JMIR Research Protocols

Impact Factor (2023): 1.4
Volume 9 (2020), Issue 5 ISSN 1929-0748 Editor in Chief: Xiaomeng (Simone) Ma, PhDc, MS, BS

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Effectiveness of a Quit Vaping Text Message Program in Promoting Abstinence Among Young Adult E-Cigarette Users: Protocol for a Randomized Controlled Trial

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Abstract

Background: Millions of young adults currently vape electronic cigarettes (e-cigarettes), yet little research on vaping cessation interventions exists. Text messaging is a promising, scalable intervention strategy for delivering vaping cessation treatment.

Objective: This study evaluates the effectiveness of a text message quit vaping program (*This is Quitting*) in promoting abstinence from e-cigarettes among young adults; examines changes in self-efficacy, perceived social norms, and social support for quitting as hypothesized mediators of effectiveness; and examines if treatment effectiveness is moderated by gender, race, ethnicity, or sexual minority status.

Methods: Overall, 2600 young adult (aged 18-24 years) e-cigarette users in the United States will be recruited via web advertisements to participate in the study. Participants will be randomized to *This is Quitting* or an assessment-only control condition. The primary outcome measure is 30-day vaping abstinence at 7 months post enrollment.

Results: Study recruitment began on December 18, 2019, and is projected to be completed by spring 2020. The final 7-month follow-up is anticipated to be completed by fall/winter 2020. Because this is the first-ever evaluation of a quit vaping program, we were unable to draw on existing literature to determine the appropriate sample size. Therefore, we examined abstinence rates among an initial pilot sample of 269 participants (*This is Quitting*: n=148 and control: n=121) who completed the 1-month follow-up to determine the final sample size. The 1-month response rate was 79.2% (213/269), with no difference between arms. Using intention-to-treat analyses that counted nonresponders as still vaping, 30-day abstinence rates were 16.2% (24/148) among those randomized to *This is Quitting* and 8.3% (10/121) among those randomized to control. A treatment difference of 16% vs 8% is detectable with 80% power at 2-sided alpha=.05 with 260/group (520 total). To detect treatment differences of this magnitude in a 20% subsample (eg, Hispanic or sexual minority young adult e-cigarette users), we will enroll 1300/group (2600 total).

Conclusions: The scientific, clinical, and public health communities are desperate for cessation resources to address vaping among young people. This study is the first-ever comparative effectiveness trial of an intervention to help young people quit vaping. It focuses on evaluating the effectiveness of a theory-grounded, empirically informed text message intervention among young adults. The study is fully powered to examine potentially important subgroup differences among young people who are more vulnerable to e-cigarette use. Although potentially more challenging from a research ethics and pragmatic standpoint, evaluating quit vaping intervention approaches in teens is an important area for future research. Data from this trial will establish a benchmark of effectiveness for other vaping cessation programs and begin to create a body of evidence focused on how best to help young people break free from e-cigarettes.

Trial Registration: ClinicalTrials.gov NCT04251273; https://clinicaltrials.gov/ct2/show/NCT04251273
International Registered Report Identifier (IRRID): DERR1-10.2196/18327

(JMIR Res Protoc 2020;9(5):e18327) doi:10.2196/18327

KEYWORDS

e-cigarettes; tobacco cessation; young adults; text messaging; telehealth

Introduction

Background

After decades of declining smoking rates, young people are returning to tobacco by vaping electronic cigarettes (e-cigarettes). E-cigarettes are currently the most heavily used tobacco product by youth and young adults [1]. According to the 2019 National Youth Tobacco Survey, 27.5% of high school students and 10.5% of middle school students reported using an e-cigarette within the past 30 days [2]. Data from the Centers for Disease Control and Prevention's National Health Interview Survey showed an increase in e-cigarette use among young adults aged 18 to 24 years, from 5.2% in 2014 to 7.6% in 2018 [3]. Young adults are more likely to use e-cigarettes compared with adults older than 25 years. Recent data also suggest that members of some demographic groups, including men and young adults who identify as Hispanic or as a sexual minority, have a higher prevalence of e-cigarette use than others [4].

E-cigarette use among young adults is associated with future initiation of combustible tobacco use [5,6] and with increased odds of alcohol and marijuana use [7]. However, even if young e-cigarette users do not progress to other products or substances, early exposure to nicotine puts them at risk for a lifetime of addiction as well as largely unknown health risks of long-term e-cigarette use. The majority of e-cigarettes contain nicotine, and the concentrations available in popular products have increased over the past decade [8]. Nicotine has known health effects on brain development occurring into the mid-20s [9]. Specific risks include nicotine addiction, mood disorders, permanent lowering of impulse control, and negative impacts on attention and learning [10]. In addition, the aerosol produced by e-cigarettes contains cancer-causing chemicals and tiny particles that reach deep into the lungs [11].

Many young people want to quit vaping. Across social media platforms, posts, videos, tweets, and comments are ubiquitous from young people about the negative impact that vaping is having on their health and well-being and their desire to quit. Key themes include feeling addicted and unable to control their use of e-cigarettes; deleterious impacts on relationships with family, friends, and significant others; declining academic and athletic performance; concerns about job and career trajectories; and negative health experiences [12].

Unfortunately, the rapid increase of e-cigarette use among young people has left researchers, clinicians, and public health professionals without evidence to turn to about how to effectively support vaping cessation among young people, particularly at the scale necessary. A search for peer-reviewed manuscripts on e-cigarette cessation yields two case reports [13,14], both of which highlight the need for guidelines and research. The 2020 Surgeon General's Report on Smoking Cessation [15] called for research to develop and understand safe and effective e-cigarette cessation interventions. Although vaping differs from smoking in many important ways, in the absence of scientific literature on vaping cessation, decades of research on best practices for smoking cessation likely provide a useful starting point for intervention design. Smoking cessation treatment delivered via text message has been shown to be effective among young adults [16-18], impacting key psychosocial processes that impact abstinence [19]. Mobile phone ownership is at 99% among young adults [20], and text messaging is an easy-to-use, discreet, anonymous, and preferred communication modality in this age group [21,22], making it a promising modality to reach and engage young people in vaping cessation treatment.

Objectives

To our knowledge, this protocol describes the first-ever randomized controlled trial to evaluate the effectiveness of a vaping cessation intervention among young adults. The intervention is delivered entirely via text messages and is scalable at a national level. The primary aim of this study is to evaluate the effectiveness of a text message quit vaping program in promoting abstinence from e-cigarettes among young adults aged 18-24 years compared with an assessment-only control condition. Secondary aims are to examine changes in self-efficacy, perceived social norms, and social support for quitting as hypothesized mediators of program effectiveness and to examine if treatment effectiveness is moderated by gender, race/ethnicity, or sexual minority status. The primary hypothesis is that participants in the active intervention arm will be more likely to be abstinent at the 7-month postrandomization primary end point than participants in an assessment-only control arm.

Methods

Study Setting

The study is restricted to individuals in the United States. Recruitment, enrollment, and follow-up assessments are conducted via the web, and treatment is delivered via text messages. The study is conducted by Truth Initiative, and the study protocol was approved by the Advarra Institutional Review Board ([IRB] PRO00040067).

Trial Design

This study is a 2-arm randomized controlled trial conducted among 2600 young adult e-cigarette users recruited through web advertisements for a study on vaping cessation. Participants will be randomized to the active text message intervention arm

(n=1300) or to an assessment-only control arm (n=1300) in a 1:1 ratio following the methods described below.

Inclusion Criteria

Individuals will be eligible if they are aged 18 to 24 years, own a mobile phone and have an active text message plan, are currently using e-cigarettes (defined as past 30-day use), are interested in quitting vaping in the next 30 days, and are a US resident.

Exclusion Criteria

Individuals are excluded if they fail to provide contact information during the baseline assessment process (to ensure study retention), if they do not provide informed consent, or if they do not fully enroll in their assigned text message program by responding to the initial system-generated message.

Recruitment and Enrollment

Web advertisements on various platforms (eg, Facebook and Twitter) will describe the study opportunity and lead to the study website, which provides details about study participation, including incentives for participation. Interested individuals will complete eligibility screening followed by informed consent and a baseline assessment. Those who complete the baseline will be randomized into 1 of the 2 arms and instructed to text a specific keyword to the phone number corresponding to their treatment assignment. Only those who respond to an initial opt-in confirmation message from the text message program within 24 hours will be fully enrolled into the study. This requirement will be made explicit.

Informed Consent

Following eligibility screening, potential participants must provide informed consent to continue with the enrollment process. The web-based informed consent form provides details about the requirements for study participation, incentive structure, randomization process, plans for protecting human subjects data, and contact information for study staff and Advarra IRB. Agreeing to the informed consent will immediately launch the baseline assessment.

Randomization

Randomization will occur at the completion of the baseline survey. A computer algorithm embedded in the survey software will automate random allocation in a 1:1 sequence. Investigators will be blind to treatment assignment.

Interventions

Treatment attrition and loss to follow-up are particular challenges in digital interventions [23], especially among young people [24]. Differential attrition where follow-up rates are higher in one group than in another can bias results [25]. To minimize differential attrition and to optimize overall follow-up assessment completion rates, incentivized text messages asking about e-cigarette use and abstinence will be sent to all participants at 14 days post enrollment and then monthly thereafter through 6 months post randomization. At 14 days, enrollees will be asked, “Checking in: Have you cut down how much you vape nicotine in the past 2 weeks? Respond w/letter: A=I still use the same amount, B=I use less, C=I don’t use at all anymore.” At monthly intervals from 1 month post randomization to 6 months post randomization, enrollees will be asked, “How’s the quit going? When was the last time you vaped nicotine, even a puff of someone else’s? Respond w/ letter: A=in the past 7 days, B=8-30 days ago, C=More than 30 days ago.” Participants in both arms will be compensated US $5 via a digital gift card for each response to these text message assessments (total 7 assessments, possible payment US $35).

This is Quitting

In response to the youth vaping epidemic and the scarcity of available quitting resources for young people, in January 2019, Truth Initiative launched *This is Quitting*, a first-of-its-kind free e-cigarette cessation text message program designed specifically for young people [26]. *This is Quitting* is promoted nationally through *truth*, the public education campaign run by Truth Initiative for over 20 years [27], as well as through earned media and local and national outreach efforts. Since it was launched, more than 150,000 teens (aged 13-17 years) and young adults (aged 18-24 years) have enrolled. Observational data have shown that approximately 70% of enrolled users set a quit date, nearly half use one or more of the interactive keywords for on-demand support, and 68% stay enrolled for the full duration of the program. This study focuses on evaluating the effectiveness of the program among young adults.

This is Quitting is fully automated and interactive, grounded in best practices from smoking cessation research with young people [17,24,28] and our experience delivering digital tobacco cessation interventions to people of all ages, and informed by formative research with young e-cigarette users and quitters. The program is written in first-person, positioned as a nonjudgmental, supportive friend to the user. It is anchored around key constructs from the Social Cognitive Theory [29]. For example, to build self-efficacy, users receive messages that are designed to bolster confidence (eg, Matt says: “Just trust the process. It’s hard at first but it gets easier with time. And don’t get down on yourself, every day is a new day.” We all believe in you here.). To establish or reinforce perceived social norms and social support around quitting, a majority of messages come from other users who have submitted them to the program (edited by Truth Initiative personnel where appropriate). These messages reference the author and are designed to convey that many other young people are quitting and that the user is not alone (eg, Ashley says: “You can do it we are all in this together.” You’re not the only one who’s thought about quitting.). To support observational learning, users receive messages with strategies from other young people (eg, Dalton says: “Remember that stress can be dealt with in other ways! Try meditating or even writing down what the problem is and then figure out solutions.” You dealt with hard things before you started to vape, and you still can.) To grow behavioral capability, users receive messages that suggest concrete evidence-based skills and strategies users can practice (eg, Have your friends supported your quitting? Reply YES or NO. {{If user responds NO}} Practice - like actually say out loud in front of a mirror at home or in your car - how you’ll turn down a JUUL if they offer it to you.). Like this example, many of the messages are interactive in nature, encouraging users to engage with the program.

Participants typically receive 1 to 2 messages per day, with 3 messages sent on their quit date. Messages are tailored to users' age, to their enrollment date or quit date (which can be set and reset via text message), and to the vape product they use (if provided by the user). Those not ready to quit receive 4 weeks of messages focused on building skills and confidence. Users who set a quit date receive messages for 1 week preceding it and 8 weeks afterward that include encouragement and support, skill- and self-efficacy building exercises, coping strategies, and information about the risks of vaping, benefits of quitting, and cutting down to quit. For young adult users, messages about nicotine replacement therapy state that it may make quitting more comfortable, that it is available over the counter, and that they should talk to a doctor or pharmacist to help determine the best dose. Keywords such as COPE, STRESS, SLIP, and MORE can be used to request on-demand support. Users can unsubscribe to stop receiving messages anytime by texting STOP. The message confirming unenrollment instructs them how to reengage with the program at any time and solicits feedback about the program.

To isolate the treatment benefit provided by the program from any confounding effects related to its public marketing or promotion, all branding and reference to the branded name will be removed from the program. Instead, it will be generically described as the *Quit Vaping Study* to participants randomized to this arm.

Assessment-Only Control

After an initial message confirming enrollment, participants will receive the incentivized text messages asking about e-cigarette use and abstinence, as described above. They will not receive any additional text messages. At the end of the intervention period and following the last follow-up assessment, they will receive information on how to sign up for *This is Quitting* (free and publicly available) if they are interested.

Data Collection

The baseline survey will be conducted on the web and hosted on a secure server. Follow-up assessments at 1 month post randomization and 7 months post randomization will be conducted via mixed-mode follow-up. The 7-month postrandomization follow-up is designed to correspond to the 6-month posttreatment follow-up most commonly used in clinical trials and the end point used by quitlines in assessing the effectiveness of a real-world intervention where the end of treatment varies across participants [30]. Participants who do not complete the survey on the web will be contacted by phone and text message by the research staff. Telephone surveys will be conducted by research staff blind to treatment. Text messages will be used as a final means of gathering abstinence data from nonresponders.

There will be no payment for study enrollment or completion of the baseline assessment. Participants will be paid US $20 for completing each follow-up survey via the internet or over the phone with a telephone interviewer, with an additional US $10 incentive for responding within 24 hours of receiving the initial invitation.

Measures

Screening Variables

To characterize those interested in the study, we will gather information about demographics (age, education, income level, sexual and gender identity, race, and ethnicity), current e-cigarette use (use of e-cigarettes containing nicotine or marijuana in the past 30 days [31]), and interest in quitting.

Baseline Variables

To characterize study participants and explore the potential moderators of treatment effectiveness, we will gather additional demographic information beyond the screener (student status and employment status); current e-cigarette use and history (frequency and rate [31,32], motivation to quit, and quitting history [33]); nicotine dependence will be assessed with the PROMISE-E [34] and items from the Texas Adolescent and Tobacco Marketing Surveillance [35]; other substance use (other tobacco products, alcohol [36]), and mental health symptoms [37]. Given the evolving trends of e-cigarette use and perception, we will also ask about their awareness of media reports about e-cigarettes, perception about e-cigarettes, reasons for wanting to quit, and reasons for joining the study. To account for potential predictors of treatment dropout, we will ask about motivation to use or quit e-cigarettes and potential barriers to quitting (eg, social influences).

Mediating Variables

The program primarily aims to help people quit vaping by building their self-confidence through skills training and by increasing perceived social norms and social support for quitting. Accordingly, we hypothesize that changes in self-efficacy and perceived social norms and social support will mediate the relationship between treatment assignment and abstinence outcomes. These constructs will be assessed at baseline, 1 month post randomization, and 7 months post randomization, and changes will be examined in mediational analyses. Items assess how supportive of quitting vaping their friends and family are, perceptions about how many of their peers vape or want to quit vaping, and awareness about media reports of vaping-related illnesses.

Primary Outcome

The primary outcome is self-reported 30-day abstinence at 7 months post randomization. Participants are first instructed "Please note that the terms 'vape' or 'vaping' in this survey refer to use of all vaping products, including JUUL, mods, and other e-cigarettes." They are then asked to respond to the following question: "In the past 30 days, did you vape at all, even a puff of someone else's?"

Following the completion of the final 7-month follow-up assessment, after participants receive compensation for completing this survey, we will administer an exit questionnaire that queries participants about the accuracy of their self-reports. This process was used successfully by Lantini et al [38] to determine rates of misreporting of outcomes in a randomized trial with adolescent smokers. Items will address the reasons for joining the study, the extent to which they paid attention to the study questions and their answers, the extent to which they

like/dislike the way vaping makes them look, concerns about confidentiality in the study, and several items tapping social desirability bias in the context of a digital intervention.

Secondary Outcomes

In addition to the 7-month assessment of abstinence as the primary outcome, we will gather abstinence data at all other follow-ups as secondary measures. Other quitting-related outcomes include change in motivation to quit, quit attempts and quit methods, reduction in e-cigarette use, 7-day abstinence, and continuous abstinence measured at each formal follow-up as well as interim text message assessments (single items asking about current vaping status). Nicotine dependence among those still vaping will be assessed with the PROMISE-E [34] and items from the Texas Adolescent and Tobacco Marketing Surveillance [35]. We will ask about other substance use (other tobacco products and alcohol [36]) and mental health symptoms [37] as in the baseline survey. Intervention satisfaction in both conditions will be measured with items about overall satisfaction (1=very satisfied, 2=somewhat satisfied, 3=a little satisfied, and 4=not at all satisfied), how likely they would be to recommend the intervention to a friend (0=not at all likely and 10=very likely), and a rating of the number of text messages they received (1=too few, 2=just right, and 3=too many) [39]. To assess perceived message relevance, participants will be asked to provide feedback about the text messages by agreeing/disagreeing with several statements, such as if text messages "were written personally for me," [40] "suggested quitting strategies that were new to me," and "made me feel that I knew the right steps to take to quit."

Data Analysis Plan

Sample Generalizability

We will compare our final enrolled sample with those who did not complete the enrollment process to identify if study participants differ from the sample from which they were drawn [41]. These analyses will provide important information about the generalizability of our study sample to the broader population of young adult e-cigarette users interested in quitting vaping.

Pilot Analyses for Sample Size Calculations

Given that this is the first-ever evaluation of a quit vaping program, we were unable to draw on existing literature to estimate the potential effect size of our intervention against an assessment-only control to determine the appropriate sample size. Previous text message interventions for smoking cessation among young adults suggest a treatment benefit of 5 to 10 percentage points, favoring the intervention arm [42,43]. However, these studies vary by age of participants, abstinence metric, assessment end point, and obviously the nature of the behavior change being studied (smoking vs vaping). Therefore, we examined abstinence rates among an initial pilot sample of participants who completed the 1-month follow-up from our own trial to determine the final sample size. Details are provided below in the Results section.

Primary Outcome

Point prevalence abstinence at 7 months post randomization will be compared between the treatment and control groups using logistic regression. All estimates will be adjusted for baseline confounders of the intervention-outcome relationship. Missing data will be handled in 2 ways. First, we will conduct an intent-to-treat (ITT) analysis in which participants who have been lost to follow-up are assumed to be treatment failures (ie, vaping). This analysis will be conducted because ITT analyses are common in the smoking cessation literature, despite simulations demonstrating that the approach is neither conservative nor anticonservative but rather biased in favor of whichever condition contains less missingness [44]. Second, we will supplement ITT analyses with an analysis that uses a multiple imputation procedure to minimize bias in estimates and SEs, under the assumption that outcomes are not missing at random but rather more likely to be missing for treatment failures (ie, vaping) than treatment successes (ie, abstinence). Given that the magnitude of actual response bias is unknown, we will conduct a sensitivity analysis to evaluate the treatment effect on outcomes under a range of magnitudes, from equal odds of missing (odds ratio [OR] 1) to 5 times more likely to be missing (OR 5).

Secondary Outcomes

Additional outcomes related to abstinence and treatment engagement will also be analyzed with logistic regression as secondary analyses. These include the likelihood of making a quit attempt, likelihood of reducing e-cigarette use, and changes in confidence and self-efficacy in quitting e-cigarettes.

Moderators and Mediators of the Treatment-Outcome Effect

We will identify potential moderators (eg, age, gender, baseline motivation to quit) by analyzing interactions between treatment and selected variables. For all moderators found to be associated with the primary outcome, we will examine the effects of treatment/moderator interaction terms on outcomes after entering the main effects.

Our conceptual model is that treatment increases the odds of abstinence by increasing perceived social norms, perceived social support, and perceived self-efficacy for quitting. These 3 constructs will be measured at baseline, 1 month post randomization, and 7 months post randomization. Changes in these constructs from baseline will be evaluated with separate mediation analyses. Specifically, we hypothesize that the effect of treatment on abstinence will be mediated by changes in perceived social norms, perceived social support, and perceived self-efficacy, such that (1) a significant effect is found associating treatment assignment with changes in the mediator, (2) a significant effect is found associating changes in the mediator with outcome (abstinence), (3) a significant effect is found associating treatment with outcome (abstinence), and (4) the effect of the treatment-outcome relationship is significantly attenuated when the other effects (ie, 1 and 2) are simultaneously included in the model.

Results

Study recruitment began on December 18, 2019, and is projected to be completed by spring 2020. The final 7-month follow-up is anticipated to be completed by fall/winter 2020.

Between December 18, 2019, and December 28, 2019, a total of 269 participants were randomized to treatment (This is Quitting: n=148 and control: n=121). The 1-month response rate was 79.2%, with no difference between arms. Using ITT analyses, 30-day abstinence rates were 16.2% (24/148) among those randomized to *This is Quitting* and 8.3% (10/121) among those randomized to control. A treatment difference of 16% vs 8% is detectable, with 80% power at 2-sided alpha=.05 with 260/group (520 total). To be able to detect treatment differences of this magnitude in a 20% subsample (eg, Hispanic or sexual minority young adult e-cigarette users), we determined that we needed to enroll 1300/group (2600 total) in our full sample.

Discussion

Significance and Challenges

This study is the first-ever comparative effectiveness trial of an intervention designed specifically to help young people quit vaping. It is fully powered to examine potentially important subgroup differences among young people who are more vulnerable to e-cigarette use. In addition, it lays the groundwork for future intervention research and begins to build an evidence base for vaping cessation treatment.

Selection of a control condition in a behavioral trial such as this one requires careful consideration and balance between internal and external validity [45]. Masking of treatment assignment can be difficult [46], and developing an *inactive* behavioral control arm that is credible and equally preferable to participants in the context of a text message intervention is a unique challenge. Participants enrolled in the trial seeking support to quit vaping and expected to receive some form of intervention. Therefore, we elected to use an assessment-only approach for the control arm to deliver an experience that retains subjects while not being so involved that it significantly changes participant behavior.

Conducting a comparative effectiveness trial of a quit vaping program during a time when the e-cigarette product [47-49] and policy [50-52] landscape are in flux is a unique challenge. It is important to acknowledge that myriad contextual factors from the individual level up through the policy level may influence the outcomes of this trial to a greater or lesser degree. We expect that whatever factors are at play and whatever degree of influence they may have, randomization should distribute such influence evenly across both arms.

Limitations

Several aspects of our trial design and implementation are worth noting as potential limitations. First, the timing of funding availability meant that we launched the study several weeks before the new year. Recruiting during a time when motivation to quit may be higher than at other times during the year may result in somewhat inflated quit rates across the arms. Alternatively, it is possible that the motivation among individuals who attempt to quit vaping around the New Year is more ephemeral and characterized by less dedication and intensity, yielding perhaps lower quit rates than if the study was conducted at a different time of year. Previous research on smoking cessation has supported both possibilities. Regardless, we do not have any reason to believe that this seasonal influence would differentially affect participants in the 2 arms and that this potential confounding factor would be addressed via randomization.

Second, it is important to acknowledge that the active intervention arm is publicly available and being actively promoted through a national education campaign. Participants in both conditions may become aware of this national campaign at some point during the trial. Follow-up measures will assess awareness of the truth campaign and engagement in *This is Quitting* among control arm participants.

It is also important to note that we have no plans for biochemical verification of abstinence, although this is not necessarily a limitation given the context of this research. Previous digital cessation research has shown low response rates among young people despite a protocol involving minimal participant burden [53]. Indeed, biochemical confirmation is often not practical in large-scale trials with no in-person contact between participants and study staff and where the entirety of the study is conducted digitally [54,55], both of which characterize this trial. Furthermore, biomarkers are more useful for verifying brief periods of smoking abstinence than longer periods of abstinence (eg, our primary end point of 30-day abstinence). We believe that our measurement approach using the methods described by Lantini et al [38] will add important information about the veracity of self-reported cessation outcomes.

Finally, this study focuses on evaluating the effectiveness of the intervention only among young adults aged 18-24 years and does not include teens. Research among teens involves ethical and practical considerations (eg, parental assent) that are not present in research with adults aged 18 years and older. Given that the e-cigarette epidemic is largely concentrated among middle and high school students, it will be important to study this intervention among youth, with the appropriate ethical controls in place.

Conclusions

Research on e-cigarettes, to date, has largely centered on their potential benefit as an alternative to cigarettes and their potential utility as a smoking cessation strategy [15]. While this often-contentious debate continues [56-58], there is an urgent and critical need to identify effective vaping cessation strategies to support the thousands—perhaps hundreds of thousands—of young people who want to quit vaping today. To our knowledge, this study is the first randomized controlled trial that is fully powered to evaluate the effectiveness of an automated, scalable, cost-efficient text message program for vaping cessation designed specifically for young people. Observational data from this program is extremely promising, both in terms of the massive uptake and engagement seen within the first year and also with respect to signals of abstinence. The data generated from this trial will establish a benchmark of effectiveness for

other vaping cessation programs and begin to create a body of evidence focused on how best to help young people break free from e-cigarettes.

Acknowledgments

This study is funded by the Truth Initiative with support from the CVS Health Foundation. The funding sources had no role in the design of this study and will not have any role during its execution, analyses, interpretation of the data, or decision to submit results.

Authors' Contributions

AG, MJ, MA, SC, and MB conceived the study and initiated the study design. SC and MB implemented the study. AG, MA, and GP provided statistical expertise in trial design. MA and GP are conducting the statistical analyses. All authors have read and approved the final manuscript.

Conflicts of Interest

AG, MJ, MA, SC, and MB are employed by Truth Initiative, a nonprofit public health foundation that sells enterprise digital tobacco cessation programs.

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Abbreviations

e-cigarette: electronic cigarette
IRB: Institutional Review Board
ITT: intent-to-treat
OR: odds ratio

Edited by G Eysenbach; submitted 24.02.20; peer-reviewed by J Chen-Sankey, L Akers; comments to author 16.03.20; revised version received 17.03.20; accepted 21.03.20; published 01.05.20.

Please cite as:
Graham AL, Jacobs MA, Amato MS, Cha S, Bottcher MM, Papandonatos GD
Effectiveness of a Quit Vaping Text Message Program in Promoting Abstinence Among Young Adult E-Cigarette Users: Protocol for a Randomized Controlled Trial
JMIR Res Protoc 2020;9(5):e18327
URL: https://www.researchprotocols.org/2020/5/e18327
doi:10.2196/18327
PMID:32356774

Protocol

Social Media Interventions for Risky Drinking Among Adolescents and Emerging Adults: Protocol for a Randomized Controlled Trial

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Abstract

Background: Despite intervention efforts to date, the prevalence of risky drinking among adolescents and emerging adults remains high, increasing the risk for health consequences and the development of alcohol use disorders. Peer influences are particularly salient among this age group, including via social media. Thus, the development of efficacious early interventions for youth, delivered with a broad reach via trained peers on social media, could have an important role in addressing risky drinking and concomitant drug use.

Objective: This paper describes the protocol of a randomized controlled trial (RCT) testing the efficacy of a social media intervention among adolescents and emerging adults who meet the criteria for risky drinking (using the Alcohol Use Disorders Identification Test-Consumption [AUDIT-C]), delivered with and without financial incentives for participation, compared with an attention placebo control condition (ie, entertaining social media content), on alcohol consumption and consequences.

Methods: This RCT involved recruiting 955 youths (aged 16-24 years) via advertisements on Facebook and Instagram to self-administer a brief web-based screening survey. Those screening positive for past 3-month risky drinking (AUDIT-C positive: ages 16-17 years: ≥3 females and ≥4 males; and ages 18-24 years: ≥4 females and ≥5 males) were eligible for the RCT. After providing consent (a waiver of parental consent was obtained for minors), participants completed a web-based baseline survey and several verification procedures, including a selfie photo matched to Facebook profile photos. Participants were then randomized to join invitation-only secret Facebook groups, which were not searchable or viewable by parents, friends, or anyone not recruited by the study. The 3 conditions were social media intervention with incentives, social media intervention without incentives (SMI), and attention placebo control. Each condition lasted 8 weeks and consisted of bachelor's-level and master's-level therapist electronic coaches posting relevant content and responding to participants' posts in a manner consistent with Motivational Interviewing. Participants in the control condition and SMI condition did not receive payments but were blind to condition assignment between these 2 conditions. Follow-ups are ongoing and occur at 3, 6, and 12 months poststart of the groups.

Results: We enrolled 955 participants over 10 waves of recruitment who screened positive for risky drinking into the RCT.

Conclusions: The findings of this study will provide the critical next step in delivering early alcohol interventions to the youth, capitalizing on social media platforms, which could have significant public health impact by altering alcohol use trajectories of adolescents and emerging adults engaged in risky drinking.

Trial Registration: ClinicalTrials.gov NCT02809586; https://clinicaltrials.gov/ct2/show/NCT02809586.

International Registered Report Identifier (IRRID): DERR1-10.2196/16688

(JMIR Res Protoc 2020;9(5):e16688) doi:10.2196/16688

KEYWORDS

social media; alcohol consumption; adolescents; emerging adults; internet-based intervention

Introduction

Background

Despite numerous intervention and policy efforts, risky drinking (ie, hazardous levels of consumption resulting in increased risk for consequences) among youth in the United States remains a major public health issue. Although only 1.8% of youths aged 12 to 17 years and 10.0% of those aged 18 to 25 years met criteria for an alcohol use disorder in 2017 in the United States [1], risky drinking is common. For example, as one indicator of risky drinking, past-month binge (eg, ≥4 drinks for females and ≥5 drinks for males) drinking rates are 10.2% for ages 16 to 17 years, 26.2% for ages 18 to 20 years, and 45.4% for ages 21 to 25 years [2], although these may be underestimates because of possible underreporting in national surveys (eg, average past-year quantity or frequency questions) [3]. In fact, risky drinking among young people is associated with increased risk for other drug use, adverse health consequences (eg, injury and overdose), and development of substance use disorders [4-7]. Accordingly, late adolescence and emerging adulthood is a critical developmental juncture, distinct from childhood and adulthood, during which rates of alcohol and other drug use peak [8-10]. For example, 6.5% of adolescents and 22.1% of emerging adults report past-month cannabis use [1]. Thus, scalable, early interventions are urgently needed to address risky drinking and concomitant health risk behaviors (eg, other drug use and driving under the influence) among adolescents and emerging adults to disrupt risk trajectories. Here, we present the theoretical rationale and protocol for a randomized controlled trial (RCT) of social media–delivered interventions for risky drinking among adolescents aged 16 to 24 years recruited nationally.

Conceptual Model

The conceptual model guiding our intervention is rooted in social cognitive (eg, theory of planned behavior [11] and social learning [12]) and social ecological [13] theories, emphasizing the role of individual and social influences on alcohol use by adolescents and emerging adults. Furthermore, our intervention is implicitly grounded in a resiliency framework [14,15]. Across development, evolving interactions between individual and social risk and protective factors during the establishment of new roles (eg, relationships and employment) [16] can decrease or accelerate alcohol use trajectories [16-18]. Individual risk factors associated with alcohol use include low perceived risk of use, perceived norms, and mental health issues (ie, depression and anxiety), whereas disapproval of use, parenting practices, and protective behavioral strategies are protective [16,19-27]. Although parents are important during younger ages [28], peers comprise the most robust social influences on substance use among adolescents and emerging adults [16,29-38].

Over the past decade, social media has become increasingly prevalent in the day-to-day lives of young people, creating additional opportunities for exposure to positive and negative peer influences [39,40]. Social media content is user generated and constantly changing, providing frequent exposure to web-based peer influences, potentially resulting in reinforcing spirals of increasing exposure and involvement with alcohol use behaviors over time [41,42]. Although it is well known that offline peers can exert tremendous influence on alcohol use among youth [16,29-32], recent data suggest that online peers also influence alcohol use [43-45]. Emerging adults who consume more alcohol, for example, have more Facebook friends [46] and post more references to parties on Facebook than those who use less alcohol [47]. Among high school students, higher alcohol use is related to reports of friends posting alcohol content on social media [43], and in a laboratory study, researchers found that teens viewing Facebook profiles that contained positive references to alcohol had more positive attitudes and willingness to drink alcohol than teens who did not view these profiles [48]. As offline peer disapproval of risky substance use can be a protective factor [49,50], online peer disapproval of alcohol use may function similarly. Research shows that posting positive portrayals of alcohol use on social media is related to consumption among the youth [43,51]. Thus, social media provides an appealing platform for the delivery of alcohol interventions, wherein peer influences could be harnessed instead to promote harm reduction or reduced consumption. As described earlier, alcohol use is associated with other drug use; thus, social media interventions could be useful for targeting concomitant drug use, particularly because mentions of other drug use are also prevalent on social media [52,53]. For example, one study showed that more than one-third of a college student sample had seen a picture of a friend smoking cannabis posted on social media [54].

Social Media as an Intervention Platform

A common feature of social media use among adolescents and emerging adults is the frequent use of more than one platform, which reflects increased smartphone ownership and Wi-Fi access. As of 2018, 95% of teens reported having a smartphone or access to one, of which 45% reported they are on the Web almost constantly [55]. Among emerging adults (aged 18-25 years), 88% use Facebook, compared with 68% for Snapchat,

59% for Instagram, and 36% for Twitter [56]. In addition, engagement is more frequent for Facebook, with 74% of all users checking it daily, compared with 61% for Snapchat, 63% for Instagram, and 42% for Twitter [56], and 51% of Facebook users log in several times per day [57]. In contrast, among adolescents (aged 13-17 years), 51% use Facebook (which has declined in recent years) [58], compared with 69% for Snapchat, 72% for Instagram, and 32% for Twitter [56]. It may be that adolescents and emerging adults who use Facebook regularly differ from those who do not, which could affect the utility of interventions. For example, data suggest that a larger proportion of teens from lower income households use Facebook than those from higher income households [59]. Thus, when choosing a social media intervention platform to reach both adolescents and emerging adults, there is no clear single best choice. Furthermore, as trends in social media use shift over time and/or within demographic groups, there may be unique opportunities to leverage content for delivery across various emerging platforms with shared features (eg, ability to post personal content, videos, articles, etc) to reach certain at-risk groups.

To date, there a very few social media interventions to reduce risky drinking (and/or other illicit or prescription drug misuse) among young people [60], with a recent publication describing the development of a tobacco and binge drinking intervention [61]. Most prior research testing early interventions for alcohol (and other drug use) has examined interventions delivered by therapists and/or static computer programs, with demonstrated efficacy in medical and university settings [62-74]. Overall, effect sizes are modest [75], with newer studies in the substance use field and other health fields testing technology-driven methods to extend delivery [76-79]. An advantage of social media interventions is that they can be designed to blend therapist and computerized interventions to deliver dynamic, evolving content; harness online peer influences; and provide access to electronic coaches (e-coaches), which can increase exposure to content at the time the person chooses to engage. Social media interventions (typically delivered over 8-12 weeks), addressing other health outcomes (eg, exercise/weight, HIV risk reduction/sexual health, and smoking cessation) among varied samples (eg, postpartum women, college students, and general community), have demonstrated promising effects [80-88], supporting the potential of this approach to address alcohol and other drug use.

Prior social media interventions have used Facebook for delivery, likely because it remains the most popular social media site among emerging adults and it has unique features that support intervention delivery. For example, Facebook allows private, secret groups to address privacy and confidentiality concerns (which are not searchable or viewable by others and can be joined by invitation only). In addition, the content is sorted into threads, promoting group interaction, with active conversations bumped to the top of the group or one's newsfeed. Moreover, Facebook content does not disappear (eg, as in Snapchat), so it can be viewed an unlimited number of times and discussions can be revisited, as group members post new comments. Finally, Facebook does not restrict the character count of posts, which is a limitation of other platforms.

Critical issues related to designing social media interventions are exposure, dose (engagement or response showing the degree to which content may be processed), and diffusion (reach or interaction among online peers via shares, comments, etc) [89]. Exposure can be measured using metrics of reactions (eg, likes), comments, replies, and posts to Facebook groups. For instance, researchers found more than half (approximately 63%) of participants in a physical activity intervention condition reported visiting the Facebook group 2 to 3 times per month during a 12-week intervention period; among those who posted in the Facebook group more than once, they averaged 8 interactions each over 12 weeks [80]. Thus, an important methodological question is related to how to encourage engagement, increasing dose and diffusion [89]. Our study sought to accomplish this in 2 ways. First, content was informed by social marketing research tips regarding characteristics of posts that increase interaction: (1) give (eg, photo/video contests), (2) advise (useful tip for concerns, eg, coping strategies), (3) warn (dangers could affect anyone, eg, overdose and impaired driving), (4) amuse (amusing photos/videos), (5) inspire (moving quotes or stories), (6) amaze (amazing pictures or facts, eg, norms), and (7) unite (brag about group membership and social support) [90]. Second, to our knowledge, no researchers have compared intervention conditions that vary incentives for engagement. Increased interaction via incentives among peers could theoretically reinforce group interactions, increasing dose, which is thought to result in behavior change. Thus, we sought to compare an intervention condition that provided modest financial incentives for engagement as measured by daily interactions (ie, posts with status updates or comments to another's post) with a condition that did not provide incentives. Thus, in addition to comparing the interventions to an attention control condition to determine efficacy, our goal was to examine whether externally incentivized interaction produced greater engagement, and if so, whether that enhances intervention efficacy, relative to the nonincentivized intervention condition containing organic, individually motivated interactions.

Finally, sentiment analysis (eg, examining the relative positive or negative valence [tone] and arousal [activation] in text) [91,92] is a potentially useful tool to understand characteristics of engagement in social media interventions [93]. Using state-of-the-art software, natural language processing can evaluate slang and common misspellings, with 85% accuracy [94,95]. To date, sentiment analysis has been applied to smoking cessation interventions but has not been applied to alcohol interventions, although researchers are coding content of social media related to alcohol use [96,97]. Thus, because our interventions sought to encourage interaction within secret groups, sentiment analysis is an innovative approach to understanding the characteristics of engagement (eg, valence and arousal) and alcohol use outcomes.

Goal of This Study

We recruited adolescents and emerging adults using Facebook and Instagram advertisements and conducted web-based screening to enroll risky drinkers in an RCT comparing 3 conditions: (1) social media intervention (SMI) with incentives (SMI+I), (2) SMI only, and (3) attention control condition, with follow-up assessments at 3, 6, and 12 months. Interventions

comprised access for 8 weeks to unique, private secret Facebook groups facilitated by e-coaches (supervised by licensed therapists), with dynamic content addressing motives for risky drinking and reducing consumption as well as concomitant risk behaviors (other drug use). The attention control condition included access for 8 weeks to entertaining content (eg, sports, lifestyle, fun, etc). As described earlier, we used 2 intervention approaches, with and without financial incentives for participation, and we will measure engagement within the intervention groups. By providing incentives for participation in one condition, we attempted to harness participants to provide group support, thereby delivering intervention content, facilitated by e-coaches.

The specific aims are to (1) test the efficacy of the 2 intervention conditions compared with the control, in reducing alcohol consumption and alcohol-related consequences at 3-, 6-, and 12-month follow-ups; (2) compare the intervention conditions in participant engagement and efficacy in reducing alcohol consumption and alcohol-related consequences at 3-, 6-, and 12-month follow-ups; and (3) examine how level of engagement in intervention conditions (eg, engagement metrics) and characteristics of intervention engagement (sentiment analysis) relate to alcohol use outcomes in the 2 intervention conditions. The secondary aims include examining the efficacy of the interventions on other drug use, moderators of outcome, and conducting cost analyses. This paper describes the study protocol in relation to the primary aims.

Methods

Trial Registration, Ethics, Consent, and Institutional Board Approval

The study procedures were approved by the University of Michigan Institutional Review Board (IRB), and the study was registered in Clinicaltrials.gov (#AA024175). We received a waiver of parental consent for all aspects of the study for youths aged 16 to 20 years (the age of majority varied based on state residence). The rationale for this waiver was based on (1) the determination of teenage participants as *mature minors* (ie, they can understand the study risks), with decisional capacity to promote health-seeking behavior including substance use treatment [98]; (2) the fact that disclosure of high-risk behaviors may increase the risk of adverse effects on participants' well-being because of potential reactions from parents (eg, rejection and abuse); and (3) the study could not practicably be carried out without this waiver, given potential bias in participation because of fear of disclosure of risky drinking to parents [99]. Furthermore, our study involved a two-phase consent process, with separate web-based consent obtained for the screening and RCT phases. Confidentiality and privacy were also enhanced by requiring participants to agree to abide by our own User Safety Agreement (see the *Interventions* section). We obtained a Certificate of Confidentiality from the National Institutes of Health.

Design

Using recruitment via social media advertisements, we enrolled and randomized 955 adolescents and emerging adults (aged 16-24 years) in an RCT comprising the 2 intervention conditions and the control condition. Participants were assigned their conditions for a period of 8 weeks and were prompted to self-administer follow-up assessments at 3, 6, and 12 months postinitiation of groups. All assessments and interventions occurred on the Web, with surveys administered through Qualtrics [100].

Recruitment

Potential participants were recruited in 10 waves, separated by age (16-20 and 21-24 years) via paid advertisements on Facebook and Instagram. Each wave contained an average of 95.5 participants, which helped ensure that the 3 groups in each wave contained approximately 30 participants (mean=31.8 participants per group) to allow for sufficient online group interaction.

On the basis of prior work [101], Facebook/Instagram advertisements were initially placed by setting the audience location to include users in the United States. Advertisements were also specified to be displayed to users with certain demographic characteristics (ie, age groups 16-17, 18-20, 21-22, and 23-24 years and English-speaking users) and detailed targeting displayed advertisements to users who *liked* Facebook pages related to alcohol (eg, popular brands, drinking games, etc). Starting in wave 5, we added user characteristics to increase the recruitment of racial and ethnic minorities using affinity targeting within Facebook Ads Manager. After wave 6, ethnic affinity targeting was temporarily removed from the Facebook Ads Manager but was available again and used for waves 9 and 10. Each advertisement featured headlines to encourage potential participants to take the survey (eg, "Drink alcohol? Participate in a research study; earn $$$ for your time."). We used 3 images (from Facebook Ads Manager and stock photos) of alcohol/individuals with alcohol and one image of the study logo. To encourage minority representation in the sample, advertisements pictured individuals of varying races/ethnicities. Also starting in wave 5, white individuals and females were informally excluded after preset quotas were filled. Advertisements initially directed participants to the study website, but starting in wave 2, advertisements led participants directly to the consent page and screening survey. The study's website URL was provided to participants throughout the study (eg, in Facebook secret groups and texting/email communications).

Screening

Among screening-eligible participants, the 21-item web-based screening survey was used to determine RCT eligibility using a past 3-month version of the Alcohol Use Disorders Identification Test-Consumption (AUDIT-C [102-104]; where binge drinking was defined at ≥4 drinks for women and ≥5 drinks for men) embedded among other standard items querying demographics and other substance use. To ensure real people completed the survey (as opposed to bots), the web-based screening consent page included a Completely Automated Public Turing test to tell Computers and Humans Apart. Participants who reported risky drinking the past 3 months (AUDIT-C score: ages 16-17 years: ≥3 females and ≥4 males and ages 18-24

years: ≥4 females and ≥5 males [105,106]) were eligible for the study.

Participant Identity Verification Procedures and Baseline Enrollment

Before enrolling eligible participants, we reviewed their screening data as a second step to ensure data integrity and to deter fraudulent participation. Procedures included checking data for duplicate internet protocol addresses, survey completion times >60 seconds, and the existence and legitimacy of the participant's Facebook profile based on published recommendations [107,108]. Once initial identity verification procedures were passed, eligible youths were sent an email invitation to participate in the study, with a link that automatically directed them to the RCT consent form followed by a web-based baseline survey and a contact information form. Participants were informed in the consent form that "the purpose of the study is to develop and test social media interventions to help young people reduce risky behaviors, such as alcohol use." To help ensure identity and age, as part of the baseline procedures, participants were required to upload a selfie containing a handwritten sign with the date and time that included their head and shoulders. Study staff compared the selfie with the participant's Facebook profile for verification before randomization and group assignment. In rare cases where a participant's Facebook profile did not already contain a photo of themselves, we asked them to temporarily upload a second photo (different than the selfie) for real-time, immediate verification against their time- and date-stamped photo.

Randomization

Following the web-based baseline assessment and selfie verification, participants were randomized to 1 of the 3 conditions. Given differences in severity of drinking by age and sex, which could affect response to the intervention [2], computerized, stratified random assignment by sex and age group (16-20 and 21-24 years) took place within condition, in blocks of 20 within cells to equalize randomization over time. Randomization occurred by a computer algorithm generated with supervision by the data manager; thus, research staff were not able to manipulate condition assignment. Given e-coach interaction in groups, it was not possible to blind staff to condition assignment; regarding participant blinding, although participants were not told whether they were assigned to an intervention or control group, the control group did not receive alcohol content; thus, as with most behavioral trials, it is possible that participants discerned their condition assignment. Specifically, the consent form described the 2 intervention conditions, "You will have access to the secret Facebook page that will deliver health information focused on reducing risky behaviors, including alcohol use." The consent form described the control condition as, "You will have access to the secret Facebook page that will share news information about things like entertainment, sports, weather and world news." In addition, for the SMI+I group, participants were informed that they would earn points for interacting on the group page and be paid for the points earned, so participants were not blinded to being assigned to the payment condition. After randomization, participants were sent a friend request from an e-coach; once participants accepted the request, they were added to their corresponding secret group where the 8-week condition was delivered.

Follow-Up Assessments

Consecutive web-based assessments, mirroring the baseline survey measures, were distributed by a research assistant using a generic study email address at 3, 6, and 12 months after group initiation. Participants were assured that e-coaches would not view their individual outcomes on their self-administered follow-up surveys.

Incentives

Each participant received a US $30 Amazon gift card code for completing the web-based baseline survey and providing a selfie, which took approximately 30 min. Compensation for follow-up assessments was US $35 for the 3-month assessment, US $45 for the 6-month assessment, and US $55 for the 12-month assessment. Participants in the SMI+I condition received incentives to encourage interaction, earning US $1.00 for each day they posted text and/or images in the secret group (ie, status update, comment, reply, or share) for a maximum of US $56 per participant over 8 weeks. Note that *likes* or *reactions* (eg, heart and sad face) were not incentivized. Incentives were paid weekly via an electronic Amazon gift card by study staff (student research assistants, e-coaches, and/or supervisors) who reviewed posting data to confirm the number of days on which participants posted.

Interventions

Overview

The interventions consisted of interactions among participants and e-coaches within the secret Facebook group pages (separated by age group: 16-20 and 21-24 years) over 8 weeks, among approximately 30 participants per group. After 8 weeks, participation in the group ended; the ability to share new posts was turned off, but participants could still view archived content. At RCT consent, participants were required to agree to our User Safety Agreement, which provided rules of engagement for the group. These rules included prohibition of posting opportunities to engage in alcohol or other drug use (eg, parties and selling drugs) or obscene or offensive material, advertisements for making money or a business, maintaining participants' confidentiality, and treating each other with respect. Participants were informed that a single violation of the agreement would result in a reminder of these rules and that repeated violations could result in removal from the group page with redirection to an individual page so that content would still be viewable. Participants were allowed to friend each other and send messages to one another at their own discretion; we did not provide specific User Safety Agreement guidelines for these private interactions.

Electronic Coach Training and Supervision

E-coaches were trained in Motivational Interviewing (MI) and Cognitive Behavioral Therapy (CBT) skills and posted and responded to participants in a manner consistent with MI, supervised by licensed clinical supervisors in weekly individual and group supervision [109]. E-coach training included

participation in a large group (not study specific), 2-day interactive introductory training in MI led by the first author and other members of the MI Network of Trainers (MINT), one day of small group study-specific MI training with a MINT trainer, one day of small group study-specific MI training with the study coordinator, and completion of 4 web-based MI modules. Supervision included review of groups and collaborative responding to participants' comments, replies, statuses, or shares. During each 8-week intervention period, group supervision lasted 1 to 2 hours per week, and individual supervision lasted 1 to 2 hours (based on e-coach experience and/or amount of interaction occurring in the groups at a given time). In addition, depending on e-coach skills and the volume and clinical complexity of each wave, a supervisor would post with the e-coach for 1 to 2 hours weekly.

Intervention Model

Strategies from CBT [110] were structured in 3 phases: *Explore, Guide, and Choose* [111,112]. Self-determination theory (SDT) [113] is conceptualized to explain how MI works [114]; as applied to alcohol interventions, SDT would suggest that to increase intrinsic motivation to reduce alcohol use, the provider must assist the participant in increasing confidence, relatedness, and autonomy. Within each weekly topic, as part of *Explore*, e-coaches explored risk perceptions, concerns, motives, and current alcohol use along with personal goals and strengths. As part of *Guide*, e-coaches used an Elicit-Provide-Elicit framework, posting open-ended questions and responding to posts by participants, with the goal of eliciting change talk to reduce risky drinking. As part of *Choose*, CBT skills and protective behavioral strategies were elicited (eg, anticipating the consequences of use, finding alternative strategies to address motives for use) and reinforced. When the need arose, e-coaches provided community resources within the group and in private messages. A list of national resources was also available along with a copy of the consent form and User Safety Agreement within the group in a downloadable files section. Finally, a crisis text line and a reminder to call 911 for immediate emergencies were shown in the group cover photo pinned to the top of the secret Facebook page, along with a message that groups were not monitored 24/7 (although they were monitored multiples times per day).

Initially, we developed a prototype of the 8-week intervention based on theory, prior work [115], and feedback from youth advisors, who reviewed initial content in a focus group. To increase our library of content, we used Amazon's Mechanical Turk to crowdsource content appealing to the youth. Then, we refined the content and focus tested it with another group of youth advisors, who participated in a mock intervention group, followed by content editing. Although the content topics were consistent across waves (see Table 1), the intervention was flexible to address current events (eg, overdose death of a celebrity) and topics initiated by group members, which included topics such as personal struggles or celebrations. Consistent with expectations on social media, posts included links to engaging content (eg, memes, GIF images, Buzzfeed articles, YouTube videos, quizzes/polls, and other web-based articles) paired with evocative statements and questions to encourage participants to interact.

Table 1. Weekly content topics addressed in the social media interventions.

Week	Topic	Goal of weekly topic
1	Dealing with stress	Establish rapport, enhance coping to manage stress, affirm personal strengths, and elicit long-term goals
2	What young people do	Explore peer norms, elicit benefits of avoiding/reducing drinking, and enhance self-efficacy for harm reduction
3	Staying out of trouble	Elicit negative consequences of alcohol use and protective behavioral strategies
4	Handling tricky situations	Elicit motives for drinking and reinforce strategies to address motives in healthier ways
5	Free time activities	Elicit free time activities that promote healthy and valued activities while avoiding/reducing drinking
6	Friends and parents	Elicit strategies for managing relationships and situations with others
7	Staying healthy	Elicit skills to prevent life-threatening outcomes of drinking (overdose and drinking/drugged driving)
8	Getting support	Engage participants in identifying resources and promote healthy social support

Multiple times per day for 56 days, e-coaches posted new, dynamic content during morning, afternoon, and evening shifts. The same content was posted by e-coaches across both SMI and SMI+I conditions, at the same daily intervals, with some content tailored by age group. For example, posts in the younger group tended to reference school and parents, whereas posts in older groups tended to mention employment and partner relationships. During daily shifts, e-coaches used MI to respond to participants' posts and comments. In addition, e-coaches used Facebook tagging and/or sent messages to participants via text, email, or private message if they did not engage for 7 days, sharing trending topics being discussed on the intervention page with the goal of increasing participation. After initial icebreaker posts (eg, How would you describe yourself in 5 words?), the intervention primarily addressed upstream motives for alcohol use (eg, stress, negative affect, positive affect, social influences). Given our secondary aims and in recognition of the harmful health effects of combined alcohol and other drug use, other drug use was also addressed (eg, risk of overdose, drugged driving). As cannabis (followed by misuse of prescription drugs) is the most commonly reported illicit substance used by adolescents and emerging adults [116], we also addressed these other substances throughout the intervention, given the likelihood that many participants could be co-using and experience heightened risks (eg, greening out, overdose). Finally, e-coaches posted weekly polls to assess participants'

content preferences while also monitoring the ongoing popularity of posts for tailoring in future weeks and waves.

Attention Placebo Control Condition

Similar to prior work [86], participants in the control group were given access to an 8-week attention placebo entertainment condition using private secret Facebook groups. Weekly topics included posts related to nonalcohol or drug-related topics that involved entertaining content (eg, sports, lifestyle, fun, etc). E-coaches posted content within the groups daily, at the same intervals as the intervention group posts. As in the intervention groups, the User Safety Agreement was enforced, the crisis line information was displayed in the group cover photo 24/7, and the downloadable files section included national resources (eg, suicide hotlines, mental health, and substance use treatment), the User Safety Agreement, and a copy of the consent form.

Outcomes

Alcohol Use

Our primary outcome of changes in alcohol consumption (eg, quantity, frequency, binge drinking) in the past 30 days is based on a self-administered, web-based, Timeline Follow-Back (TLFB) assessment [117-119]. We programmed this self-administered measure to embed within our Qualtrics baseline and follow-up surveys, with data housed on our secure internal servers.

Alcohol Consequences

Alcohol consequences were measured via the Brief Young Adult Alcohol Consequences Questionnaire (BYAACQ) [120], which asked participants about experiences with 24 specific alcohol-related problems (eg, blackouts, hangovers) over the last 3 months (responses: *0=none* to *3=more than 5 times*). Note that we modified the BYAACQ by removing 2 items that are not frequently endorsed (ie, "My physical appearance has been harmed by my drinking" and "I have felt like I needed a drink after I'd gotten up [that is, before breakfast]"); we substituted 2 additional questions adapted from the original Young Adult Alcohol Consequences Questionnaire (ie, "I have damaged or lost property after drinking" and "I have gotten into physical fights because of drinking") [121,122].

Condition Engagement and Sentiment Analysis

Measures of intervention engagement include counts of engagement data (eg, posts, status, comments to others' posts, likes/shares). We expect that engagement level will mediate drinking outcomes, in that those who were more engaged in the intervention may respond more positively to the intervention. To examine characteristics of engagement, we will conduct sentiment analysis using software to code valance and arousal (eg, Dictionary of Affect in Language, Affective Norms for English Words) [94,95]. When initially starting the study, we considered using third-party applications to collect these data; however, our IRB did not allow for storing participant identities on third-party servers. Thus, we developed our own automated software application housed on our internal servers to count each user's likes/reactions, status updates, shares, replies, and comments to monitor engagement (and to assist in calculating incentive payments in the SMI+I condition) and to code sentiment within secret groups. However, midway through the study, Facebook restricted access to our program and all other third-party applications to secret groups. Therefore, study staff hand coded engagement to provide weekly incentives to participants in the SMI+I condition. To complete sentiment analyses (eg, code valence and arousal) and calculate engagement totals, we are currently revising our automated software application to code group conversations.

Intervention Acceptability and Perceived Helpfulness

At the 3-month follow-up, as done in prior work [123], participants were asked to rate perceived helpfulness of interactions with Facebook groups and e-coaches and the 8 weekly intervention topics. Example items include, "How helpful was it to interact with other peers in the group?" and "I felt the e-coaches understood me," with response options ranging from *not at all* to *extremely*. The SMI+I condition received additional questions to assess the perception of incentives for engagement. Finally, the 12-month survey asked participants how many friends they made from the group that they still keep in touch with, with response options ranging from none to 21 or more.

Secondary Outcomes of Other Drug Use

Several measures were collected at baseline and follow-ups, which may be used to explore the impact of the interventions on other drug use as a secondary outcome. First, the TLFB described earlier also assessed past 30-day daily cannabis use. In addition, we made minor modifications to items from the Tobacco, Alcohol, Prescription medications, and other Substance tool to query other substances used in the past 3 months [124].

Statistical Analyses for Primary Aims

We will use generalized linear mixed models (GLMMs) to examine treatment effects and changes in the dependent measures (for both primary and secondary outcomes). We chose GLMMs for 2 primary reasons: (1) GLMMs adjust for correlations between data points (eg, repeated measurements on individuals); and (2) within GLMMs, one can retain participants who do not complete all follow-up assessments in analyses. As the primary outcome variable, alcohol consumption, is unlikely to have normally distributed errors and is effectively integer valued, the Poisson distribution, allowing for overdispersion [125], is a natural choice. This assumption will be scrutinized, and, as needed, modifications (eg, zero inflation) [126] and alternative families of distributions (eg, negative binomial) will be considered. For models treating level of interaction, quantified by engagement metrics, as the dependent variable (aim 2), we do not have any *a priori* judgments about the appropriate distributional family, and this will be assessed based on the observed distribution. Our initial choice will be the Gaussian (normal) distribution. In all cases, we will implement an intent-to-treat analysis [127]. Analyses pertaining to secondary outcomes of other drug use will be conducted in parallel manner to the primary outcomes analysis.

Aim 1: Develop and Test the Efficacy of Intervention Conditions (Social Media Intervention With Incentives and Social Media Intervention Only) Compared With

Control, in Reducing Alcohol Consumption and Alcohol-Related Consequences

Hypothesis

Compared with the control group, the intervention conditions will have significantly less alcohol use and consequences.

Statistical Analysis

We will assess intervention effects at 3-, 6-, and 12-month follow-ups using the bivariate analyses comparing the 2 intervention conditions to the control condition. We will then examine treatment effects using a Poisson GLMM to account for correlations between repeated measurements. If preliminary bivariate analyses suggest that the effect of the intervention may vary over time, we will model an interaction of intervention by time.

Aim 2: Compare the Intervention Conditions (Social Media Intervention With Incentives and Social Media Intervention Only) in Participant Engagement and Efficacy in Reducing Alcohol Consumption and Alcohol-Related Consequences at Follow-Up

Hypotheses

Compared with participants in the SMI condition, participants in the SMI+I condition will have (1) greater levels of involvement and (2) have significantly less alcohol use and consequences.

Statistical Analysis

As mentioned earlier, we will assess intervention effects at 3-, 6- and 12-month follow-ups using bivariate analyses and also examine the distribution of outcome variables. We will then examine intervention effects over the study using a Poisson GLMM to account for correlations between repeated measurements and an indicator for the intervention group (SMI+I and SMI). As mentioned earlier, we will examine interaction effects as appropriate, including intervention by time.

Aim 3: Examine How the Level of Engagement in Intervention Conditions and Characteristics of Engagement Relate to Alcohol Use Outcomes in the 2 Intervention Conditions

Hypothesis

Participants in the intervention who have more frequent engagement and more positive valence and arousal will have significantly less alcohol consumption and consequences over 12 months of follow-up than participants with less interaction.

Statistical Analysis

We will examine the level of intervention involvement (eg, number of posts) and valence/arousal from the 8-week intervention period as predictors of alcohol outcomes at 3, 6, and 12 months using GLMMs. We will conduct sensitivity analyses by stratifying models by intervention condition. We will create graphs of the outcomes by treatment group to inform how potential variation in the effect of the intervention conditions on the outcome over time is examined in GLMMs (eg, consider interaction terms of condition with time that test for linear or quadratic increases or decreases in effect size over time).

Sample Size for Primary Aims

Power was estimated based on an N value of 900 and approximately 75% follow-up rate (conservatively based on our team's prior alcohol brief intervention, which had >80% compliance with interventions and follow-ups over 12 months) [62], which does not take into account imputations and other strategies for handling missing data without reducing sample size. All power analyses were conducted using G*Power 3.1.7. software and assumed a two-sided test with an alpha of .05. Although we conservatively estimated effect sizes based on the brief intervention literature, we hope that the 8-week intervention period will enhance effect sizes. Although we were not able to locate software for calculating power for GLMMs, we estimated power assuming one follow-up and using traditional statistical tests and anticipate that the greater number of observations will be partially offset by correlation of observations within participant, resulting in similar power. For aim 1, we estimated that we will have >80% power to detect an 11.1% difference between intervention and control groups on alcohol consumption and a 12.5% in alcohol consequences. For aim 2, we estimated we will have >80% power to detect alcohol consumption that is 11.3% lower in the SMI+I group than the SMI group. For aim 3, we estimated we will have >80% power to detect intervention engagement as a continuous variable predicting a reduction in alcohol consumption and consequences.

Results

Recruitment for the RCT began on January 5, 2017, and was completed on April 20, 2019, with 10 waves of recruitment to enroll the final sample. Across all waves, 11,914 individuals self-administered the web-based screening survey, and we sent baseline invitations to 1541 participants who screened positive on the AUDIT-C and passed initial verification processes. There were 1015 participants who completed the baseline survey; however, 46 individuals did not send a selfie for verification, 8 did not pass selfie verification procedures, 4 indicated they were too busy to join the study, and 2 timed out (did not complete all baseline procedures by group start). Thus, a total of 955 completed all baseline procedures (survey and selfie verification) and were randomized to one of 3 conditions: SMI+I (N=321), SMI (N=321), and attention control (N=313). The 8-week groups were completed in June 2019, and follow-up assessments are ongoing.

There were a total of 5 User Safety Agreement violations during the course of the groups, which resulted in removing a post and reminding participants of this agreement (eg, a public post to the group and/or private message). These violations included 1 individual posting an advertisement for a business, 1 individual posting a personal fundraising page, 1 individual posting a disturbing image, 1 individual using derogatory language regarding mental health, and 2 individuals arguing about politics that included swearing and name calling.

Discussion

Although social media has been used to deliver interventions addressing other health behaviors [80-82,86], this RCT is one of the first to examine the efficacy of SMIs to reduce risky drinking among adolescents and emerging adults. Given the popularity and daily use of social media among young people [55,56], our intervention capitalizes on a highly used medium that is already routinely a part of their daily lives, unlike prior computerized interventions or alcohol-specific smartphone apps. Furthermore, addressing limitations of prior expensive computer applications that use software that quickly becomes out of date, these SMIs allow for ease of integration into common Web applications by nontechnical staff to facilitate sustainability.

The study protocol described here creates a recipe for future SMIs, as applied to early interventions for substance use. Similar to studies of HIV risk reduction [88], our interventions harness the Facebook feature of secret groups that preserve privacy and facilitate group interaction with other participants in real time, catalyzed by e-coaches who post dynamic content daily. The incentive condition harnesses participants to engage with other participants, which will provide interesting comparison with the nonincentivized intervention condition. In addition, unlike many prior alcohol interventions, which ignore concomitant other drug use, our intervention primarily addresses alcohol while also addressing the use of other drugs and associated health consequences (eg, injury, impaired driving, overdose prevention). Future papers will examine the efficacy of these innovative SMIs, which could have a significant public health impact by altering the alcohol use trajectories of adolescents and emerging adults.

Acknowledgments

The funding for this study was provided by the National Institute on Alcohol Abuse and Alcoholism R01 (#024175). During her work on this study, EB was supported by a National Institute on Drug Abuse Career Development Award (#036008). The funding sources had no role in the design, data collection, analysis, or interpretation of results. Research reported herein was also supported by a grant to the University of Michigan Injury Prevention Center by the Centers for Disease Control & Prevention Award Number R49-CE-002099. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Centers for Disease Control & Prevention or the Department of Health and Human Services.

Authors' Contributions

EB and MW and DS wrote the initial drafts of this paper; however, all authors have contributed to the writing and editing of this manuscript and approve the final manuscript.

Conflicts of Interest

The authors do not have any personal financial interests related to the subject matters discussed in this manuscript, with 2 exceptions. MW is a minor shareholder in Facebook and has a conflict of interest plan approved by the University of Michigan. SY has received an unrestricted gift from Facebook, on file with the University of California, Los Angeles (his prior academic appointment).

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Abbreviations

AUDIT-C: Alcohol Use Disorders Identification Test-Consumption
BYAACQ: Brief Young Adult Alcohol Consequences Questionnaire
CBT: cognitive behavioral therapy
e-coach: electronic coach
GLMM: generalized linear mixed model
IRB: institutional review board
MI: Motivational Interviewing
MINT: MI Network of Trainers
RCT: randomized controlled trial
SDT: self-determination theory
SMI: social media intervention
SMI+I: social media intervention with incentives
TLFB: Timeline Follow-Back

Edited by G Eysenbach; submitted 15.10.19; peer-reviewed by D Litt, K Tassiopoulos, T Filipowicz; comments to author 12.12.19; revised version received 30.01.20; accepted 16.02.20; published 13.05.20.

Please cite as:
Bonar EE, Schneeberger DM, Bourque C, Bauermeister JA, Young SD, Blow FC, Cunningham RM, Bohnert ASB, Zimmerman MA, Walton MA
Social Media Interventions for Risky Drinking Among Adolescents and Emerging Adults: Protocol for a Randomized Controlled Trial
JMIR Res Protoc 2020;9(5):e16688
URL: https://www.researchprotocols.org/2020/5/e16688
doi:10.2196/16688
PMID:32401225

Protocol

Development of a Digital Content-Free Speech Analysis Tool for the Measurement of Mental Health and Follow-Up for Mental Disorders: Protocol for a Case-Control Study

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Abstract

Background: The prevalence of mental disorders worldwide is very high. The guideline-oriented care of patients depends on early diagnosis and regular and valid evaluation of their treatment to be able to quickly intervene should the patient's mental health deteriorate. To ensure effective treatment, the level of experience of the physician or therapist is of importance, both in the initial diagnosis and in the treatment of mental illnesses. Nevertheless, experienced physicians and psychotherapists are not available in enough numbers everywhere, especially in rural areas or in less developed countries. Human speech can reveal a speaker's mental state by altering its noncontent aspects (speech melody, intonations, speech rate, etc). This is noticeable in both the clinic and everyday life by having prior knowledge of the normal speech patterns of the affected person, and with enough time spent listening to the patient. However, this time and experience are often unavailable, leaving unused opportunities to capture linguistic, noncontent information. To improve the care of patients with mental disorders, we have developed a concept for assessing their most important mental parameters through a noncontent analysis of their active speech. Using speech analysis for the assessment and tracking of mental health patients opens up the possibility of remote, automatic, and ongoing evaluation when used with patients' smartphones, as part of the current trends toward the increasing use of digital and mobile health tools.

Objective: The primary objective of this study is to evaluate measurements of participants' mental state by comparing the analysis of noncontent speech parameters to the results of several psychological questionnaires (Symptom Checklist-90 [SCL-90], the Patient Health Questionnaire [PHQ], and the Big 5 Test).

Methods: In this paper, we described a case-controlled study (with a case group and one control group). The participants will be recruited in an outpatient neuropsychiatric treatment center. Inclusion criteria are a neurological or psychiatric diagnosis made by a specialist, no terminal or life-threatening illnesses, and fluent use of the German language. Exclusion criteria include psychosis, dementia, speech or language disorders in neurological diseases, addiction history, a suicide attempt recently or in the last 12 months, or insufficient language skills. The measuring instrument will be the VoiceSense digital voice analysis tool, which enables the analysis of 200 specific speech parameters, and the assessment of findings using psychometric instruments and questionnaires (SCL-90, PHQ, Big 5 Test).

Results: The study is ongoing as of September 2019, but we have enrolled 254 participants. There have been 161 measurements completed at timepoint 1, and a total of 62 participants have completed every psychological and speech analysis measurement.

Conclusions: It appears that the tone and modulation of speech are as important, if not more so, than the content, and should not be underestimated. This is particularly evident in the interpretation of the psychological findings thus far acquired. Therefore, the application of a software analysis tool could increase the accuracy of finding assessments and improve patient care.

Trial Registration: ClinicalTrials.gov NCT03700008; https://clinicaltrials.gov/ct2/show/NCT03700008

International Registered Report Identifier (IRRID): PRR1-10.2196/13852

(JMIR Res Protoc 2020;9(5):e13852) doi:10.2196/13852

KEYWORDS

voice detection; depressive disorder; content-free speech analysis; mobile health app

Introduction

Human Language

Human language is a fundamental ability which, in addition to social interaction, primarily serves the exchange of feelings; however, in the sense of an inner dialogue, it also serves as a means of self-perception and self-reflection [1]. This establishes a relationship between pure content as an expression of cognitive performance and emotional content in the sense of affective meaning. This close connection between emotion and cognition, especially with language and speech, has been scientifically researched within the framework of relational frame theory for many years [2]. Human language as a form of expression, with human listening on the other side, has been the basis of professional therapeutic support for mental disorders for more than 100 years [3,4]. The recent treatment developments regarding linguistic and psychological research in relational frame theory have been acceptance-based treatments, such as acceptance and commitment therapy [5].

Due to the increasing global frequency of mental disorders, their safe detection and treatment is very important. According to World Health Organization calculations [6], depression alone will be the second greatest burden of disease in the world in 2020. Other mental disorders, such as neurodevelopmental disorders (attention deficit hyperactivity disorder [ADHD], autism spectrum disorders, etc [7,8]) or personality disorders [9], which have been increasing in recent years, also cause significant individual stress and have a societal impact due to the loss of potential productivity and treatment costs [10]. Early detection and treatment of mental disorders is, therefore, a major factor in preventing these problems, as is the avoidance of deterioration. However, there is currently no objective, ideal physiological parameter available for this task.

Since the 1990s, attempts have been made to determine the emotional state of a speaker by analyzing the content of their speech and the linguistic structure [11]. There have been positive results thus far, with high specificity and sensitivity in some subjects when using suitable parameters, like in cases where depressive disorders have been detected [12-14]. As a result, there has been intensive development in the automation of such analyses, with continuing positive results [14]. However, so far dissemination of such analyses, such as in the early detection, diagnosis, or assessment of mental disorders, has not occurred in broad clinical practice but has been described in a few single cases [15,16]. The reasons for this may be complex, but it may be due to the high technical effort required to perform these analyses that have led to them not being well reflected in outpatient care practice [17]. Also, resentment against machine diagnosis or very technical measurements may have played a role that should not be underestimated. Finally, the diagnostic and prognostic validity of such measures still needs to be proven.

In the last decade, electronic assistants have taken up considerable space in all areas of life, first through computerization and later via smartphones [18]. In medicine, and especially in psychiatry and psychotherapy, numerous programs, online tools, and coaching applications are now available and have seen increasing acceptance [19]. At the same time, the technical effort that needs to be expended to create a high-quality, medically or psychologically useful application for use in the clinic has decreased [20,21]. The applications that can be implemented in this way are even more complex and extensive than previously thought possible. It may, therefore, make sense to use these new technical possibilities and examine whether the analysis of language, especially the noncontent aspects (eg, speech flow, speech melody, expression), can be used by a differentiated algorithm to assess the mental state of a subject. It is possible that they could also measure the course of mental illness, the quality of life of patients with chronic mental illnesses, and patients' well-being [22].

The study presented here uses a noncontent linguistic analysis algorithm developed by VoiceSense, a company specializing in prosodic speech analysis, which links speech patterns to behavioral tendencies. The analysis is commercially used for personal risk assessment by banks and insurance companies, for candidate assessment by human resources companies, and customer analytics by enterprise call centers. The current study would provide a structured setting for the differentiated evaluation of psychopathological factors (effects, personality aspects, psychomotor factors, etc) by this speech pattern analysis.

Research Objectives

The primary objective of this study is to evaluate the measurements of the mental state of the participants by comparing the analysis of noncontent speech parameters to the results of several psychological questionnaires (Symptom Checklist-90 [SCL-90], the Patient Health Questionnaire [PHQ], and the Big 5 Test). We hypothesized that the emotional state of mind, the behavioral patterns, the well-being, and some of the personality traits of the participants could be identified using the prosodic analysis algorithm. A second hypothesis is that the diagnosis could be confirmed by the application of the analysis program, and a distinction can be made between different psychopathologically-defined syndromes.

Methods

Participants

A total of 166 outpatients will be recruited in one center (Neuropsychiatric Center of Hamburg), following the invitation of their treating physician or psychotherapist, to use a new method to measure their mental state and distress. Inclusion and exclusion criteria for the study are listed in Textbox 1.

Textbox 1. Inclusion and exclusion criteria.

Inclusion criteria:

- A regular outpatient with a mental disorder or neurological disease
- Native German speaker
- Aged 18-65 years old
- In good general health (absence of cancer, acute myocardial infarction, unstable angina, severe cardiac arrhythmia, recent cerebrovascular incident, or severe atherosclerosis).

Exclusion criteria:

- Schizophrenia
- Dementia
- Current or recent (less than 1 year) history of alcohol or drug abuse
- Current or recent (less than 1 year) history of suicide attempts
- Other significant comorbidities according to the Investigator's clinical assessment (eg, cancer, acute myocardial infarction, unstable angina, severe cardiac arrhythmia, recent cerebrovascular incident, or severe atherosclerosis).

For the exclusion criteria, both schizophrenia and dementia have shown indications that a patient's speech patterns are influenced by these disorders. Therefore, we decided to consider these two groups of patients separately in a future study to see whether there is a comparable difference to the general population on a content-free linguistic level.

Linguistic Algorithm and Recording System

Audio Collection

Speech utterances of the subjects will be sampled using the VoiceSense mobile app, which will be installed on the tablets (BENEVE Co, 10.1-inch screen, 32 gigabytes of memory, Android version 7.0) of the research examiners. The recordings will be taken over 1-3 separate sessions throughout the study: the initial interview, the first follow-up session after 2-4 weeks, and the second follow-up session after another 2-4 week period. In each of those sessions, the research examiners will activate the app by logging into it with a dedicated username and password that was prepared in advance for each subject (the username and password do not reveal the subject's identification). The app then presents 9 general questions (eg, "Please describe in a few sentences how was your day yesterday"). The subject presses record and answers, and when finished they will press stop and the app will present a second question for the subject to answer. The app will count the recorded time to verify that at least 120 seconds are recorded, but if after nine answers there is still not enough recording time then the app will present an increasing number of questions till the time requirement is met. Once enough speech is recorded, the app will send the recorded audio to the VoiceSense cloud server for analysis. The content of the subject's answers is not important for the analysis; therefore, the questions are designed in a general manner to enable collection of the natural speech patterns of the subjects. The recordings will be done in a quiet room in the Neuropsychiatric Center Hamburg, which is reserved for diagnostic purposes. The examiner will leave the room while the recording is done, to make the subjects feel more comfortable and to not influence their free speech.

Speech Analysis

The audio that will be sent to the server will be analyzed using VoiceSense proprietary speech analysis. This analysis produces raw data of over 200 prosodic parameters for each call. The raw data parameters will be sent back to the research center for the statistical analysis, with a sampling frequency of 8 kilohertz.

VoiceSense speech analysis focuses on speech prosody, the noncontent aspects of the speech, such as intonation, pace, stressing, and other aspects. The analysis is language independent and has been tested successfully in many languages (different European languages, different Asian languages, etc). The analysis was validated versus various personality tools, such as Big 5 [23], Holland [24], Hogan [25], WPI [26], and linked speech patterns (clusters of the raw speech parameters) with the personality scales as measured by these tools. The analysis is based on several granted patents regarding measurement of emotional state [27] and behavioral tendencies [28] through speech analysis. This proprietary speech anal ysis is the basis for commercial products in the fields of enterprise, big data analytics, customer analytics, human resources, and others.

Study Design and Data Protection

This study is a case-controlled study with a case group and a control group to identify the best target population for measuring speech patterns with the VoiceSense app. We adhered to the Consolidated Standards of Reporting Trials (CONSORT) guidelines in the design of the trial.

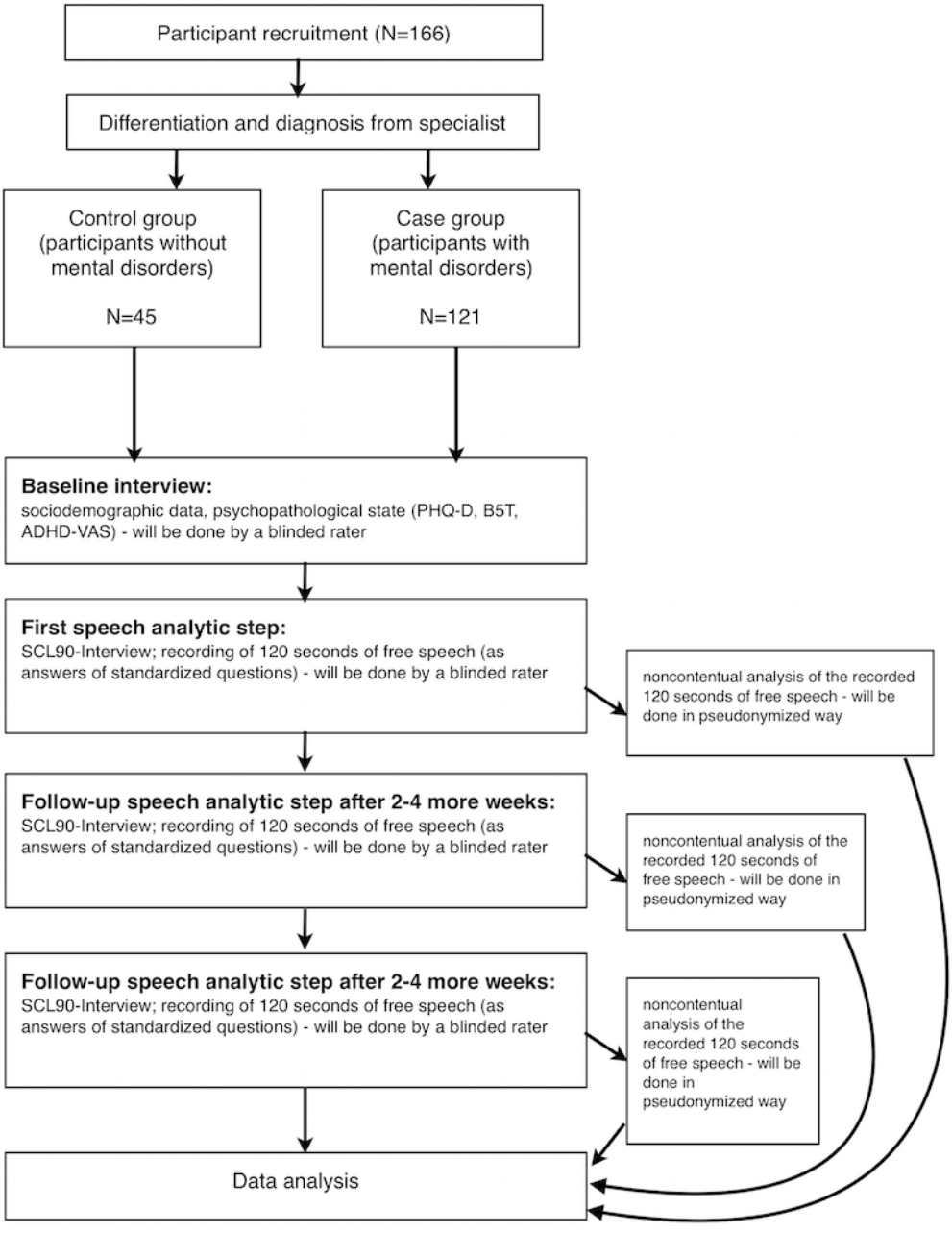
In the first step, the participants will be grouped by the physician or psychotherapist into a control group (participants without mental disorders) or a case group (participants with mental disorders). All participants will provide written informed consent after being given detailed information by the treating therapist or physician. The original forms will be stored in a closed cabinet, but the participants will receive a copy. Second, they will receive a pseudonymized label for the blinded inhouse-rater to work with the questionnaires, and for the data center for the speech-analysis. Neither the rater nor the data center will know

the name and diagnosis of the participant. Data security and availability will be ensured every time, according to the European Union (EU) rules [29]. The participants' data will be stored in a MySQL-Database. Within the project database, identifying data will be stored separately from the collected data, with only project staff with specifically conferred access rights able to access the identifying data. It is envisioned that the distribution of participants will correspond to the clinical distribution in the Neuropsychiatric Center with different degrees of severity of mental disorders (about 25% mild, about 50% moderate, about 25% severe). This should be checked by the study nurse every 2 weeks.

For documentation purposes, the presence or absence (in the case of neurological outpatients) of any psychiatric diagnosis will be screened using the PHQ-D [30]. Personality traits will then be measured with the Big 5 Test [23]. In the case of ADHD, we added a Visual Analogue Scale (ADHD-VAS) to identify the three main affective states (impulsivity, inattention, and hyperactivity). This will be done at baseline only.

At baseline, at follow-up one (2-4 weeks after baseline), and follow-up two (2-4 weeks after follow-up 1), participants will be measured for mental distress using the SCL-90 [31]. They will then be asked to freely answer nine standardized questions, with a few sentences per question. These answers will be recorded for evaluation. If less than 120 seconds of free speech is possible, three more standardized questions will be asked and the answers to these will also be recorded. The recorded sentences will then be sent to the server to carry out the prosodic analysis. The results of the questionnaires and the results of the prosodic analysis will be stored in the patients' records on file. Figure 1 shows the flow chart of the study.

Figure 1. Flowchart of the study protocol. PHQ-D: Patient Health Questionnaire. B5T: Big 5 Test. ADHD-AS: attention deficit hyperactivity disorder-visual analogue scale. SCL-90: Symptom Checklist-90.



Statistical Methods

It should be possible for the study team to evaluate the efficacy and effectiveness of the raw data from the linguistic analysis in correlation with the clinical data collected with the questionnaires. All statistical tests will be two-tailed and will be considered statistically significant at $P<.05$. A sample size of 166 subjects was calculated (effect size medium=0.30; alpha=0.05; 1–beta=0.95), and considering a drop-out rate of 15%, a total sample size of 190 patients was determined.

Statistical analysis will be performed with R version 3.5.3 (The R Project, Vienna, Austria), and epidemiological data will be evaluated. Continuous variables will be described with the mean, standard deviation, median, minimum, maximum, and the 25th and 75th percentiles. Categorical variables will be described with percentages and absolute frequencies. The differences in continuous variables between the two groups will be evaluated with the Kruskal-Wallis test, followed by the Dunn multiple comparison test. The differences between the two diagnostic groups (psychiatric versus neurological diagnosis) for normally distributed data will be evaluated with a one-way analysis of variance (ANOVA), followed by the Newman-Keuls multiple comparison test. The normality of the distribution will be evaluated with the Kolmogorov-Smirnov test. Any correlation between the variables under evaluation will be assessed by the Spearman r correlation. To compare qualitative data, we will use the Chi-square test with the Yates correction or the Fisher exact test. Lastly, the variables will be grouped to their diagnostic groups according to the 10th edition of the International Statistical Classification of Diseases and Related Health Problems or the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders, and a confirmative factor analysis will be done comparing these groups with the prosodic parameters.

Ethics Approval

This study protocol has been approved by the ethical committee of the Neuropsychiatric Center under the Declaration of Helsinki. Written informed consent will be collected from the participants before they will be included in the study.

Results

The study is ongoing as of September 2019, and as of this date, we have enrolled 254 participants. The dropout rate has been acceptable, with 161 participants having thus far completed every questionnaire and the speech analytical measurements at time point one. Overall, 67 participants have reached time point two and 62 participants have reached the end of the study. We believe we can close recruitment and start final statistical calculations by November 2019.

Discussion

The prevalence of mental disorders has increased in recent decades, and thus their importance in society has also grown. This can be traced back to the reduced stigma surrounding them and the associated growing acceptance, as well as to a growing social awareness of the problem. Undoubtedly, early detection in the development of mental illness, as well as adequate follow-up for relapse prevention, is one of the most important tools in reducing the burden of disease for the individual as well as for society. If the use of linguistic analysis, in the presented form of an app or as an online tool, can enable the possibility of validating the emotional state and behavioral patterns of a patient, this screening could be used for an initial assessment. Also, due to its low threshold of access, it could end up providing valuable support for those who might not otherwise be able to access any assessment.

The importance of linguistic parameters for the detection of the emotional or behavioral state of a patient has been proven in the light of previous literature, at least for patients with depressive disorders. However, the analyses carried out with content-free voice recordings have thus far been associated with a high level of technical and personnel expenditure. This study wants to examine whether mental distress measured by voice analysis compared with standard questionnaires could be an appropriate tool with validated results, and also whether other mental disorders have specific linguistic patterns (in addition to patients with depression) which could differ from each other.

Conflicts of Interest

YD, SH, and AK were involved in the production of the VoiceSense digital analysis tool.

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Abbreviations

ADHD: attention deficit hyperactivity disorder
ANOVA: analysis of variance
CONSORT: Consolidated Standards of Reporting Trials
EU: European Union
PHQ: Patient Health Questionnaire
SCL-90: Symptom Checklist-90
VAS: visual analog scale

Edited by G Eysenbach; submitted 27.02.19; peer-reviewed by Y Omiya, F Lamers; comments to author 27.04.19; revised version received 14.08.19; accepted 19.08.19; published 14.05.20.

Please cite as:
Tonn P, Degani Y, Hershko S, Klein A, Seule L, Schulze N
Development of a Digital Content-Free Speech Analysis Tool for the Measurement of Mental Health and Follow-Up for Mental Disorders: Protocol for a Case-Control Study
JMIR Res Protoc 2020;9(5):e13852
URL: https://www.researchprotocols.org/2020/5/e13852
doi:10.2196/13852
PMID:32406862

Protocol

Investigating the Efficacy and Cost-Effectiveness of Technology-Delivered Personalized Feedback on Dietary Patterns in Young Australian Adults in the Advice, Ideas, and Motivation for My Eating (Aim4Me) Study: Protocol for a Randomized Controlled Trial

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Abstract

Background: Web-based health interventions may be easier to access and time efficient relative to face-to-face interventions and therefore may be the most appropriate mode to engage young adults.

Objective: This study aims to investigate the impact of 3 different levels of personalized web-based dietary feedback and support on changes in diet quality.

Methods: The Advice, Ideas, and Motivation for My Eating (Aim4Me) study is a 12-month assessor-blinded, parallel-group randomized controlled trial evaluating the impact of 3 levels of web-based feedback on diet quality, measured using the Australian Recommended Food Score (ARFS). Participants (N=2570) will primarily be recruited via web-based methods and randomized to 1 of 3 groups. Group 1 (control) will receive the Healthy Eating Quiz, a web-based dietary assessment tool that generates a *brief* feedback report on diet quality. Individuals randomized to this group can use the *brief* feedback report to make positive dietary changes. Group 2 will receive the Australian Eating Survey, a web-based dietary assessment tool that generates a *comprehensive* feedback report on diet quality as well as macro- and micronutrient intake. Group 2 will use the *comprehensive* feedback report to assist in making positive dietary changes. They will also have access to the Aim4Me website with resources

on healthy eating and tools to set goals and self-monitor progress. Group 3 will receive the same intervention as Group 2 (ie, the *comprehensive* feedback report) in addition to a tailored 30-min video consultation with an accredited practicing dietitian who will use the *comprehensive* feedback report to assist individuals in making positive dietary changes. The self-determination theory was used as the framework for selecting appropriate website features, including goal setting and self-monitoring. The primary outcome measure is change in diet quality. The completion of questionnaires at baseline and 3, 6, and 12 months will be incentivized with a monetary prize draw.

Results: As of December 2019, 1277 participants have been randomized.

Conclusions: The web-based delivery of nutrition interventions has the potential to improve dietary intake of young adults. However, the level of support required to improve intake is unknown.

Trial Registration: Australian New Zealand Clinical Trials Registry ACTRN12618000325202; https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=374420

International Registered Report Identifier (IRRID): DERR1-10.2196/15999

(JMIR Res Protoc 2020;9(5):e15999) doi:10.2196/15999

KEYWORDS

young adults; web-based; dietary feedback; nutrition; eHealth; diet

Introduction

Background

In Australia, young adults (aged 18-24 years) are gaining weight and at a faster rate than any other adult age group [1,2], with 31.5% [3] affected by overweight or obesity. Studies report weight gain of around 0.5 kg to 1 kg (1-2 lbs) per year over a 5- to 10-year period in young adults [4-6]. Becoming overweight or obese at a young age increases the risk of noncommunicable chronic diseases, including metabolic syndrome, type 2 diabetes, cardiovascular disease, and specific cancers [7].

Diet quality is currently poor among young adults [8], with the high consumption of sugar-sweetened beverages (SSBs) and low intake of fruit and vegetables [3]. Discretionary foods (predominantly SSBs, alcohol, and takeaway and convenience foods) account for over one-third of total energy intake in Australia [9]. Globally, similar patterns of dietary intake have been observed, with young adults having the lowest diet quality [10]. Dietary patterns also differ by income status and ethnicity across regions [11], but when comparing the diet quality of low- and high-income countries, young adults still have the poorest diet across income levels [11]. Poorer diet quality is linked to poor physical and mental health [12-14], and considering that the dietary habits of young adults have been shown to track throughout life when disease risk is higher [15], intervening during young adulthood is crucial [16].

Young adults are faced with multiple life-stage challenges, including moving out of or away from home, commencing study or employment, developing new social interactions or cohabitations, and increased independence and financial responsibilities [2]. These changes can interfere with the adoption of healthy eating behaviors. Young adults reported the following key barriers to eating healthy: lack of time (because of balancing work, study, and a social life); lack of skills and knowledge to plan, shop, prepare, and cook healthy foods; relative low cost and availability of less healthy foods; peer influences and lack of motivation to eat healthy; and competing priorities [2,17,18]. Strategies to help overcome these barriers are required, and because of the unique characteristics of this group and the challenge with reaching and engaging them in health behavior change, an appropriate set of strategies for this age group needs to be selected. The self-determination theory (SDT) supports self-directed motivation by satisfying an individual's need for autonomy, perceived competence, and relatedness and focuses on the extent to which behaviors are self-initiated (autonomous) versus influenced by external factors (external motivators) [19]. At the center of the Behavior Change Wheel framework is a system comprising 3 key factors that influence behavior change: capability, opportunity, and motivation (COM-B) [20]. It provides a framework for selecting appropriate intervention strategies, such as goal setting, tracking, and action planning, which are essential for building long-term positive behavior changes in young adults. A recent review reported that the most frequently used behavior change techniques for improving the dietary intake of young adults included goal setting and feedback on behavior [21]. Goal setting includes setting or agreeing on a goal, defined in terms of the behavior to be achieved (eg, *increase serves of fruit by one serve per day*). Feedback on behavior is where goals and behaviors are monitored and informative or evaluative feedback is provided on the performance of the behavior (*eg, frequency or quantity of intake of fruit*) [22]. Interventions including behavior change techniques have been shown to be more effective at improving dietary intake compared with those without [21].

Beyond the selection of appropriate strategies, interventions targeting young adults need to consider the ideal mode of delivery for optimal engagement. The uptake of web-based technologies to support health is still increasing in young adults, and web-based technologies continue to evolve to meet this demand. Websites offer a platform for information delivery via various modes, including written, audio, and video, and advances in technology allow web-based programs to be accessed via mobile devices, such as smartphones [23]. Additional benefits of web-based interventions include greater reach in terms of geographical location and population groups and the ability to maximize the collection of complete data [23].

The Advice, Ideas, and Motivation for My Eating (Aim4Me) study aims to recruit young adults and provide nutrition interventions with varying levels of feedback, nutrition education, goal setting and tracking, and interaction with a dietitian in a web-based environment. The extent to which these types of interventions can successfully recruit, engage, and effect positive dietary change in this population has not been investigated.

Aim

Thus, the primary aim is to investigate the impact of 3 levels of personalized dietary feedback and support on changes in diet quality, as measured by the Australian Recommended Food Score (ARFS). The secondary aim is to investigate intervention reach, participant engagement, retention, satisfaction, and cost-effectiveness.

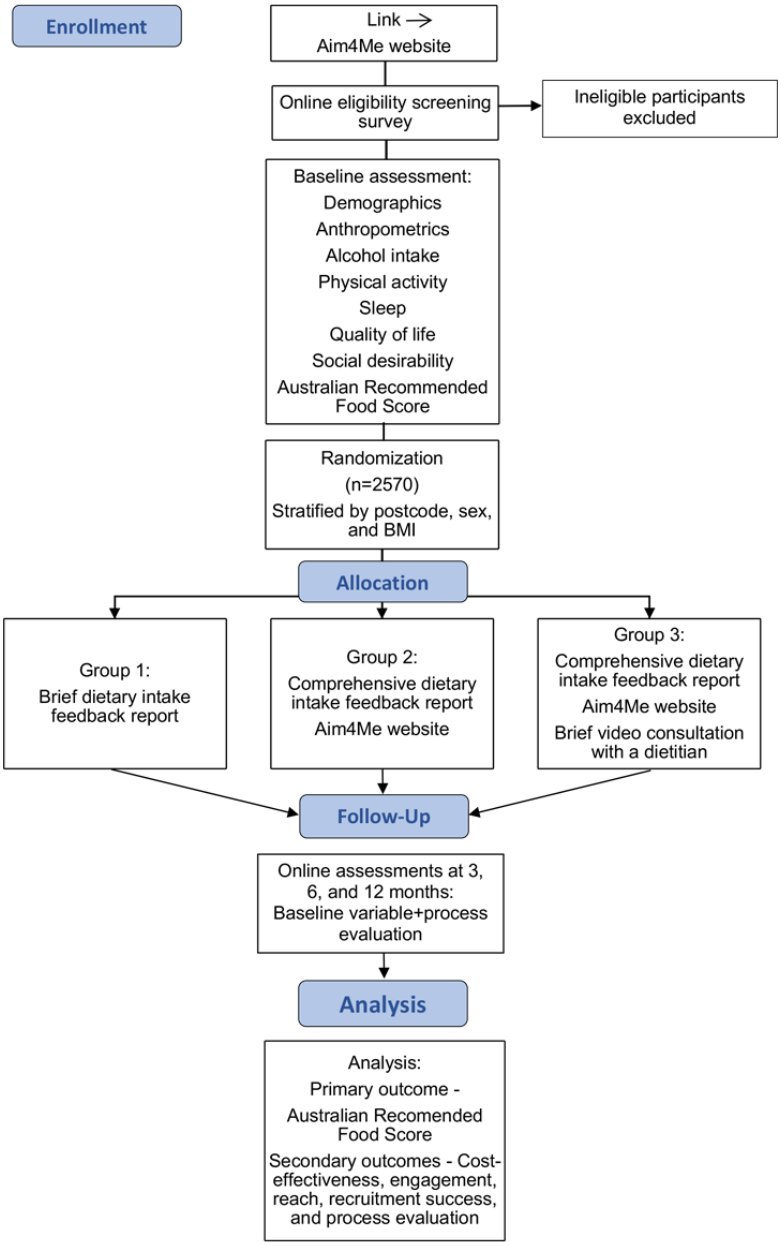
Methods

Study Design

Aim4Me is a 12-month assessor-blinded, parallel-group randomized controlled trial assessing the impact of varying levels of web-based feedback on diet quality. The study is approved by the University of Newcastle Human Research Ethics Committee (H-2017-0087). This study was prospectively registered with the Australian New Zealand Clinical Trials Registry and is consistent with the Consolidated Standards of Reporting Trials guidelines (ACTRN #12618000325202) [23]. The study was performed in accordance with the Declaration of Helsinki. All patients enrolled in the study provided written consent.

Participants (N=2570) will be recruited nationally across Australia. After informed consent and baseline data are collected, eligible participants will be randomized to 1 of 3 groups (Figure 1). Group 1 will receive a *brief* feedback report on their current dietary intake, whereas groups 2 and 3 will receive a *comprehensive* personalized feedback report on their usual intake as well as get access to the study website. Group 3 will also be offered a 30-min video consultation with a dietitian.

Figure 1. Study flowchart. Aim4me: Advice, Ideas, and Motivation for My Eating.



Participants

Recruitment and Setting

A total of 2570 young adults (aged 18 to 24 years) will be recruited across Australia using multiple strategies. Given the target age group, a large focus of the recruitment is on using social media platforms, including Facebook, Instagram, and Twitter. An Aim4Me account will be created for each of these platforms, and specific posts suitable to each of the platforms will be developed. Paid Facebook advertising will also occur [24], delivered by institutional marketing and media teams. Study information and links to social media accounts will be shared on the websites of universities and research institutes. Flyers will be distributed around universities and to professional organizations and communities aimed at young adults and student associations, with requests that they advertise and share study information on their social media platforms, websites, or email lists. In addition, study information will be disseminated using local and national media releases via printed newspapers, magazines, and radio stations. A snowball method, in which individuals who visit the Aim4Me website will be able to share the link with their colleagues and friends via Facebook, Twitter, or email, will also be used. Finally, email campaigns will be distributed to contacts who have previously signed up to receive notifications of nutrition-related research studies through members of the research team.

Through each strategy, interested individuals will be directed to a study website to access information about what participation entails, check their eligibility, and provide informed consent, if eligible and interested.

Screening and Baseline Assessments

Potential participants will complete a web-based screening survey to determine whether they meet the eligibility criteria.

Once deemed eligible, they will register their contact details and provide informed consent to participate in the research. A confirmation email will be sent to the address specified by the participant with their log-in details and password, allowing them to access the participant portion of the study website and commence the baseline assessment questionnaires. Email and text reminders will be sent to registered participants on an automated schedule if they have not completed the baseline assessments post screening and consent.

Inclusion Criteria

Eligibility criteria include being aged 18 to 24 years, residing in Australia, computer/internet access, self-reported BMI ≥18.5 kg/m^2, not pregnant or planning pregnancy in the next year, no medical conditions, and no diagnosis of current or previous eating disorder. Participants with medical conditions, such as type 1 diabetes or Crohn's disease, who require specific nutrition advice, will be advised to visit their general practitioner to obtain medical clearance before participating in the study.

Randomization

Eligible participants will be randomly allocated (1:1:1) to a control group or 1 of 2 intervention groups. Randomization will occur in permuted blocks using random blocks of varying size and be stratified by postcode location (using the Monash Modified Model) [25], sex, and BMI (18.5-24.9 kg/m^2 vs ≥25 kg/m^2). Randomization will be coded by an independent statistician who will provide the coding to the software developers to program the web-based environment. The research team will remain blinded to the randomization code.

Interventions

The intervention components are based on SDT, which focuses on the extent to which behaviors are self-initiated (autonomous) versus influenced by external factors (external motivators) [19]. SDT supports self-directed motivation by satisfying an individual's need for autonomy, perceived competence, and relatedness. Autonomy will be satisfied by providing opportunities for participants to choose their own goals, reflect on progress and revise goals, access a range of resources that they self-select, and choose their level of engagement with the website. For Group 3, engagement with the dietitian will reinforce the importance of nutrition relative to personal motivators. The graphic design of the Aim4Me website and resource materials related to the motivators for, and barriers to, healthy eating among young adults. Website images, wording, and content have been selected based on feedback from this age group. In groups 2 and 3, perceived competence will be addressed by the self-development of personalized goals and regular self-monitoring of progress toward these goals to support progressive and small behavior change toward healthy eating.

Healthy Eating Quiz Brief Dietary Intake Feedback Report (Group 1)

The Healthy Eating Quiz (HEQ) [26] will be available via a link on the Aim4Me dashboard, which will direct Group 1 to this intervention component outside of the website. The HEQ is a 5-min web-based dietary assessment tool that provides *brief* general feedback on current eating patterns and diet quality using the ARFS [27,28]. Group 1 will have access to the brief report to identify the key areas for improving diet quality (eg, increase the variety of vegetable intake). These participants will have access to the HEQ throughout the study and will be prompted to complete it at baseline and at 3, 6, and 12 months.

Australian Eating Survey Comprehensive Feedback Report (Groups 2 and 3)

The Australian Eating Survey (AES) is an automated web-based food frequency questionnaire (FFQ) that assesses usual dietary intake in adults [29]. Following completion of the AES, participants randomized to groups 2 and 3 will be provided with a real-time *comprehensive* personalized feedback report that compares usual dietary intake with Australian dietary recommendations (percent energy from 5 core healthy food groups and 10 energy-dense, nutrient-poor food groups) and nutrient reference value targets (percent energy from protein, fat, saturated fat, carbohydrate, daily grams of fiber, 7 minerals, and 5 vitamins) [30], based on age and sex. The report provides feedback on diet quality, giving a total diet quality score and scores for individual food groups. Participants will be encouraged to set goals around improving diet quality. Participants in Group 2 will receive the report but no further support on the interpretation of the report or how to use the report to set goals. Group 3 will be offered additional support in the form of a video consult with an accredited practicing dietitian (APD), which will focus on using the diet quality results from the AES report to set specific goals around improving diet quality. The control group will also complete the AES to allow measurement of change in the primary outcome (see the Primary Outcome Measures section) but will not receive the AES personalized feedback report.

Advice, Ideas, and Motivation for My Eating Website

Participants in groups 2 and 3 will have access to the Aim4Me website for 12 months (Textbox 1). Images of the web interface are provided in Multimedia Appendix 1.

Textbox 1. Description of the components of Advice, Ideas, and Motivation for My Eating website.

Personalized dietary feedback

- An automated (computer-generated) personalized feedback report on dietary intake will be available to access through the website
- The feedback report will be provided at baseline and at 3, 6, and 12 months if the appropriate dietary assessment tool is completed. This will allow the individual to compare their previous reports and self-assess change

Healthy eating resource materials

- A web-based resource library of evidence-based materials will include links to apps, articles, fact sheets, recipes and information related to healthy eating, and targeting motivators and barriers to behavior change expressed by young males and females, for example, in relation to the key barriers of cost and time, the website will include resource tips on eating healthy on a budget, quick and easy meals, and budget recipes
- Other accessible content will include *Theme of the month*, which provides educational information on a new topic each month (eg, Love your Heart is May content); *Food*, which provides short snippets of information on specific food groups, for example, how to eat more fruits and vegetables; and *Explore*, which contains other useful information such as cooking tips, app suggestions, and recipes

Goal setting

- Setting dietary goals—Participants set short-term goals based on feedback from their personalized dietary report and can either self-select from predetermined generic goals that have been developed to target each of the food groups or write their own goal
- The food groups include vegetables and salad, fruit, dairy, breads and cereals, meat and alternatives, alcoholic beverages, fatty meats, sweetened drinks, packaged snacks, confectionary, baked sweet products, fried and takeaway food, and spreads and sauces
- The listed generic goals have been designed as specific-measurable-achievable-realistic-timely goals
- They can select up to 3 goals to focus on at any one time
- At 3 and 6 months, they will be prompted by email and/or text message to revise and update their goals after they have received their personalized feedback report for intake over the preceding 3 months

Self-monitoring

- Monitoring of dietary goals—Participants will be prompted by email and text message to self-monitor their goals by going to their dashboard
- Using a 5-point scale from *very poor* to *very good*, participants will be asked to reflect on how well they did in achieving their goals and how important their goal is to them (*very important* to *not important*)
- On the basis of their responses, they will be provided with generic feedback, which will either direct them to update their goals or provide them with information that will support them in achieving their goals

Video Consultation With a Dietitian (Group 3 Only)

Participants randomized to Group 3 will be encouraged to book one web-based, personalized 30-min video consultation with an APD, within 14 days of enrolling in the study. Participants will be prompted via an automated email to book their appointment on receiving their personalized feedback report. This structured consultation session will entail a review of the goals the participant has set based on the personalized feedback report from the AES and assistance in setting personalized strategies to overcome self-identified barriers to healthy eating. The resources used to streamline the personalization of the session include a brief self-administered Personalized Nutrition Questionnaire (PNQ) [31] and a Personalized Nutrition Toolbox (PNT) of resources used by the dietitian to support intervention strategies tailored to the characteristics of the population of interest. The PNQ draws upon the Behavior Change Wheel theory, which comprises the COM-B system [20]. In completing the PNQ, participants will be asked to self-identify and prioritize 18 factors (capability=7, opportunity=5, and motivation=6) that they perceive to affect their ability to achieve healthy eating. The PNT is a dietitian resource that consists of intervention strategies mapped out to each factor of the PNQ and the behavior change techniques required to deliver the intervention functions. The dietitian uses the individual's PNQ responses to guide the selection of interventions from the PNT and personalize associated strategies to address individual goals. Each dietitian was trained in the consultation protocol to ensure consistency in consultation delivery.

Outcome Measures

Outcome measures will be completed via the Aim4Me website at baseline and at 3, 6, and 12 months, along with a process evaluation (Multimedia Appendix 2). In addition to text message and email reminders, participants may also receive a follow-up phone call to prompt the completion of questionnaires at follow-up time points.

Primary Outcome Measures

Diet Quality

Diet quality will be measured using a validated brief diet quality index, the ARFS [27,29]. The ARFS uses a subset of 70 questions related to core nutrient-dense foods recommended in the Australian Dietary Guidelines [32]. The ARFS score is calculated by summing the points within 8 subscales, with 20 questions related to vegetable intake, 12 related to fruit, 13 related to protein foods (7 to meat and 6 to vegetarian sources of protein), 12 related to breads/cereals, 10 related to dairy foods, 1 related to water, and 2 related to spreads/sauces. The total score ranges from 0 to a maximum of 73 points [33].

Secondary Outcome Measures

Dietary Intake

Australian Eating Survey

Nutrient intake will also be assessed using the AES. The AES is a 120-item semiquantitative FFQ, which has been validated in adults, children, and adolescents [29,34]. The frequency of food consumption for the previous 3 or 6 months (as specified) is self-reported, using options ranging from *never* to *4 or more times per day* for foods and *7 or more glasses per day* for beverages. In total, 19 questions are related to vegetables and 11 are related to fruit, with separate questions about seasonality, total daily number of fruit and vegetable serves, bread and cereals, dairy products, eggs, fat spreads, beverages, snack foods, and discretionary items. An additional 12 questions are related to food behaviors, such as the frequency of consuming takeaway foods and eating while watching TV. Nutrient intakes are computed using the Australian food composition database to generate individual mean daily macro- and micronutrient intake using food portion sizes derived from the Australian Bureau of Statistics data [29].

Alcohol Intake

Alcohol consumption will be reported using the validated 3-item Alcohol Use Disorders Identification Test-Consumption to assess usual weekly alcohol consumption in grams [35].

Weight and Height/BMI

Weight and height will be self-reported as part of the web-based assessment questionnaire and BMI calculated (kg/m^2). Web-based self-reported height and weight have been shown to be relatively valid in relation to the measured height and weight [36].

Quality of Life

Quality of life will be assessed using the 6-dimensional Assessment of Quality of Life scale (AQoL-6D), which examines 20 items across 6 domains of independent living, relationships, mental health, coping, pain, and senses and provides utility scores that can be used in economic evaluations [37].

Self-Determination Factors

Self-determination constructs, including dietary self-regulation, habit automaticity, perceived competence, and social support related to healthy eating, will be measured. The Regulation of Eating Behaviors Scale will be used to assess motivational orientation toward regulating diet and reasons across 6 regulatory styles, with participants asked to what extent each item corresponds to a reason for regulation using a 7-point Likert scale [38]. The Self-Report Behavioral Automaticity Index measures a 4-item change in habitual behavioral patterns with regard to learned, automatic responses to situational cues [39]. The Perceived Competence Scale is a 4-item questionnaire assessing the degree to which participants feel confident about being able to make, maintain, or change participation in healthy eating [40]. Social support from family, friends, partners, or significant others will be measured using the 12-item Multidimensional Scale of Perceived Social Support questionnaire [41].

Covariates

Sociodemographic Characteristics

Participants will be asked questions about their age, sex, postcode, ethnicity, education level, employment and income status, relationship status, living arrangements, and food security at 3, 6, and 12 months.

Self-Reported Physical Activity, Sitting Time, and Sleep

Physical activity (PA) and sitting time during the previous 7 days will be self-reported using the 7-item Godin Leisure-Time Exercise (frequency and duration of time in light/moderate/vigorous PA) [42] and the Marshall Sitting Time Questionnaire, respectively [43]. The Epworth Sleepiness Scale will be used to measure self-reported sleep [44]. This 8-item scale measures the general level of daytime sleepiness or average sleep propensity in daily life [44].

Smoking

Two items will be used to measure smoking: (1) Do you currently smoke any tobacco products? and (2) Would you have smoked 100 or more cigarettes or equivalent tobacco in your life? [45]. Moreover, 7-day abstinence will be measured at follow-up: “Have you smoked at least part of a cigarette in the last 7 days?” [46].

Depression, Anxiety, and Stress

Participants will complete the 21-item Depression, Anxiety and Stress Scale, which is a set of 3 self-report scales designed to measure the emotional states of depression, anxiety, and stress [47]. Each of the 21 items in the scale asks participants to report how much each item applied to them over the previous week using 4 responses (*never*, *sometimes*, *often*, or *almost always*) [47]. For example, “I found it hard to wind down.”

Social Desirability and Approval

Social desirability and approval have emerged as sources of bias in self-reporting of dietary intake [48]. Social desirability will be measured using the 13-item Marlowe-Crowne Social Desirability Scale [49] in which participants are prompted to answer true or false to a number of statements concerning personal attitudes and traits [49]. The Martin-Larsen Approval Motivation Scale, a 20-item 5-point Likert scale, will be used to measure social approval [50].

Social Influences on Food Intake

The Social Eating Scale will be used to measure influences such as culture, family, or peers on food intake, requiring participants to select the appropriate response from 6 questions using a 5-point Likert scale [51].

Economic Measures

There is no basis for anticipating that health service utilization will vary between trial arms as a result of the interventions. As a consequence, health service engagement is assumed to be randomized, and the requirement to collect health service engagement or medication use is excluded. The additional costs relating to the intervention and implementation of the

intervention, including materials, labor, and other expenditures, will be collected through project management and project team records. The economic analysis will use either the change in ARFS or AQoL-6D as the outcome of interest. If the change in either is not statistically significant, all consequence measures, primary and secondary, will be reported alongside the cost estimates.

Engagement

Engagement will be measured using usage statistics captured by the website. The outcomes will include completion of the HEQ (control group only), the number of log-ins to the website, clicks on resources and links, views of personalized dietary feedback, and views and completion of goal setting and tracking (intervention groups 1 and 2). In addition, for intervention Group 2, engagement will be measured by attendance at the brief video consultation.

Reach and Recruitment Success

The number of people who engage with the various online recruitment strategies will be measured by using Bitly links [52], and the number of people who access and engage with the website will be measured by using Google Analytics. Bitly links allow the creation of customized URLs, which track back to the Aim4Me website and allow tracking of engagement with various strategies. Recruitment success will be measured by the time to recruit per strata, representativeness of the sample, number of people who expressed interest, percentage of eligible participants, and the number of those who consented. As part of the baseline assessment questionnaires, eligible participants will be asked how they found out about the study to capture which recruitment strategies were most successful.

Retention

Retention will be assessed as the proportion of participants who complete the AES at 3, 6, and 12 months.

Satisfaction

Self-reported satisfaction with study components will be evaluated at 3, 6, and 12 months using a process evaluation developed by the research team. Group 1 will be asked about their satisfaction with the HEQ if it was completed. For groups 2 and 3, questions will cover the personalized dietary feedback report, resources on the Aim4Me website, goal setting and tracking, and overall intervention satisfaction. Intervention Group 3 will also self-report satisfaction with the video consultation with the APD.

Scheduled Reminders and Prize Draw

All groups in the study will receive scheduled email and text message reminders to prompt the completion of assessment questionnaires at each time point (baseline and 3, 6, and 12 months). Emails will be sent 3, 6, and 9 days following the commencement of each phase, and text messages will be sent on day 9. Follow-up phone calls may also be scheduled at follow-up time points to prompt the completion of questionnaires. As an incentive to complete questionnaires and to promote retention, participants will automatically be entered into a gift voucher prize draw. Each draw will have a 1 in 100 chance of a prize, with the value of the gift voucher increasing in value over time (from Aus $100 [US $66.10] and up to Aus $400 [US $264.40] at 12 months).

Sample Size

The sample size calculation was based on detecting changes in the primary outcome of diet quality score (AFRS), with adequate power to assess differences in daily servings of fruit and vegetables. The study aims for a between-group increase in ARFS of 2.2 (baseline SD 9.6) and fruit and vegetables serves per day of 0.56 (baseline SD 2.4) compared with no change in the control group [53]. To detect this between-group AFRS difference with an alpha of .05 and 80% power, 300 participants per arm across 3 arms are required, totaling 900 participants. Given that we also wish to examine this effect a priori in male and female subgroups separately, we will require 900 participants of each gender or 1800 in total. To allow for 10% loss to follow-up at 3 months, 20% at 6 months, and 30% at 12 months, the study requires a total sample of 2570 (1285 males and females each).

Statistical Analysis

The outcome effects will first be evaluated using independent *t* tests, followed by repeated measures within-group changes in the ARFS diet quality score and modeling between-group changes over time using the generalized linear mixed model. The model will be fitted with ARFS at all follow-up points as the outcome variable, with fixed effects for group, time, baseline ARFS, and time by group interaction. Covariates, including PA, sleep, smoking, and social desirability, will be included in the statistical model as potential confounders. Statistical significance of the primary efficacy analysis will be based on Hochberg multiple testing procedures with a family-wise error rate for each time point held at 2.5%. The main analysis will use a generalized linear mixed model with the outcome at all time points and intention-to-treat principle. Sensitivity analyses will be conducted with the last observation carried forward, with multiple imputations, and for completers only. Analyses will be performed using SAS version 9.4 or later (SAS Institute Inc). All variables will be checked for plausibility and missing values. Data will be presented as mean (SD) for continuous and count variables.

Health Economic Analysis

The economic analysis will be conducted from a health service perspective. Cost estimation will follow a categorize:quantify:value approach. In the absence of health service implications, the costs will reflect the resources required to generate, implement, and deliver the respective interventions. The valuation will be founded on the concept of opportunity cost, that is, the value of the benefit forgone in not employing labor, services, or materials in alternative uses. Market prices will be used as a proxy for this value. Labor costs will reflect relevant skills, such as dietician time and administration time, and will incorporate additional employee benefits such as superannuation. Services include expenditure such as Facebook advertising. Materials capture nonlabor cost items such as flyers. Costs will be reported separately and jointly.

If a statistically significant difference in AQoL-6D is found, a within-trial cost analysis will be conducted using

quality-adjusted life years (QALYs) as the primary outcome. The incremental cost-effectiveness ratio (ICER) will report an incremental cost per QALY, reflecting the incremental outcome and cost differences between the comparator groups. The ICERs will be calculated as the arithmetic mean difference in cost between the intervention and control arm divided by the arithmetic mean difference in effect. Groups 2 and 3 will be compared individually with Group 1 and each other. If a significant change in AQoL-6D is not observed, the ARFS outcome measure will be used. If neither measure realizes a statistically significant change, the economic method will default to a cost-consequence analysis, with incremental costs reported against all primary and secondary outcomes. The economic analysis will be conducted, and the results will be reported in accordance with best practice guidelines [54,55].

Results

Data collection commenced in February 2018 and is ongoing. As of December 2019, 1277 participants have been randomized.

Discussion

Principal Findings

The aim of this study is to evaluate the efficacy of delivering varying levels of personalized dietary feedback and support on improving the diet quality of young adults. Young adulthood is a period of major transition whereby changes during this period influence diet and eating behaviors that contribute to the weight gain trajectory that is common in this age group. Changes include social influences, changes to the home and school/work environment, and changes in financial circumstances, which add additional stresses during this period. The perceived effort, cost, peer influence, lack of time, and feelings of inferiority are barriers to making positive changes in eating patterns and other health-related behaviors [17]. Further complexity is added when we start to consider the many other layers that shape a person's eating behaviors, including the food and beverage industry, access to health care, education, and social and cultural norms, and it needs to be acknowledged that active engagement from various segments of society is required. Approaches need to be incorporated into existing organizational structures to influence change at the population level.

Strengths and Limitations

This protocol has been designed to address some of the major challenges related to improving dietary patterns of young adults, including the ease of access to personalized nutrition advice, education on cooking skills, and practical nutrition strategies such as how to eat on a budget and goal setting and tracking to ensure dietary changes remain realistic and achievable. What is novel is the use of validated web-based dietary assessment tools to connect young adults with personalized real-time feedback on their dietary intake, an online library of resources about healthy eating, goal setting, and access to a health professional.

Conclusions

The results of this study will strengthen the current evidence related to improving nutrition by using technology-driven tools to address common barriers and motivators related to healthy eating and accessing personal dietary advice and support in young adults. The findings from testing efficacy and cost-effectiveness will inform approaches to reach and engage young adults. These will have major implications for future design and conduct of programs that target improved health and well-being in young adults.

Acknowledgments

The Aim4Me study is supported by a 3-year National Health and Medical Research Council (NHMRC)–targeted research grant (APP1115519). CC is supported by an NHMRC Senior Research Fellowship. BB is supported by an NHMRC Career Development Fellowship (1063206). BB and MH are both supported by a University of Newcastle, Faculty of Health and Medicine Gladys M Brawn Career Development Fellowship.

Authors' Contributions

CC, HT, JA, MH, TB, RC, LH, BB, DK, DL, SK, MR, and TM were involved in the study conception and design. RH and KP drafted the paper, with CC, HT, JA, MH, TB, RC, LH, BB, DK, SK, MR, and TM contributing to intellectual content. All authors have read and approved the final manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Web interface.
[PDF File (Adobe PDF File), 1237 KB - resprot_v9i5e15999_app1.pdf]

Multimedia Appendix 2
Summary of Web-based measures and timing of data collection.
[DOCX File , 16 KB - resprot_v9i5e15999_app2.docx]

Multimedia Appendix 3
CONSORT-eHEALTH checklist (V 1.6.1).
[PDF File (Adobe PDF File), 1510 KB - resprot_v9i5e15999_app3.pdf]

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Abbreviations

AES: Australian Eating Survey
Aim4Me: Advice, Ideas, and Motivation for My Eating
APD: accredited practicing dietitian
AQoL-6D: 6-dimensional Assessment of Quality of Life scale
ARFS: Australian Recommended Food Score
COM-B: capability, opportunity, and motivation
FFQ: Food Frequency Questionnaire
HEQ: Healthy Eating Quiz
ICER: incremental cost-effectiveness ratio
NHMRC: National Health and Medical Research Council
PA: physical activity
PNQ: Personalized Nutrition Questionnaire
PNT: Personalized Nutrition Toolbox
QALY: quality-adjusted life year
SDT: self-determination theory
SSB: sugar-sweetened beverage

Edited by G Eysenbach; submitted 26.08.19; peer-reviewed by YH Kwan, D Leightley, I Gabashvili; comments to author 18.10.19; revised version received 31.01.20; accepted 04.02.20; published 22.05.20.

Please cite as:
Haslam RL, Pezdirc K, Truby H, Attia J, Hutchesson M, Burrows T, Callister R, Hides L, Bonevski B, Kerr DA, Lubans D, Kirkpatrick S, Rollo M, McCaffrey T, Collins CE
Investigating the Efficacy and Cost-Effectiveness of Technology-Delivered Personalized Feedback on Dietary Patterns in Young Australian Adults in the Advice, Ideas, and Motivation for My Eating (Aim4Me) Study: Protocol for a Randomized Controlled Trial
JMIR Res Protoc 2020;9(5):e15999
URL: http://www.researchprotocols.org/2020/5/e15999/
doi:10.2196/15999
PMID:32441659

Protocol

Daily Self-Monitoring of Symptoms and Skills Learning in Patients With Borderline Personality Disorder Through a Mobile Phone App: Protocol for a Pragmatic Randomized Controlled Trial

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Abstract

Background: Patient self-monitoring via mobile phones during psychotherapy can enhance and provide an overview of psychotherapeutic progress by graphically displaying current and previous symptom scores, providing feedback to the patient, delivering psychoeducative material, and providing timely data to the therapist or treatment team.

Objective: This study will aim to assess the effects of using a mobile phone to self-monitor symptoms and acquire coping skills instead of using pen and paper during psychotherapy in patients with borderline personality disorder (BPD). Dialectical behavior therapy will be performed to treat BPD. The primary outcome is the mean time needed to learn coping skills directed at emotion regulation; the secondary outcome is changes in the BPD symptom score as measured by the Zanarini Rating Scale for Borderline Personality Disorder.

Methods: This study is a pragmatic, multicenter randomized controlled trial. Participants were recruited through five public general psychiatric outpatient treatment facilities in Denmark. Patients are randomly assigned, on a 1:1 basis, to either the mobile phone condition (using the Monsenso mDiary mobile app) or pen-and-paper condition. Patients will complete several self-report questionnaires on symptom severity; assessments by trained raters on BPD severity will be performed as well. Survival analysis with a shared frailty model will be used to assess the primary outcome.

Results: Recruitment began in June 2017 and was completed in February 2019 after 80 participants were recruited. The study ended in February 2020. It is expected that the benefits of mobile phone–based self-report compared to the pen-and-paper method will be demonstrated for skill learning speed and registration compliance. To our knowledge, this is the first trial exploring the impact of cloud-based mobile registration in BPD treatment.

Conclusions: This trial will report on the effectiveness of mobile phone–based self-monitoring during psychiatric treatment. It has the potential to contribute to evidence-based clinical practice since apps are already in use clinically.

Trial Registration: ClinicalTrials.gov NCT03191565; https://clinicaltrials.gov/ct2/show/NCT03191565

International Registered Report Identifier (IRRID): DERR1-10.2196/17737

(JMIR Res Protoc 2020;9(5):e17737) doi:10.2196/17737

KEYWORDS

borderline personality disorder; dialectical behavior therapy; mobile app; psychotherapy; patient-reported outcome measures; mhealth

Introduction

The prevalence of borderline personality disorder (BPD) in the general Scandinavian population is estimated to be 1% to 5% [1,2]. The consensus is that approximately 1.5% of the western population meets the criteria for BPD [2]. The prevalence in clinical populations is considerably higher and is estimated to be around 28%, ranging between 9.3%-46.3% of patients, according to current studies [3,4]. In Scandinavia, the mortality risk of patients with a mental disorder is 2-3 times higher than in the general population [5]. The suicide rate for BPD patients is estimated to be between 8%-10%, almost 50 times higher than in the general population [6].

BPD is characterized by instability in emotion and mood, interpersonal relationships, self-image and identity, and impulse and behavioral control [7]. A 3-factor structure has been found empirically and supported by confirmatory factor analysis; the factors were disturbed relatedness, behavioral dysregulation, and affective dysregulation [8]. In dialectical behavioral therapy (DBT), these problems are viewed as skill deficits that result from problems with regulating emotion [9].

DBT has demonstrated effectiveness and is regarded as one of the most well-researched, evidence-based treatments for BPD [10-12]. The treatment includes the “five functions” of DBT—skill acquisition, skill generalization, motivation to implement new and skillful behaviors, interventions in the social and family environment to allow for treatment progress, and a consultation team to facilitate skillful treatment delivery and reduced burnout among therapists. Thus, the central focus is on learning skills that target self-management through mindfulness skills, healthier relationships with family and peers through interpersonal skills, handling of severe emotional dysregulation through distress tolerance and crisis survival skills, and proactive, effective management of emotional reactions through emotion regulation skills [13]. All of these types of skills are typically trained in a group format, and motivation and implementation are the foci of individual therapy.

Self-Monitoring During Therapy

Self-monitoring of skill use and accompanying changes in suicidality, self-harm, and emotional reactivity during DBT therapy have traditionally been done using paper-based diaries. Technological advances in mobile apps have made new modes of self-monitoring possible and may reduce the burden on patients, increase data quality, and generate new opportunities for registration [14,15], like enhanced overview [16], ecological momentary assessment [17], and research investigating predictors of the course of therapy to facilitate future development [18,19]. However, monitoring of patients with BPD on mobile phone diary apps should be explored and evaluated before they are implemented in clinical practice in a broader sense [20].

Recent studies on pain management have demonstrated good usability in using digital self-monitoring [21,22]. Furthermore, studies using digital diaries in the treatment of bipolar disorder [19,23] in pain and weight management, sleep, and chemotherapy have all shown promising results [24-27]. Apps specifically targeting emotional awareness, posttraumatic stress reduction, and suicidality in borderline personality disorder are currently being investigated [28-30]. DBT skills have been shown to mediate improvements in BPD defining behaviors [31-35]. DBT-related apps supported by scientific inquiry have been developed at Rutgers University (Pocket Skills) [36] and the University of Washington (DBT Coach) [37]. These apps have been reported to show promise and acceptability among users. They are specialized in training and coaching skills, include diary card data as a secondary feature, and are self-contained within the app. The end users in the Pocket Skills usability study requested enhanced visualization of diary card scores as well as aggregated scores.

In this study, we used the mDiary app to fill this gap in research as well as to eliminate conventional paper diary cards through new technology. The mDiary app has a cloud-based self-monitoring system that is sharable with a therapist in real time. To our knowledge, this app is the first BPD-focused mobile app to provide sharable self-monitoring.

The Monsenso system used in our study is a modified version of the system used in the 2009 MONARCA trial, which tested a system aimed at self-monitoring bipolar disorder [38]. The MONARCA-project was developed at the IT University of Copenhagen as part of a PhD project, and a modified version of the MONARCA software is now sold by the Danish company Monsenso. The Svendborg DBT Unit modified the Monsenso mobile app to suit the needs of patients with BPD; modifications were made to the DBT treatment skills-training modules and psychoeducation content, and an enhanced therapist overview screen was added to the Monsenso system. Patients were involved in the design of the solution. A consistent focus on emotion regulation, the monitoring of progress in skills training, and compliance with standard DBT treatment [39] were prioritized in the mDiary app. The resulting solution was tested in a pilot feasibility study and showed adequate usability among patients and therapists [40].

Objectives

The objectives of the current study are to evaluate (a) if patients randomized to use the Monsenso mobile app learn DBT skills faster compared to patients randomized to the pen-and-paper version; (b) if patients using the app report higher reductions in BPD criteria; (c) if registration compliance improves with a mobile phone, and (d) if use of the mobile app is cost-effective compared to the pen-and-paper version. We expect that use of a mobile phone–based digital diary will reduce the time it takes for patients to acquire DBT skills, improve therapy outcomes, and be cost-effective.

Methods

Study Design

The study is a pragmatic 2-arm, multicenter, open-label, evaluator-blind, superiority randomized controlled trial (RCT), with the active arm being self-registration done through the Monsenso mDiary mobile app and the control arm being self-report done by pen-and-paper diary cards. Figure 1 presents the CONSORT (Consolidated Standards of Reporting Trials) flowchart and details on patient inclusion, and Table 1 provides an overview of the study.

Figure 1. CONSORT (Consolidated Standards of Reporting Trials) flowchart. DBT: dialectical behavioral therapy; DERS: Difficulties in Emotion Regulation Scale; BSL-23: Borderline Symptom List; ZAN-BPD: Zanarini Rating Scale for Borderline Personality Disorder.

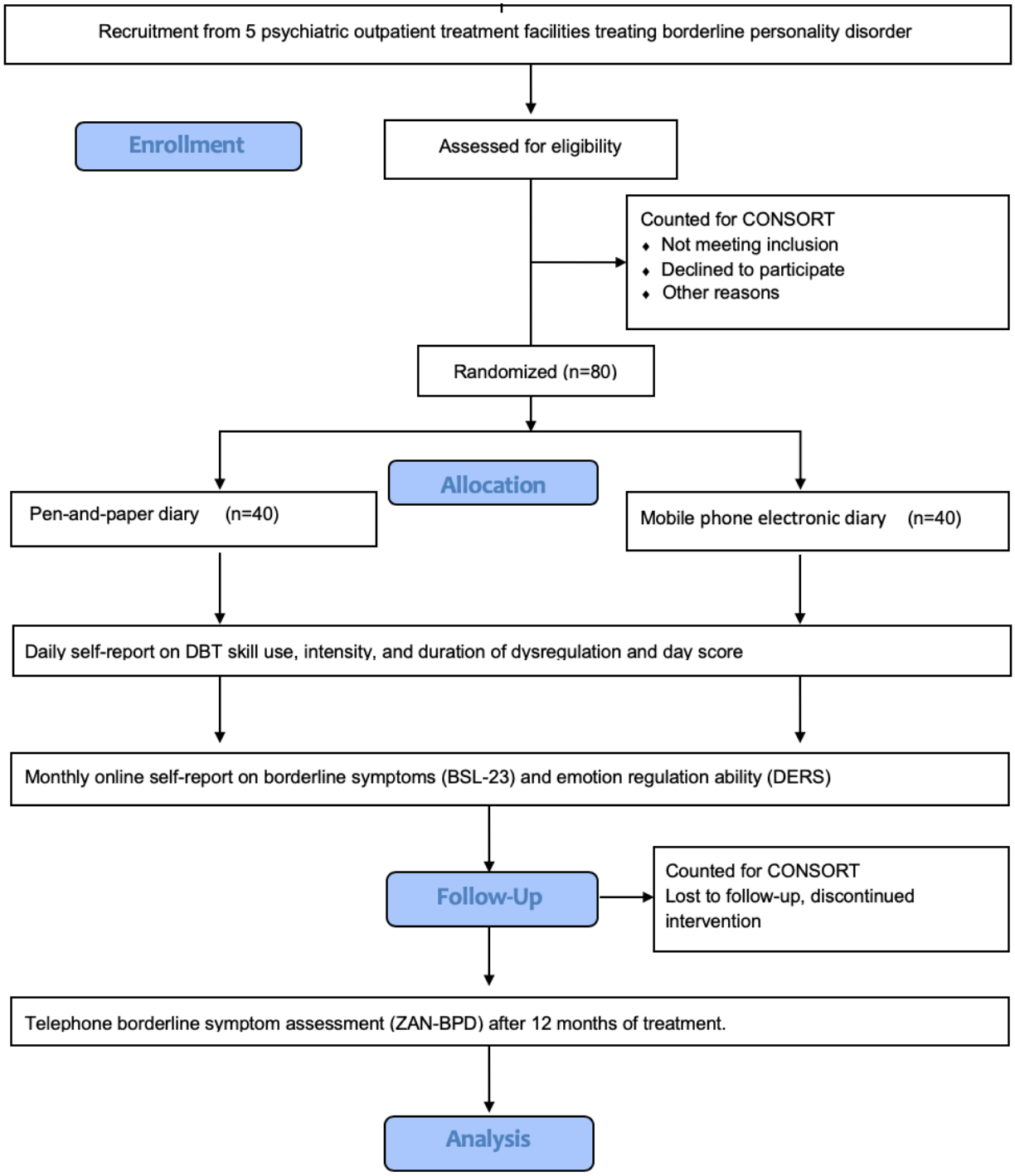


Table 1. Items from the trial registration data set.

Data category	Information
Primary registry and trial identifier	• ClinicalTrials.gov (NCT03191565)
Date of registration in primary registry	• June 19, 2017
Secondary identification numbers	• S-20160085 • 5159-00002B • 2008-58-0035
Source of monetary or material support and sponsor	• The Danish National Innovation Fund (grant number 5159-00002B)
Contact for public queries	• Centre for Telepsychiatry, Odense, Denmark
Contact for scientific queries	• Research Unit for Telepsychiatry and E-mental Health, Odense, Denmark
Public title	• Differences in electronic and paper-based self-monitoring in borderline personality disorder: which is most effective?
Scientific title	• Daily Self-Monitoring of Symptoms and Skills Learning in Patients With Borderline Personality Disorder Through a Mobile Phone App: Protocol for a Pragmatic Randomized Controlled Trial
Countries of recruitment	• Denmark
Health condition(s) or problem(s) studied	• Borderline personality disorder
Intervention(s)	• Active comparator: self-monitoring by mobile phone • Placebo comparator: *self-monitoring by pen and paper*
Key inclusion and exclusion criteria	• Inclusion criteria: adult patient (≥18 years), emotionally unstable personality disorder (ie, ICD-10-CM[a] diagnosis code: F60.3); referred to psychiatric treatment (ie, DBT[b] psychotherapy); suicide attempt within the last 3 years • Exclusion criteria: patients with schizophrenic spectrum disorders and bipolar disorder; substance abuse as primary problem (no desire to stop); intellectual problems (ie, IQ below 70)
Study type	• Interventional • Allocation: pragmatic, 2-arm, multicenter, open-label, evaluator-blind randomized controlled trial • Active arm: self-registration with the Monsenso mobile app; control arm: self-report by pen-and-paper diary cards • Primary purpose: intervention • Phase III
Date of first enrollment	• June 2017
Target sample size	• 80
Recruitment status	• Active, not recruiting
Primary outcome(s)	• Mean number of days required to learn a new DBT skill (time frame: 1 year)
Key secondary outcomes	• Borderline severity (ZAN-BPD[c]), ability to regulate emotion (DERS[d]), compliance filling out diary cards

[a]ICD-10-CM: International Classification of Diseases, 10th Revision, Clinical Modification.

[b]DBT: dialectical behavior therapy.

[c]ZAN-BPD: Zanarini Rating Scale for Borderline Personality Disorder.

[d]DERS: Difficulties in Emotion Regulation Scale.

Recruitment

Patients in the DBT treatment group for BDP and related problems will be recruited from five psychiatric outpatient units treating BDP (ie, Svendborg, Haderslev, Vejle, Silkeborg, and Glostrup) between August 2017 to December 2019. All sites have comprehensive DBT programs that have functioned as standard DBT programs for more than 7 years and include all

five modes of DBT (ie, weekly consultation team; skills training groups; individual therapy, along with telephone coaching available outside of therapy sessions; and help structuring clients' social and family environments if relevant [41]).

All patients will be informed orally and in writing about the research project. Consent for participation will be obtained not from the therapist of the patient but from an unbiased research assessor from the mDiary team. Patients were involved in designing the mDiary app.

Patients will be included in the study provided they fulfill all of the inclusion criteria and none of the exclusion criteria; they must also provide written informed consent, which will be collected by the therapists. Inclusion criteria are as follows: aged 18 years or older; a primary diagnosis of Emotionally Unstable Personality Disorder (F60.3 according to ICD-10-CM [International Classification of Diseases, 10th Revision, Clinical Modification] criteria) and diagnosed by a specialist in psychiatry (referred to as BPD here, the more common diagnostic label); referral for psychiatric treatment at the DBT treatment sites involved in the study; willingness to sign a commitment contract for DBT treatment; having had problems with self-harm or suicidal behavior within the last 3 years. Self-harm is defined as any form of self-inflicted tissue damage, excluding superficial scratching. Comorbid depression, anxiety, PTSD, antisocial traits or micro-psychotic episodes are not exclusion criteria as long as BPD is primary diagnosis. The above criteria will be screened through the Symptom Checklist-90-R (SCL-90-R) questionnaire subscores as well as targeted questions during the assessment interview. Patients with secondary substance use will be included if they agree to work on reducing their abuse.

The exclusion criteria are as follows: any diagnosis of schizophrenic spectrum disorders (any type of schizophrenic disorder or schizotypal personality disorder); any diagnosis involving bipolar disorder or a comorbid diagnosis of substance abuse disorder without a wish to change the associated behavior. The exclusion criteria will be checked in the electronic patient journal and through structured interviews during the intake procedure. Patients with intellectual problems comparable to an IQ below 70 will be excluded. Screening for intellectual disability will be done with the Danish Adult Reading Test (DART) [42]. Lack of a mobile phone or participation in other concomitant psychotherapy will also be reasons for exclusion.

Statistical Analysis

The primary endpoint is the skills learning rate—the amount of time (in days) taken to learn a new skill (ie, progress from "started learning the skill" to "have learned the skill"). Patients assess and switch status using a button on the mobile phone app when they consider the skill is of use to them; at this time, the skill is considered learned, which will then be discussed and confirmed with the therapist during the preceding session.

The secondary endpoints are (a) BDP symptoms, including the ability to regulate emotion, will be evaluated with the interview-based ZAN-BPD; (b) percentage of completed diary questions, measured as a day with an entry in the mDiary app or in the paper-based diary; (c) quality of life measured by the EuroQoL five-dimension, five-level (EQ-5D-5 L) instrument; and (d) depression measured with the Patient Health Questionnaire (PHQ-9).

Power

We are planning a study of 80 patients with equal allocation to each arm, an accrual interval of 360 days, and an additional follow-up of 360 days. The sample size of 80 patients is a realistic recruitment goal for the given timeframe. To our knowledge, no studies have previously investigated DBT skill acquisition time through the use of mobile phones. Based on pilot data and relevant noticeable clinical differences, it is estimated that the mean time to learn a DBT skill will be 1.5 month (44 days) for mobile phone registration versus 2 months (60 days) for the control condition. Using an alpha of .05 and a power of .90, we will need 437 events of learned skills in total to reject the null hypothesis. With an expected attrition rate during follow-up of 20%, each remaining patient (n=64 will on average need to generate 7 learned skills. A very cautious estimate would be that half of the patients (32 patients) will learn half of the skills (16 skills) during one year of therapy. This would generate 512 events, meaning that an inclusion of 80 patients will be able to generate sufficient power. A more realistic expectation is that 75% of the patients following protocol will learn 75% of the skills, which will generate 1188 events and will leave ample room to adjust for shared frailty. It is estimated that at least 15,000 episodes of a specific skill use will contribute to the survival analysis. The power analysis was performed using R statistical software and gsDesign. The power calculation is based on the log-rank test [43].

Randomization

All BPD patients in DBT treatment group are offered participation in the study. All patients are followed from the beginning of their therapy. Randomization and initial assessments are done by an independent research assistant. Initial assessment is completed by a blinded assessor since it is done before randomization. Stratification is done by site as well as by severity, aiming for equal distribution of severe and less severe cases within each site. Severity is assessed by the general severity score from the SCL-90-R questionnaire with a Global Symptom Index cut-off score of ≥1.75. Blocks of four are randomized with a ratio of 1:1. The allocation sequence is generated by a random number computer algorithm transferred to two stacks of sealed envelopes (severe and less severe) for each site that is opened by the participant immediately after the first assessment. The study needs to be open label since it is not possible to withhold the treatment condition (paper or mobile phone), but the analysis will be performed blinded.

Training of Therapists

The therapists at the five sites will be trained to use the app during two meetings, each one hour in length, and agree to refer patients to the research project. The sites have an estimated intake of 20 patients per site per year. In case of reduced enrollment, the recruitment period will be prolonged. Each site has 4-7 active therapists, typically 1 psychiatrist, 1-2 psychologists, and 1-2 nurses specializing in DBT. Referrals to the clinics are from either a primary care physician or from the

inpatient section of the hospital ward dealing with acute psychiatry. All therapists are trained in standard DBT.

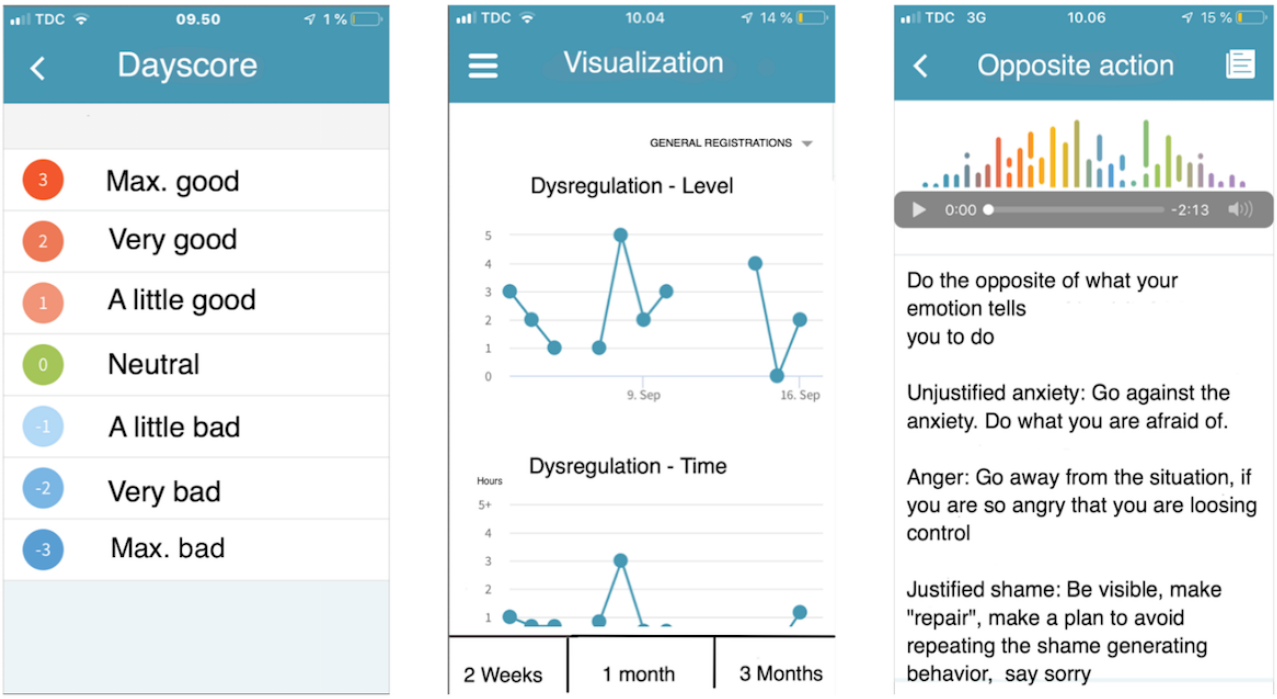
Intervention

All patients in the mDiary trial will receive standard DBT treatment. The difference between the two conditions in the trial is whether self-monitoring is done with the pen-and-paper method or the Monsenso system. There is a higher degree of interactivity and available information on the Monsenso system, as it is possible to access submenus on a mobile phone app to learn more about what patients report. Descriptions of the skills to be learned include more details, as well as a larger psychoeducative element. Skills explanations are supported by sound files.

Content of the Monsenso System

Figure 2 displays three mobile phone screenshots of the Monsenso system. The screen to the left is an example of registering one of the required variables (ie, day score). Under normal circumstances, this is one of 10 variables participants would register daily. This score is a general rating of the day in terms of good or bad. The middle screenshot is a visualization of variables entered that can be seen after registering all variables of the day. It is possible to scroll down to see more registered variables. The right-hand screenshot explains one of the DBT skills (ie, opposite action). This is delivered in both text and podcast format.

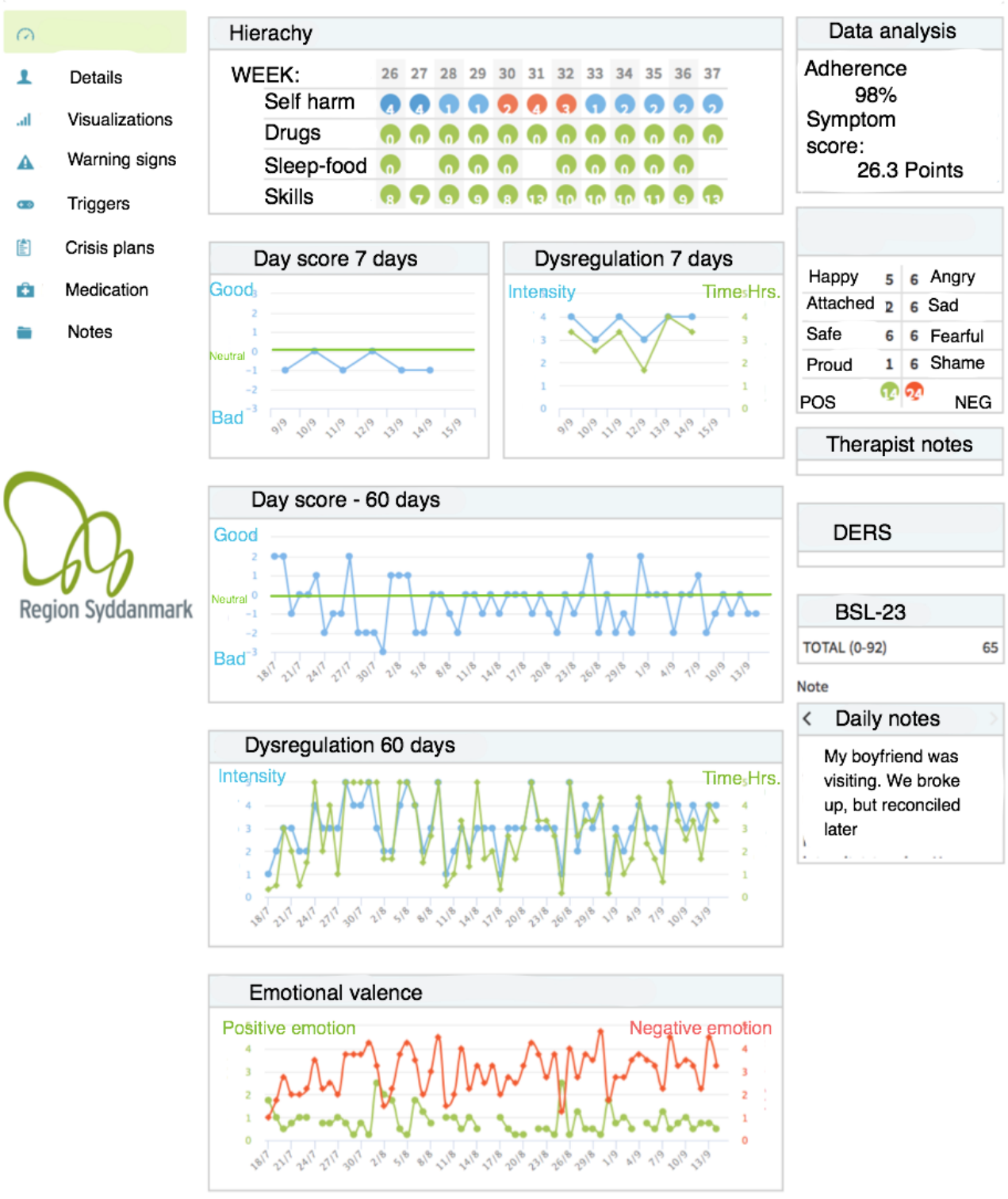
Figure 2. Screenshots of the Monsenso system.



An overview screen for the therapy session is provided in Figure 3. Summed scores for the treatment and the DBT hierarchy by week number are displayed. Red dots signal self-harm or suicidal behavior. Aggregated scores for drug use, vulnerability factors, and skill use are shown as well. The next row presents visualizations of dysregulation and day scores by day. Taken together, this provides a quick overview of the week. The next two rows display the day score and dysregulation for the past 60 days, providing a longer overview of development. A separate, dedicated screen can be accessed for even longer time spans (ie, two years or more). The bottom row shows aggregated scores for positive and negative emotions in the past 60 days. The top right side of the screenshot provides the compliance percentage (adherence) for completed diary cards in the past 60 days, as well as a total aggregated score of severity (symptom score). Below that, the aggregated scores of positive and negative emotions are broken down based on the number of days different emotions were registered. Below that, there is room for therapist notes and the Borderline Symptom List (BSL-23) and the Difficulties of Emotion Regulation (DERS) summed scores. In the bottom right, patient notes from their diary dating to the last 7 days is accessible. If a score from the previous week is particularly interesting, there will be a quick way to gain more information through a link to the comments for that specific day. All patient diary notes are accessible via a separate, dedicated screen.

The left-hand row is a menu for accessing other overview screens like the long-term overview of variables, program notifications like triggers and warning signs, a dedicated screen for diary notes, medication, and construction of action plans.

Figure 3. Overview screen for the therapy session.



Data Collection and Management

Daily registrations for the diary are collected through the Monsenso system or on a piece of paper that closely resembles the standard DBT paper diary sheet. Collected variables are listed in Table 2. The column “Always” shows which variables are always collected through the mobile phone on a daily basis. The column “When relevant” shows variables that can be switched off when they are no longer relevant. Patients for whom emotions are too painful to register at the start of the treatment can switch off the variable in the beginning. “Self-harm” can be switched off when treated to a completely extinct level; patients are instructed to switch this registration on, if they are to relapse.

Questionnaires for overall assessment of all participants are collected through the REDCap (Research Electronic Data Capture) system. All data collected are monitored through the Odense Patient Data Exploratory Network (OPEN) using a logged secure database run by the Region of Southern Denmark.

Paper diaries will be entered by double data entry into the OPEN database, securing data quality and data safety. The OPEN team ensures that the data are stored according to the European Union's General Data Protection Regulation (GDPR) standards and CONSORT guidelines. The research data will only be accessible to the research team. An anonymized version will be stored at the Danish National Archives (Rigsarkivet) in order to revisit, extend, and validate conclusions from the RCT.

Table 2. Outcomes collected daily from the mobile phone–based or paper diary.

Covariate	Always	When relevant
Skill use (3 factors: unknown, started learning it, have learnt it)	✔	
Dysregulation, intensity	✔	
Dysregulation (duration in hours/day)	✔	
Numbness	✔	
Day score (–3 to +3)	✔	
Qualitative short description of the day	✔	
Suicide thoughts and actions (0-5)		✔
Self-harm thoughts and actions		✔
Basic emotions (anger, joy, shame, pride, love, sad, anxious, safe; 0 to +3)		✔
Eating (too little, balanced, or too much; –3 to +3)		✔
Drugs		✔

Deviations from participating in the intervention will not be addressed in order to mirror normal participation in outpatient treatment as closely as possible. Patients who decline to participate in the study will be assessed by their therapist, who will fill out a form stating reasons for not wanting to participate.

A dedicated data safety monitoring board to protect participants from aversive consequences of the intervention will not be necessary since the study is open label. Patients are followed on a day-to-day basis by psychotherapists and patient safety will be monitored weekly by therapists, which makes an unblinded double check redundant. Adherence to filling out forms on paper and through the mobile phone app (days with entries) will be part of the secondary outcome measurements and will not be sought or influenced during data collection.

Outcomes Collected

Patients are asked to complete a set of questionnaires during the study period (Table 3). These are delivered by mobile phone, thereby posing a smaller burden than standard questionnaires. Questionnaires are sent out automatically to the patients' mobile phone and does not require the patient to meet with an assessor at a specified time and place. It can be filled out when convenient during the day.

Table 3. Questionnaires used in the study.

Questionnaire	Questions, n	Frequency	Endpoint	Reference
Danish Adult Reading Test (DART)	40	Only pre	DART measures the number of correctly pronounced words when the patient reads out loud	Hjorthøj et al [42]
Zanarini Rating Scale for Borderline Personality Disorder (ZAN-BPD)	9	Pre, post	ZAN-BPD measures clinician rated BPD[a] severity	Zanarini et al [44]
Suicide Behaviors Questionnaire-Revised (SBQ-R)	4	Pre, post	SBQ-R measures suicide behavior	Osman et al [45]
Posttraumatic Stress Disorder-8 items (PTSD-8)	8	Pre, post	PTSD-8 consists of 8 questions from the Harvard Trauma Questionnaire for screening PTSD[b] severity	Hansen et al [46]
Symptom Checklist-90-R (SCL-90-R)	90	Pre, post	SCL-90-R measures self-perceived psychiatric symptom load	Brophy et al [47]
EuroQoL five-dimensions, five-levels (EQ-5D-5L)	5	Pre, post	EQ-5D-5L measures quality of life for health economic evaluation	Janssen et al [48]
Patient Health Questionnaire (PHQ-9)	9	Pre, post	PHQ-9 measures suicidality and depressive symptoms for health economic evaluation	Kroenke et al [49]
Treatment Inventory Cost in Psychiatric patients (TIC-P)	11	Pre-post	TIC-P measures treatment costs and loss of productivity for health economic evaluation	Bouwmans et al [50]
Self-Harm Inventory (SHI)	12	Pre, post	SHI measures lifetime self-harm type and count	Sansone et al [51]
Borderline Symptom List (BSL-23)	23	Monthly	BSL-23 measures BPD core symptoms	Wolf et al [52]
Difficulties in Emotion Regulation Scale (DERS)	36	Monthly	DERS measures ability to regulate emotion	Weiss et al [53]
Positive and Negative Affect Schedule short form (PANAS SF)	10	Weekly	PANAS SF comprises 10 items and measures positive and negative affect	Watson et al [54]

[a]BPD: borderline personality disorder.

Statistical Analysis

All analyses will be conducted according to the intention-to-treat principle. Comparison between the active and control conditions on the primary endpoint will be performed by means of survival curves, as time-to-event models analyzed by Cox proportional hazards regression models with multiple events per patient. Significance tests are based on a frailty mixed effects approach [55]. Since missing data is not expected to be missing randomly, data will be modelled with multiple imputations, if missing data is to be included.

The level of dependence or heterogeneity among patterns of skill acquisition speed within the same site will also be explored by the intracluster correlation coefficient (ICC) [56]. Apart from intervention type (mobile phone or paper), treatment site, intellectual ability (DART score), level of BPD (ZAN-BPD), and level of PTSD (PTSD-8) are used as interaction terms in the Cox proportional hazards regression models.

A secondary analysis of differences in compliance in filling out daily registrations between mobile phone and paper groups will use Wilcoxon rank sum to test the hypothesis of improved compliance in the active arm of the intervention. The problem of backfilling paper diary entries [57] cannot be easily controlled in the pen-and-paper version, but in the mobile phone condition, it will only be possible to back fill 2 days' worth of entries, so clusters of 3-day fill-outs will signal backfilling. This bias in the study will be addressed in the interpretation of the results.

On an explorative level, time series data from daily data collection will be used to predict a binary classification of treatment in responders and nonresponders. In this analysis, the classification of responders and nonresponders will be based on the definitions provided by Jacobson et al [58] and and Schmitgen et al [59].

Adverse Effects

Due to the nature of BPD, self-harm and suicidal behavior might appear during psychotherapy, but the DBT treatment is aimed at dealing with this type of behavior. It is safe to assume that monitoring symptoms and skills acquisition on a mobile phone instead of paper forms will not subject patients to additional risk. During the DBT treatment, patients are coached in dealing with suicidal and self-harm behaviors. Furthermore, a therapist or an acute team is available by telephone 24/7 for patients. Even if suicidal ideation should emerge, there is a very quick path to rapid crisis intervention. If unforeseen adverse effects should emerge due to the study, these problems will be quickly presented to the mDiary RCT advisory board for evaluation, and matters will be responded to immediately.

Patient Involvement Statement

Patients were involved in the pilot and development phases, by engagement in the codevelopment of the mobile app. The research question reflects a reoccurring wish for mobile phone registration from patients in DBT treatment, making

self-monitoring less like homework from school and more technologically up to date.

Data Availability

The data sets generated and analyzed during the current study are not publicly available due to the highly sensitive nature of the content. Psychiatric diagnosis, suicidality, self-harm, and alcohol and drug use are disclosed in the diary registrations. It is not possible to do this kind of research without promising the research subjects the highest level of confidentiality, that is, complete data anonymization. Relatively few study subjects were treated at each site, thus making it possible to infer site location by looking at the number of subjects treated at the sites. Very few men participated in the study, so the identity of single individuals may be inferred by looking at the sex and location data. However, the data can be made available in a nonidentifiable form from the corresponding author on reasonable request.

Ethics and Dissemination

The study was approved by the regional Committees on Health Research Ethics for Southern Denmark (Journal number: S-20160085) and the Danish data registry (Journal number: 2008-58-0035). The trial was registered on ClinicalTrials.gov (NCT03191565) on June 19, 2017 and is conducted in agreement with the Declaration of Helsinki. Informed consent material is available in Danish with the approved protocol. If a patient sustains any trial-related harm, they are covered by Danish law. The Committees on Health Research Ethics select and audit a number of studies on an annual basis. Independent investigators and sponsors conduct the audit process. The primary investigator has unrestricted access to the full data set. There are no contractual limitations regarding access of the full data set for relevant investigators. There are no restrictions regarding the dissemination of results. Primary authorship will be held by the primary investigator when reporting the results of the study.

Funding

This study is part of a larger project (the ENTER [Programme for E-meNTal hEalth Research] project) at the Centre for Telepsychiatry in the Region of Southern Denmark. In January 2016, €2.7 million for the ENTER program was obtained from the Danish Innovation Fund Denmark [60] (grant number 5159-00002B). The funding body does not have any ownership or authority over the data collected.

Results

All results will be written up for publication and submitted to international peer-reviewed journals. Positive as well as negative or inconclusive findings will be published. Results will be reported according to the updated guidelines for reporting parallel group randomized trials—the CONSORT 2010 Statement—and the guidelines for the inclusion of patient-reported outcomes in clinical trial protocols—the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) extension. Significant protocol amendments will be reported back to the ethics committee, the Danish data registry, and ClinicalTrials.gov, and will be reported in the primary results paper. Authorship will be granted to all participating authors, according to the current principles stated by the International Committee of Medical Journal Editors.

Discussion

The present effectiveness trial focuses on individuals with BPD, who have a high level of service utilization, much subjective suffering, a high suicide rate, and high-cost treatments [61].

The results of the RCT will be a first attempt at giving an internet-based, mobile phone solution an evidence base to operate from. This study adds to the literature by providing and assessing best practice in terms of self-monitoring during BPD psychotherapy. The exploration of trajectories of improvement or deterioration may point to new uses of diary registration during psychiatric treatment. A promising aspect of the approach is the collection of diary data through the patients' own mobile phones. Data is entered directly into a database without further action from the clinician. Thus, data is stored very conveniently on a server making both short- and long-term review accessible, as well as facilitating bench marking and detailed record keeping. As databases will naturally grow with the passing of time and data collection, this data collection method will be increasingly amenable to machine learning. In future psychotherapy treatments, this mode of self-monitoring could inform us of predictors and relevant classification from start to follow-up.

Acknowledgments

We would like to thank all patients and clinicians for their participation in the study. We would also like to thank Mickey Kongerslev, PhD, and Rune Andersen, PhD, from the Psychiatric Research Unit of Region Zealand for an early-stage reviewing of the protocol and pointing out important therapist rating scales.

Authors' Contributions

SHJ and SSP conceived the trial and authored the first draft of the trial protocol. AEF and MBL have revised and optimized this protocol. CMD has approved and improved the statistical analysis plan. All authors contributed to and approved the final manuscript.

Conflicts of Interest

None declared.

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Abbreviations

BPD: borderline personality disorder
BSL-23: Borderline Symptom List
CONSORT: Consolidated Standards of Reporting Trials
DART: Danish Adult Reading Test
DBT: dialectical behavior therapy
DERS: Difficulties in Emotion Regulation Scale
ENTER: Programme for E-meNTal hEalth Research
EQ-5D-5L: EuroQoL five-dimension, five-level

GDPR: General Data Protection Regulation
ICC: intracluster correlation coefficient
ICD-10-CM: International Classification of Diseases, 10th Revision, Clinical Modification
OPEN: Odense Patient Data Exploratory Network
PANAS SF: Positive and Negative Affect Schedule short form
PHQ-9: Patient Health Questionnaire
PTSD-8: Posttraumatic Stress Disorder-8 items
SBQ-R: Suicide Behaviors Questionnaire-Revised
SCL-90-R: Symptom Checklist-90-R
SHI: Self-Harm Inventory
SPIRIT: Standard Protocol Items: Recommendations for Interventional Trials
TIC-P: Treatment Inventory Cost in Psychiatric patients
ZAN-BPD: Zanarini Rating Scale for Borderline Personality Disorder

Edited by G Eysenbach; submitted 10.01.20; peer-reviewed by P Santangelo, D Streiner; comments to author 12.02.20; revised version received 27.02.20; accepted 11.03.20; published 25.05.20.

Please cite as:
Helweg-Jørgensen S, Beck Lichtenstein M, Fruzzetti AE, Møller Dahl C, Pedersen SS
Daily Self-Monitoring of Symptoms and Skills Learning in Patients With Borderline Personality Disorder Through a Mobile Phone App: Protocol for a Pragmatic Randomized Controlled Trial
JMIR Res Protoc 2020;9(5):e17737
URL: http://www.researchprotocols.org/2020/5/e17737/
doi:10.2196/17737
PMID:32449690

Protocol

Reducing Antibiotic Prescriptions for Urinary Tract Infection in Nursing Homes Using a Complex Tailored Intervention Targeting Nursing Home Staff: Protocol for a Cluster Randomized Controlled Trial

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Abstract

Background: Urinary tract infection (UTI) is the most common reason for antibiotic prescription in nursing homes. Overprescription causes antibiotic-related harms in those who are treated and others residing within the nursing home. The diagnostic process in nursing homes is complicated with both challenging issues related to the elderly population and the nursing home setting. A physician rarely visits a nursing home for suspected UTI. Consequently, the knowledge of UTI and communication skills of staff influence the diagnosis.

Objective: The objective of this study is to describe a cluster randomized controlled trial with a tailored complex intervention for improving the knowledge of UTI and communication skills of nursing home staff in order to decrease the number of antibiotic prescriptions for UTI in nursing home residents, without changing hospitalization and mortality.

Methods: The study describes an open-label cluster randomized controlled trial with two parallel groups and a 1:1 allocation ratio. Twenty-two eligible nursing homes are sampled from the Capital Region of Denmark, corresponding to 1274 nursing home residents. The intervention group receives a dialogue tool, and all nursing home staff attend a workshop on UTI. The main outcomes of the study are the antibiotic prescription rate for UTI, all-cause hospitalization, all-cause mortality, and suspected UTI during the trial period.

Results: The trial ended in April 2019. Data have been collected and are being analyzed. We expect the results of the trial to be published in a peer-reviewed journal in the fall of 2020.

Conclusions: The greatest strengths of this study are the randomized design, tailored development of the intervention, and access to medical records. The potential limitations are the hierarchy in the prescription process, Hawthorne effect, and biased access to data on signs and symptoms through a UTI diary. The results of this trial could offer a strategy to overcome some of the challenges of increased antibiotic resistance and could have implications in terms of how to handle cases of suspected UTI.

Trial Registration: ClinicalTrials.gov NCT03715062; https://clinicaltrials.gov/ct2/show/NCT03715062

International Registered Report Identifier (IRRID): DERR1-10.2196/17710

(JMIR Res Protoc 2020;9(5):e17710) doi:10.2196/17710

KEYWORDS

urinary tract infection; nursing home; antibiotics; antibiotic resistance; drug prescription; communication; communication barriers; interprofessional relationship; elderly

Introduction

Urinary tract infection (UTI) is the most common reason for antibiotic prescription in elderly individuals living in nursing homes in Europe, and many of these prescriptions are considered inappropriate [1-3]. Overall, excessive use of antibiotics causes antibiotic-related harms, such as selection of resistant bacteria, in those who are treated and others residing within the same nursing home [4,5]. The excessive use of antibiotics for suspected UTI could be connected with the interplay between properties specific to the elderly population and the nursing home setting.

Two dominant factors associated with elderly individuals living in nursing homes contribute to overtreatment. First, it is widely accepted by nursing home staff that unspecific changes in behavior indicate UTI [6]. However, guidelines recommend that unspecific symptoms in elderly individuals should not be treated, and the link to UTI remains debated [7-9]. Second, health professionals frequently use urinary tests as screening tools for UTI [10]. As asymptomatic bacteriuria is common in nursing home residents, these tests are frequently positive [11]. Asymptomatic bacteriuria should not be treated with antibiotics, and it is commonly confused with UTI [11,12]. Therefore, urinary testing becomes a driver for overtreatment [13,14].

In the Capital Region of Denmark, most nursing homes are public, but private homes also follow municipality regulations, making labor coverage similar. A home with 60 residents employs 2 to 3 nurses and 20 to 25 health care helpers and health care assistants (in Danish, “SOSU-hjælper” and “SOSU-assistent,” respectively). Health care helpers and assistants attend to the residents’ everyday needs. Only if a resident appears unwell, a nurse gets involved. When UTI is suspected, the staff usually contacts the residents’ general practitioner (GP), the affiliated nursing home physician, or the out-of-hour service. In addition, physicians often prescribe antibiotics for UTI without directly evaluating the patients themselves, and therefore, rely on the clinical history provided by the nursing home staff [15,16].

Owing to the interaction between the properties of the elderly population and the nursing home setting, diagnosis and treatment are directly influenced by the knowledge and communication skills of the staff [17]. If nursing home staff do not have sufficient knowledge about UTI in elderly individuals or fail to communicate important clinical observations, unnecessary antibiotic prescription could be exacerbated [18]. Although the responsibilities of the staff vary, health care helpers, assistants, and nurses are engaged in the diagnostic process and treatment of elderly residents, and therefore, all staff members should be targeted in an intervention. Some antibiotic stewardship programs have improved the knowledge of UTI and have implemented decision algorithms and communication tools to reduce inappropriate antibiotic prescription for UTI, but none of the programs have randomized and tailored the intervention to the setting, in addition to targeting all groups of nursing home staff [19,20].

We hypothesize that a tailored complex intervention improving the knowledge of UTI and communication skills in nursing home staff will decrease the number of antibiotic prescriptions for UTI in residents, without changing hospitalization and mortality. The aim of this study is to describe a protocol for measuring the effect of this intervention.

Methods

Trial Details

The protocol describes an open-label cluster randomized controlled trial with two parallel groups and a 1:1 allocation ratio. Originally, we planned recruitment and allocation of nursing homes to be completed by the end of 2017. We aimed to complete the planning of the start-up phase (ie, the tailoring process of the intervention and scheduling of the workshops) by the summer of 2018 and finish the start-up phase by the fall of 2018. The trial was planned to last for 4 months. Data collection, analysis, and dissemination were to commence in the spring of 2019 and end in the spring of 2020.

Recruitment

There is no central registry of nursing homes in Denmark; therefore, we use a convenience sample method. We seek volunteers through the network of hygiene nurses in the Capital Region of Denmark, who organize local meetings and conferences and have direct contact with key hygiene personnel at nursing homes.

Eligibility Criteria

Nursing homes enrolling in the trial should not participate in other UTI projects during the trial period. Nursing homes should be situated in the Capital Region of Denmark. They should have common areas with attending staff 24 hours a day. The living spaces for residents with dementia are included, but living spaces for other special needs are not included. Nursing home eligibility screening is to be completed during the recruitment period. Residents should be over 65 years of age and should permanently occupy a living space at an eligible home. According to Danish law, this study is a communication study. Therefore, residents meeting the eligibility criteria are included in the study, unless they or their legal guardians decline access to health information for the trial. Residents’ eligibility screening is to be performed during collection of informed consent permitting sharing of health care data.

Intervention

The primary components are a dialogue tool and a workshop. They target all staff members who have nursing responsibilities in the intervention group. The supporting components relate to communication with stakeholders (Table 1).

Table 1. Primary and supporting components of the intervention.

Components	Intervention	Control
Primary components		
Dialogue tool	+	−
Workshop	+	−
Supporting components		
Letter to nursing home physicians	+	−
Letter to all staff members	+	−
Poster for staff members	+	−
Letter to the liaison officer in the municipality	+	+
Letter to local coordinators	+	+
Letter to residents and relatives	+	+
Poster for residents and relatives	+	+

Each component of the intervention is described below, and the components received by the intervention group and those received by both the intervention and control groups are presented. Examples of the components are provided in Multimedia Appendices 1-9.

Interventions Received by the Intervention Group

Dialogue Tool

The dialogue tool consists of a reflection and a communication section. The reflection section has three parts. First, a form that enables systematic gathering of signs and symptoms exhibited by the resident. Second, a flowchart to determine if UTI is likely or unlikely. These two parts are based on the revised Loeb Minimal Criteria for ordering urinary culture [21]. Third, four questions that are designed for the staff to be able to reflect on the next actionable step. The communication section uses the communication concept called ISBAR (Identification, Situation, Background, Assessment, and Recommendation) that has previously been used in combination with a decision-making aid for UTI prescription [22]. ISBAR is used to communicate clinical information accurately among health care professionals (between staff and the prescribing physician in this case) [23].

The tool is tailored through an iterative process that involves focus groups with stakeholders. Whenever UTI is suspected, a paper copy of the tool will be available for use at the staff office. If any adverse events occur because of the tool, the local coordinators will contact the principal investigator (PI). At least two members of the study group will evaluate the main cause of the adverse event. If the tool is deemed responsible, the entire group is gathered to determine if the trial should be terminated.

Workshop

The tool is introduced to the staff in a 75-minute workshop. At each nursing home, we aim to include as many staff members as possible within three separate workshops. The PI will facilitate all workshops. The focus of the workshop is threefold. First, the staff members learn the distinction between UTI and asymptomatic bacteriuria. Consequently, diagnostic caveats regarding urinary testing, odor, and urine clarity will be discussed. Second, an approach to evaluate unspecific symptoms is discussed. This approach specifically considers the importance of excluding other reasons for the observed signs and symptoms. Finally, the staff members receive training on how to use the tool for test cases.

Letter to Nursing Home Physicians

All nursing home physicians in the intervention group receive letters that include an open invitation to participate in the workshop, information about the trial, and contact details of the study group. The letters are emailed to the nursing home physicians.

Letter to Staff Members

All staff members receive letters that describe the trial and their role from the management of the home and the PI.

Poster for Staff Members

Posters are provided in each home to remind the staff when and how to use the tool. The posters also direct the staff to local coordinators for questions. Posters are visible at staff offices.

Interventions Received by Both Groups

Letter to the General Practitioner Liaison Officer in the Municipality

In 2016, the state, the regions, the municipalities, and the General Practitioners' Organization in Denmark agreed to employ affiliated nursing home physicians in nursing homes [24]. By 2019, the ambition was that a physician should make regular rounds at each home. However, owing to the shortage of physicians, not all homes are covered yet. Moreover, although nursing homes have affiliated physicians, some residents continue with their usual GP. Therefore, we inform nursing home physicians and GPs in the participating municipalities about the trial. In all municipalities with participating homes, we ask the GP liaison officer ("praksiskonsulent" in Danish) or another physician in the GP network to distribute a short letter informing all GPs about the trial.

Letter to Local Coordinators

Each home appoints a local coordinator. There are no prespecified eligibility criteria. This pragmatic approach is

adopted owing to the heterogeneity of the internal organization of the home. Local coordinators in each arm receive letters describing the trial and the UTI diary.

Letter to Residents and Relatives

Residents and relatives are informed about the trial through letters posted in the nursing home newspaper or website containing a description of the trial and contact information of research group members.

Poster for Residents and Relatives

Posters containing information about the trial are prepared for residents and relatives. They are visible in common areas.

To prevent dropout, unedited trial data are returned to the homes when data collection is complete. Optionally, the PI can facilitate workshops in the control group after evaluation.

Data Collection

In this trial, data are collected from three different sources as presented below.

Background Information About Nursing Homes

Background information about nursing homes is collected from the management during the enrollment period and includes the following:

1. number of living spaces for residents
2. number of livings spaces designated for normal care needs, dementia, and psychiatry
3. owner status of the home (public/private)
4. availability of dipstick (yes/no)
5. affiliated physician (yes/no)

Data From Nursing Home Medical Records of Residents

Collection of background information on residents commences during the trial and is collected from the nursing home medical records. The following information is obtained:

1. social security number
2. use of catheter (yes/no), and if yes, type of catheter (indwelling catheter, intermittent clean catheter, intermittent sterile catheter, or suprapubic catheter)
3. use of incontinence aids (eg, diapers and condom catheter) (yes/no)
4. mobility status (bedridden, wheelchair bound, or walking)
5. capability of providing informed consent to share health care data (yes/no)
6. treatment for diabetes (yes/no), and if yes, the type of treatment (generic drug name)
7. number of acute and prophylactic treatments for UTI (lower, upper, and urosepsis) 1 year prior to the trial
8. prophylactic treatment for UTI (yes/no), and if yes, the type of treatment (generic drug name)

Data on prescriptions for UTI, all-cause hospitalization, and all-cause mortality during the trial period are also retrospectively registered. With regard to antibiotic prescriptions for UTI, the following information is obtained:

1. generic drug name
2. start date (yyyymmdd)
3. duration of treatment (number of days)
4. strength, dosage, and frequency (mg per tablet, number of tablets per dosage, and number of doses per day)
5. prescriber background (primary physician, out-of-hour service, or hospital physician)
6. indication (curative/prophylactic UTI)

With regard to all-cause hospitalization, the following information is obtained: date of hospitalization (yyyymmdd); date of discharge (yyyymmdd); and suspected cause of hospitalization according to staff. With regard to all-cause mortality, the following information is obtained: date of death (yyyymmdd).

Urinary Tract Infection Diary

During the trial, local coordinators complete a diary for each resident with suspected UTI during an 8-day period. The diary is introduced to local coordinators at the nursing home during a 30-minute meeting with the PI. The diary includes the following:

1. Signs and symptoms on days 1-8
   - new urinary symptoms [dysuria, incontinence, urge, frequency, lower back pain, gross hematuria, shaking chills, suprapubic pain, and none of these]
   - other new severe symptoms [severe back pain, rigors, delirium, and none of these]
   - new onset signs of other infectious diseases [respiratory, gastrointestinal, skin, and none of these]
   - other new observations [malodorous urine, unclear urine, unspecific symptoms, and none of these]
   - temperature [degrees Celsius]
   - blood pressure [systolic/diastolic]
   - pulse [beats per minute]
   - urinary dipstick result [positive or negative for nitrite, leucocytes, and blood]
2. Events on days 1-8
   - increased observation/triage [yes/no]
   - preventive measures [yes/no]
   - dipstick test [yes/no]
   - physician contacted [yes/no]
   - urinary sample [yes/no]
   - change of catheter [yes/no]
   - antibiotic [yes/no]
   - change of antibiotic [yes/no]
   - antibiotic discontinued [yes/no]
   - result of urine culture [positive/negative/unknown/not done]
3. Prescriptions for UTI on days 1-8
   - generic drug name
   - start date [yyyymmdd]
   - duration of treatment [number of days]
   - strength, dosage, and frequency [mg per tablet, number of tablets per dosage, and number of doses per day]
4. Hospitalization on days 1-8 (day of hospitalization)
5. Death on days 1-8 (day of death)

The UTI diaries are collected once during the trial period and once after the trial has ended. Examples of UTI diaries are presented in Multimedia Appendices 10 and 11.

Outcomes

The primary outcome is the number of antibiotic prescriptions for acute UTI per resident in 4 months following contact between the staff and a prescriber. Antibiotics prescribed during hospital visits are not included, because prescriptions by hospital physicians are independent of those by nursing home staff. Prophylactic treatments are also excluded.

The secondary outcomes are as follows: number of all-cause hospitalizations per resident in 4 months; number of all-cause deaths per resident in 4 months; and comparison of suspected UTI during the trial. Groups are compared with regard to the numbers of acute antibiotic treatments for suspected UTI, antibiotic treatments for urinary tract symptoms, UTI-related hospitalizations, and UTI-related deaths.

Data Management

Data collected from medical records and diary entries are subjected to double data entry. A data manager performs merging, anonymization, and range checks. Trial data are stored in accordance with the data policy of the University of Copenhagen [25]. Data will be saved for 5 years after publication of the results.

Sample Size

Our primary outcome involves clustered count data, and we determined a minimum sample size according to the method for clustered Poisson regression [26]. In Denmark, the number of prescriptions for UTI in 2015 was 90 per 100 persons among those aged above 80 years [27]. Assuming no seasonal variation and generalizability to residents, the average number of prescriptions per resident during a 4-month period is 0.3. We assume that an average nursing home accommodates 60 residents. The intraclass correlation coefficient (ICC) of antibiotic prescription in nursing homes included in similar studies varies between 0.04 and 0.17 [28-30]; the higher estimates are based on the general population and prescriptions for respiratory tract conditions, whereas the lower estimates are based on nursing home data on prescriptions for UTI. With a conservative estimate of ICC of 0.07 and a significance level of 5%, we will have a power of 80% to detect a 50% decrease in the antibiotic prescription rate for the intervention group (from 0.30 to 0.15 prescriptions per resident in 4 months). This estimation is based on the inclusion of at least 11 nursing homes and 637 residents in each arm.

Sequence Generation, Blinding, and Statistical Analysis

The study statistician randomly assigns the nursing homes to the two study arms with a 1:1 computer generated randomization schedule stratified by municipality. Owing to the nature of the intervention, the trial is open labelled. The statistical analysis is blinded. Primary and secondary outcomes are analyzed using a Poisson regression model and generalized estimating equation.

Ethical Approval and Sharing of Health Care Information

Because the study is not a health science project as defined in the Danish Committee Act § 2, the Research Ethics Committee of the Capital Region of Denmark has waived the need for full ethical approval (journal no: 17013412). The Danish Patient Safety Authority has approved data collection for those residents unable to participate in informed consent for sharing of their health care information (journal no: 3-3013-2409/1 and amendment no: 3-3013-2704/1). We have collected informed consent from the rest of the residents from the start-up phase until the data collection phase. The study has been reported to the Danish Data Protection Agency.

Results

The timeline of the trial deviated slightly from the original plan. Particularly, enrollment and allocation were completed in June 2018. The trial ended at the end of March 2019; data have been collected and are being analyzed. We expect the results of the trial to be published in a peer-reviewed journal in the fall of 2020. Figure 1 shows the schedule of enrollment, interventions, and assessments.

Figure 1. Preliminary schedule of enrollment, interventions, and assessments (February 2020).

The original idea for the intervention was to provide nursing home staff with a biomarker for severe infection (C-reactive protein as a point-of-care test) in addition to the dialogue tool. Moreover, the primary outcome was originally appropriate prescription for UTI, but this was changed to number of prescriptions for UTI. The changes had been decided prior to registration at ClinicalTrials.gov.

Discussion

The aim of this study is to describe a protocol for evaluating the effects on antibiotic prescription, hospitalization, and death of a tailored complex intervention to improve the knowledge of UTI and communication skills among staff caring for residents with suspected UTI. The dialogue tool is based on a decision aid and a communication tool tested in clinical trials that have previously reduced antibiotic prescriptions [21,22]. The trial was performed from December 2018 through March 2019, and the results are expected to be submitted for publication in the fall of 2020.

We apply a tailoring process to develop the intervention and decrease barriers to implementation. In order to facilitate the collection of data and to tailor the intervention process to nursing homes, the research group decided to modify the original project plan slightly. This strategy is recommended to increase the impact of complex interventions [31]. We primarily target UTI knowledge and communication skills among all staff members, which differs from the approach in previous trials [20]. Because off-site prescription in nursing homes is common, staff members collect the information the physician receives and influence the diagnosis [17]. Hence, focusing on this group may prove to be an impactful strategy. We acknowledge the hierarchy in the prescription process. If prescribers continue with inappropriate prescription for asymptomatic bacteriuria despite improved quality of information, it may overrule the effect of the intervention. To avoid this, we inform all GPs in participating municipalities about the trial and invite nursing home physicians to participate in the workshop.

The greatest strength of the study is the randomized design. On the other hand, blinding can only be introduced in the data analysis. Owing to the format of the intervention, the open-label design is indispensable but introduces the control group to the potential risks of contamination and selection bias. This bias cannot influence the primary outcome, because it is obtained from the nursing home medical records. The medical record extracts information on prescribed drugs from “Fælles Medicin Kort,” which registers all prescriptions in the past 2 years [32]. Thus, another strength of using medical records is that if an indication is unclear, background information about the prescription decision is accessible. Finally, the PI facilitates all workshops and all introductions to the UTI diary. This ensures a high degree of homogeneity in the trial start-up for all included nursing homes.

The trial is pragmatic. First, the eligibility criteria for both homes and individual residents are broad, which may result in a heterogeneous population. Second, the implementation of the intervention is left to the individual homes after completion of the workshop. Third, during the trial period, the homes are visited only once by the PI, unless they initiate contact. As the homes differ in organizational structure, a uniform and strict design was not feasible.

Nursing home medical records only include information about all-cause hospitalization and all-cause mortality. The drawback

is that the information may be unrelated to UTI and that a relevant change may be diluted. We gain access to the social security numbers of residents, thereby permitting a long-term follow-up of residents through national registries. This could reveal any indirect effects on hospitalization or death. However, it is beyond the scope of this study.

Because of the Hawthorne effect, participating in a trial poses a challenge when evaluating the effect of the intervention [33]. Control groups commonly experience a behavioral change with knowledge of trial participation alone [34]. In this trial, the stakeholders in the control group are informed about the trial in general terms and both intervention and control groups have local coordinators, who complete the UTI diary. Thus, some impact of the trial design on antibiotic prescription in the control group is likely.

The use of a UTI diary may induce diagnostic bias. The diary is used for suspected UTI in both groups, but staff in the intervention group may be more alert to the discovery of potential UTI. There is a risk that staff members in the intervention group complete more diaries than staff members in the control group. The diary is extensive, and both groups may find it too bothersome to complete. This is why the research group changed the primary outcome from appropriate prescriptions to number of prescriptions, which can be found in the medical records. Nevertheless, a UTI diary is the best way to capture important clinical data about patients. Among other things, the diary includes information about signs and symptoms, which are rarely reported in medical records.

The problem of excessive and inappropriate antibiotic use is common in nursing homes. The study offers a strategy to tackle the challenges of increased antibiotic resistance and has implications in terms of handling suspected UTI. Some retailoring should be expected when transferring this intervention to an alternate setting.

In conclusion, this trial will test the hypothesis that a tailored complex intervention targeting the knowledge of UTI and communication skills of nursing home staff will improve antibiotic prescription for suspected UTI in residents. The results may provide new insights and prove to be an important addition to the current strategies to limit superfluous antibiotic treatment for suspected UTI in nursing homes.

Acknowledgments

The project is funded by the Danish Ministry of Health and The Velux Foundations. The funding bodies have no influence on the design of the study; collection, analysis, and interpretation of data; or writing of the manuscript.

Authors' Contributions

AH conceived the original study idea. SHA is the principal investigator and drafted the first version of this article. LB is the grant holder. SHA, AH, and LB provided clinical expertise. MBK and JNJ provided expertise in development and evaluation of the dialogue tool. JNJ provided expertise on nursing homes. VS provided statistical expertise on cluster randomized controlled trial design, allocation, and statistical analysis. All authors contributed to the review of the study protocol and approved the final manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Reflection section of the dialogue tool.
[PNG File , 509 KB - resprot_v9i5e17710_app1.png]

Multimedia Appendix 2
Communication section of the dialogue tool.
[PNG File , 298 KB - resprot_v9i5e17710_app2.png]

Multimedia Appendix 3
Letter to nursing home physicians.
[PNG File , 382 KB - resprot_v9i5e17710_app3.png]

Multimedia Appendix 4
Letter to all staff members.
[PNG File , 391 KB - resprot_v9i5e17710_app4.png]

Multimedia Appendix 5
Poster for staff members.

[PNG File , 632 KB - resprot_v9i5e17710_app5.png]

Multimedia Appendix 6
Letter to the liaison officer in the municipality.
[PNG File , 371 KB - resprot_v9i5e17710_app6.png]

Multimedia Appendix 7
Letter to local coordinators.
[PNG File , 378 KB - resprot_v9i5e17710_app7.png]

Multimedia Appendix 8
Letter to residents and relatives.
[PNG File , 372 KB - resprot_v9i5e17710_app8.png]

Multimedia Appendix 9
Poster for residents and relatives.
[PNG File , 490 KB - resprot_v9i5e17710_app9.png]

Multimedia Appendix 10
Urinary tract infection diary day 1.
[PNG File , 393 KB - resprot_v9i5e17710_app10.png]

Multimedia Appendix 11
Urinary tract infection diary days 2-8.
[PNG File , 259 KB - resprot_v9i5e17710_app11.png]

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Abbreviations

GP: general practitioner
ICC: intraclass correlation coefficient
ISBAR: Identification, Situation, Background, Assessment, and Recommendation
PI: principal investigator
UTI: urinary tract infection

Edited by G Eysenbach; submitted 06.01.20; peer-reviewed by M Bakhit, H Strauven; comments to author 13.02.20; revised version received 27.02.20; accepted 28.02.20; published 08.05.20.

Please cite as:
Arnold SH, Jensen JN, Kousgaard MB, Siersma V, Bjerrum L, Holm A
Reducing Antibiotic Prescriptions for Urinary Tract Infection in Nursing Homes Using a Complex Tailored Intervention Targeting Nursing Home Staff: Protocol for a Cluster Randomized Controlled Trial
JMIR Res Protoc 2020;9(5):e17710
URL: https://www.researchprotocols.org/2020/5/e17710
doi:10.2196/17710
PMID:32383679

Protocol

Mindfulness-Based Cognitive Therapy for Improving Subjective Well-Being Among Healthy Individuals: Protocol for a Randomized Controlled Trial

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Abstract

Background: Previous studies have indicated that higher subjective well-being works as a protective factor for health. Some studies have already shown the effects of mindfulness-based interventions on improving subjective well-being. However, these studies targeted specific populations rather than the general public. Furthermore, they assessed either life evaluation or affective aspects of subjective well-being rather than the concept as a whole, including the eudemonic aspect of well-being.

Objective: This study aims to investigate the effectiveness and cost-effectiveness of mindfulness-based cognitive therapy (MBCT) for improving the wholistic aspects of subjective well-being in healthy individuals.

Methods: This study was an 8-week, randomized, parallel-group, superiority trial with a 2-month follow-up. Healthy individuals aged 20-65 years with scores lower than 25 on the Satisfaction With Life Scale (SWLS) were eligible to participate and randomly allocated to the MBCT group or the wait-list control group. The intervention program was developed by modifying an MBCT program to improve the well-being of a nonclinical population. The primary outcome was the difference between the two groups in mean change scores from the baseline on the SWLS. The secondary outcomes included scores on the Flourishing Scale and the Scale of Positive and Negative Experience as well as the incremental cost-effectiveness ratio.

Results: This study began recruiting participants in July 2018 and recruitment was completed at the end of September 2019. Data collection and dataset construction was completed by the end of March 2020.

Conclusions: This study is unique in that it investigates MBCT's effects on the three different aspects of subjective well-being: life evaluation, affect, and eudemonia. It is limited, as the specific effect attributable to MBCT cannot be detected because of the lack of an active control group.

Trial Registration: University Hospital Medical Information Network Clinical Trials Registry (UMIN-CTR) UMIN000031885; https://upload.umin.ac.jp/cgi-open-bin/ctr_e/ctr_view.cgi?recptno=R000036376

International Registered Report Identifier (IRRID): DERR1-10.2196/15892

(JMIR Res Protoc 2020;9(5):e15892) doi:10.2196/15892

KEYWORDS

mindfulness-based cognitive therapy; subjective well-being; healthy individuals; randomized controlled trial; cost-effectiveness

Introduction

Background

Subjective well-being has become a central issue in the development of public policy. In this context, there are concerns about the adequacy of current measures of economic performance, such as gross domestic product (GDP), to indicate societal well-being [1]. The Organisation of Economic Co-operation and Development (OECD) proposed that subjective well-being should be considered in addition to these objective scales as a complementary indicator of people's well-being [2]. Following this initiative, several countries have launched challenges to propose a substitute indicator that complements GDP by measuring the progress of society [1,3-7].

Although arguments about the definition of subjective well-being are still in progress, the most widely accepted one is "good mental states, including all of the various evaluations, positive and negative, that people make of their lives, and the affective reactions of people to their experiences" [2]. There is a general consensus among experts that subjective well-being consists of at least two aspects: life evaluation and affect. In addition, several researchers have insisted that the eudemonic aspect, reflecting people's sense of purpose and engagement, should also be included in subjective well-being [8]. Thus, subjective well-being consists of three dimensions: life evaluation, affect, and eudemonia.

The importance of subjective well-being is not limited to economics. Several studies have indicated that subjective well-being affects the health of the general public. Steptoe et al revealed that impairment of subjective well-being by depression and life stress elevates the risk of premature death [9]. In addition, higher eudemonic well-being may work as a protective factor for health [10-12]. Therefore, improving the subjective well-being of the general public is significant from a public health perspective.

What We Already Know

Several interventions, such as a positive events diary [13], life coaching and attainment of goals [14], and positive future thinking [15], have proven effective in the improvement of subjective well-being for nonclinical populations. Furthermore, mindfulness-based intervention (MBI) is another measure that potentially improves people's subjective well-being. Although MBI was originally developed for the treatment of clinical populations, such as patients with chronic pain [16], depression [17], or anxiety disorders [18], its scope has recently expanded to nonclinical populations. Some studies have already shown its effects on decreasing stress and improving subjective well-being [19-30].

Rationale for the Study

The studies discussed above, however, have several limitations. First, because they tended to target specific populations, such as students [20,22,26,28,29], schoolteachers [21,23], health care professionals [19,27], and workers in the workplace [31-34], the generalizability of the results to the community is limited. Second, although two studies targeted healthy individuals in the community [24,25], they assessed either the life evaluation or affective aspect of subjective well-being rather than all three aspects (ie, cognitive, affective, and eudemonic aspects). Thus, no study has evaluated the eudemonic aspect of well-being, which has been proven to have a relationship with health [35]. Finally, although the effect of mindfulness-based stress reduction (MBSR) on subjective well-being has been evaluated, no study has assessed the effect of mindfulness-based cognitive therapy (MBCT) [36], which is the other major MBI currently practiced. Therefore, we decided to conduct a randomized controlled trial to demonstrate MBCT's effectiveness on three different aspects of subjective well-being (ie, life evaluation, affect, and eudemonia) for healthy individuals sampled from community residents.

Aim

The primary objective of this study is to investigate the effectiveness and cost-effectiveness of MBCT for improving the subjective well-being of healthy individuals in a randomized, wait-list, and controlled trial.

Methods

Participants

The study is being conducted at Keio University Hospital in Tokyo, Japan. Participants will be recruited through the Center for Stress Research at Keio University (Keio CSR). Eligible participants are people (1) between the ages of 20 and 65 years, (2) without a history of psychiatric disorders or who have been recovered from psychiatric disorders for more than 2 years, (3) with scores lower than 25 on the Satisfaction With Life Scale (SWLS), and (4) who can provide written informed consent.

Participants will be excluded if they (1) are difficult to follow up with 4 months after the start of the intervention, (2) have a past history of MBIs equivalent to the program provided in the study, and (3) have severe physical conditions.

Enrollment

Prospective participants who apply to the study through the form at the Keio CSR's website will be asked to fill out screening questionnaires via the Web (ie, the first screening). If the participants pass the first screening, they will meet a member of the study team who will conduct a face-to-face interview (ie, the second screening) to establish if they meet the inclusion criteria. The Japanese version of the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV), Axis I Disorders [37], will be used for diagnostic assessment. The first, second, and third authors (MS, TK, and AN) will conduct the second screening. The eligibility of the participants will be judged based on the results of this second screening. All participants will provide written informed consent after receiving a detailed explanation of all the procedures and will be able to withdraw their consent at any time without negative consequences.

Baseline Assessment

Overview

The participants will complete a battery of questionnaires assessing demographic and psychosocial data. Psychological

measures to be obtained will include the SWLS, the Flourishing Scale (FS), the Scale of Positive and Negative Experience (SPANE), the Rosenberg Self-Esteem Scale (RSES), the Five Facet Mindfulness Questionnaire (FFMQ), the Connor-Davidson Resilience Scale (CD-RISC), the Self-Compassion Scale (SCS), the 16-item Quick Inventory of Depressive Symptomatology (QIDS), the Generalized Anxiety Disorder 7-item scale (GAD-7), the Perceived Stress Scale (PSS), the World Health Organization Health and Work Performance Questionnaire (WHO-HPQ), the Multidimensional Assessment of Interoceptive Awareness (MAIA), and the European Quality of Life Five-Dimension Five-Level Scale (EQ-5D-5L). All measures have been validated in Japan [38-49]. The details of each scale are described below.

Satisfaction With Life Scale

The SWLS is a self-reported questionnaire with five questions. The scale focuses particularly on assessing one's life satisfaction. Total scores range from 5 to 35, with higher scores indicating higher satisfaction [50].

Flourishing Scale

The FS consists of eight items describing important aspects of human functioning, ranging from positive relationships to feelings of competence, meaning, and purpose in life. Each item is answered on scale ranging from 1 (*strong disagreement*) to 7 (*strong agreement*). Total scores can range from 8 (*strong disagreement* with all items) to 56 (*strong agreement* with all items). Although the scale does not provide separate measures for distinct facets of well-being, it does yield an overview of positive functioning across diverse domains that are widely believed to be important [51].

Scale of Positive and Negative Experience

The SPANE measure is a brief 12-item scale with six items devoted to positive experiences and six items designed to assess negative experiences. Because the scale includes general positive and negative feelings, it assesses the full range of positive and negative experiences, including specific feelings that may have unique labels in particular cultures [51].

Rosenberg Self-Esteem Scale

The RSES was developed as a brief self-rated assessment to determine self-esteem, self-worth, acceptability, and confidence. It comprises 10 items that allow four responses on a Likert scale, ranging from 1 (*strongly disagree*) to 4 (*strongly agree*). Total possible scores range from 10 to 40; higher scores represent higher self-esteem [52].

Five Facet Mindfulness Questionnaire

The FFMQ is a self-report questionnaire used to assess mindfulness ability. It consists of five factors, which were designed based on a factor analytic study of five independently developed mindfulness questionnaires. The five facets are observing, describing, acting with awareness, not judging inner experience, and not reacting to inner experience [53].

Connor-Davidson Resilience Scale

The CD-RISC was developed as a brief self-rated assessment to help quantify resilience. The scale contains 25 items, all of which feature a 5-point range of responses, ranging from 0 (*not true at all*) to 4 (*true nearly all of the time*). The total score ranges from 0 to 100, with higher scores reflecting greater resilience [54].

Self-Compassion Scale

The SCS assesses individuals' ability to be kind and understanding toward themselves as opposed to harsh and self-critical in instances of pain or failure. It consists of 29 items and generates scores on six subscales: self-kindness, self-judgment, common humanity, isolation, mindfulness, and overidentification. Participants' responses are based on the frequency of certain thoughts and feelings. Total subscale scores range from 1 to 5, with higher scores indicating more self-compassion [55].

16-Item Quick Inventory of Depressive Symptomatology

The QIDS is one of the most widely used self-reported questionnaires assessing depressive symptoms. The scoring system for the QIDS converts responses to 16 separate items into the nine DSM-IV symptom criterion domains. Total scores range from 0 to 27. Higher scores indicate higher levels of depressive symptoms [56].

Generalized Anxiety Disorder 7-Item Scale

The GAD-7, a 7-item questionnaire, was developed by asking patients how often, during the preceding 2 weeks, they had experienced a set of symptoms. There were four response options on a Likert scale, ranging from 0 (*not at all*) to 3 (*nearly every day*). Scores range from 0 to 21, with scores of 5, 10, and 15 representing mild, moderate, and severe anxiety symptoms, respectively [57].

Perceived Stress Scale

The PSS is designed to measure the degree to which situations in one's life are appraised as stressful. Among two versions of the PSS—the 14-item version (PSS-14) and the 10-item version (PSS-10)—the PSS-10 was recommended because the four additional items of the PSS-14 show relatively low factor loading [58]. Therefore, the PSS-10 was used in our study. This scale assesses perceived stressful experiences or stress responses over the previous month. Total possible scores range from 0 to 40. Higher scores represent high stress levels [59].

World Health Organization Health and Work Performance Questionnaire

The WHO-HPQ is a self-report instrument designed to estimate the workplace costs of health problems in terms of self-reported sickness absences and reduced job performance (ie, presenteeism). The WHO-HPQ measures presenteeism with the following two questions: "On a scale from 0 to 10, where 0 is the worst job performance anyone could have at your job and 10 is the performance of a top worker, how would you rate the usual performance of most workers in a job similar to yours?" and "Using the same 0-10 scale, how would you rate your overall job performance on the days you worked during the past 4 weeks?" A low presenteeism score indicated poorer performance [60].

Multidimensional Assessment of Interoceptive Awareness

Interoceptive awareness has been regarded as an essential factor in meditation and stress reduction. The MAIA was developed as a self-report instrument for experimental interoception research and for assessment of mind-body therapies [61]. It is a 32-item self-report measure that assesses interoceptive awareness on the following eight subscales: noticing, not-distracting, not-worrying, attention regulation, emotional awareness, self-regulation, body listening, and trusting. Each item is assessed on a 6-point Likert scale, ranging from 0 (*never*) to 5 (*always*). Higher scores indicate better interoceptive awareness [62].

European Quality of Life Five-Dimension Five-Level Scale

The EQ-5D-5L is a standardized instrument used to measure health-related quality of life [63]. Applicable to a wide range of health conditions and treatments, it provides a simple descriptive profile and a single index value for health status.

Randomization

Eligible participants will be randomly assigned, at a 1:1 ratio, to the MBCT group or the wait-list control group. A computer-generated random number stratified by the baseline score of the SWLS will be allocated to each participant. The Keio Center of Clinical Research Project Management Office, which is not associated with this study, will manage the process of the randomization. The flow diagram of the study participants is shown in Figure 1.

Blinding

Due to the nature of this psychological intervention, the randomization status of participants and program instructors cannot be blinded. Because all measures obtained through the study period are self-reported, there will be no assessors to judge the state of participants.

Intervention and Control Groups

Mindfulness-Based Cognitive Therapy Group

The intervention program used in the study is the modified version of MBCT based on the book *Mindfulness: A Practical Guide to Finding Peace in a Frantic World* [64]. This program has been developed by modifying an MBCT program to improve the well-being of a nonclinical population. The contents of the program are shown in Table 1. The main differences of this program from MBCT are that (1) the lecture relevant to depression will be skipped and (2) compassion meditation and activity records (ie, pleasant, unpleasant, appreciation events, and nourishing and depriving activities) will be introduced. In the program, participants will learn both cognitive approaches and mindfulness practices (eg, raisin exercise, body scan, sitting meditation, mindful walking, and three-step breathing space).

The program will consist of eight weekly sessions. Each session will be in a group format—15 participants at the most—and will last for 2 hours. The participants will be asked to practice mindfulness meditation for 30-60 minutes as their daily homework and to keep a record of the type of meditation and the amount of time they practiced.

The first author (MS) will lead the sessions as the principal instructor. Dr Sado has been qualified to teach MBSR through a program at the University of Massachusetts, Boston, USA; is on the training path for MBCT teachers at Oxford University, Oxford, UK; and has 9 years of experience in mindfulness practice. The second (TK) and third (AN) authors will join the course as assistant instructors.

Control Group

Participants on the wait list will have no interventions during the intervention period. They will be asked not to take part in other mindfulness or meditation activities. After the first intervention term is completed, the participants in the control group will be given an opportunity to attend the MBCT program.

Figure 1. Flowchart of the effectiveness and cost-effectiveness of mindfulness-based cognitive therapy (MBCT) for improving subjective well-being among healthy individuals.

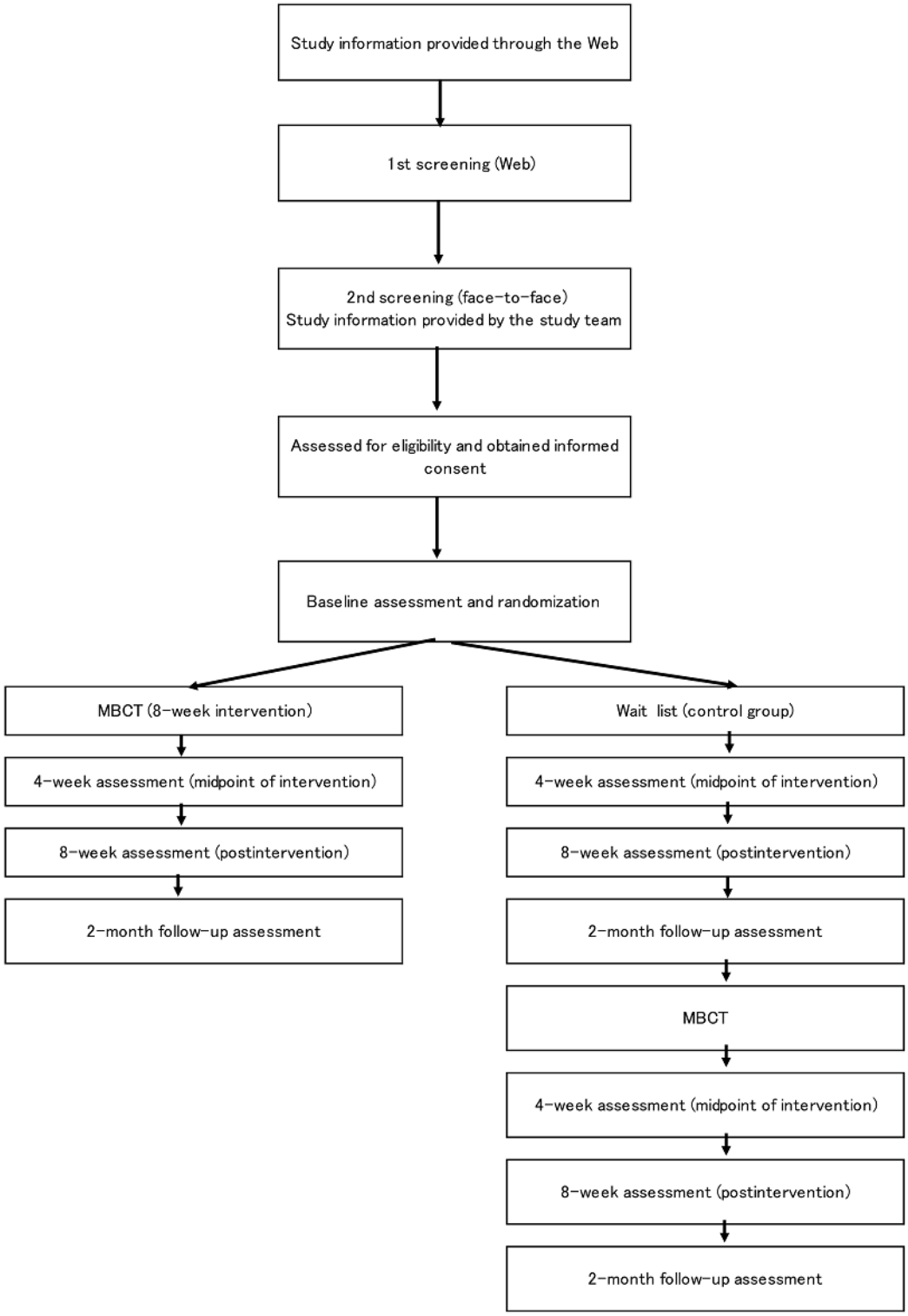

Table 1. Contents of the intervention program.

Session	Theme	Contents
1	Waking up to the automatic pilot	Psychoeducation: What is mindfulness? Exercise: Mindful eating (ie, *raisin exercise*), asking yourself why you are here now, and mindfulness of body and breath Homework: Mindfulness of body and breath, mindfulness of a routine activity, and let go of habits
2	Keeping the body in mind	Psychoeducation: Association of mood and thoughts Exercise: Mindfulness of body and breath, thoughts and feelings exercise, and body scan Homework: Body scan, pleasant event calendar, mindfulness in everyday life, and let go of habits
3	The mouse in the maze	Psychoeducation: Awareness of mind wandering and focusing on the breath Exercise: Breathing meditation, meditation of sounds, gentle yoga, and mindful walking Homework: Three-step breathing space, gentle yoga, mindful walking, diary of appreciation and gratitude events, and let go of habits
4	Moving beyond the rumor mill	Psychoeducation: Staying present Exercise: Mindfulness meditations (ie, breathing as well as sounds and thoughts) Homework: Mindfulness meditations (ie, breathing, sounds and thoughts, and three-step breathing space), unpleasant events calendar, and let go of habits
5	Turning toward difficulties	Psychoeducation: Exploring difficulty Exercise: Mindfulness meditations (ie, breathing, sounds and thoughts, and exploring difficulty) Homework: Mindfulness meditations (ie, breathing, sounds and thoughts, exploring difficulty, and three-step breathing space) and let go of habits
6	Trapped in the past or living in the present	Psychoeducation: Cognitive biases and compassion for myself Exercise: Mindfulness meditations, compassion meditation, and watching the movie *Happy* about subjective well-being Homework: Mindfulness meditations (ie, sounds and thoughts, exploring difficulty, compassion, and three-step breathing space) and diary of your kind behavior
7	When did you stop dancing?	Psychoeducation: Choosing functional behaviors, behavioral activation, and identifying triggers Exercise: Mindfulness meditations (ie, breathing as well as sounds and thoughts) Homework: Mindfulness meditations (ie, choose what you like and three-step breathing space) and diary of activity that nourishes you
8	Your wild and precious life	Personal reflections of the course, plans for future practice, strategies for maintaining momentum, and farewell Exercise: Body scan and asking yourself why you are here now and what you realized through the program

Outcomes

Primary Outcome

The primary outcome is the difference in mean change scores between the baseline and postintervention assessments on the SWLS for the MBCT group as compared to the control group.

Secondary Outcomes

The secondary outcomes are the differences in mean change scores between the baseline and postintervention assessments on the FS, SPANE, RSES, FFMQ, CD-RISC, SCS, QIDS, GAD-7, PSS, WHO-HPQ, MAIA, and EQ-5D-5L for the MBCT group as compared to the control group.

Cost-Effectiveness

Cost-effectiveness will be assessed based on the incremental cost-effectiveness ratio that represents the incremental cost divided by the incremental effectiveness between the groups. With respect to cost, we only include the human resource cost to deliver the sessions, since the study targets healthy individuals. Because the population targeted in the study is composed of healthy individuals, incremental effectiveness will be evaluated primarily using the measures of subjective well-being, such as the SWLS. However, we will also use the quality-adjusted life years mapped from the results of the EQ-5D-5L and so on, representing health-related quality of life as the secondary incremental effectiveness outcome. The analyses will be conducted from a third-party payers' perspective.

Schedule of Visits and Assessments

All participants will be asked to complete these psychological self-reporting measures at 4 weeks (ie, the intervention midpoint), 8 weeks (ie, postintervention), and 2 months (ie, 16 weeks) after the completion of the intervention, as well as at their baseline assessments (ie, week 0). The assessment schedule is shown in Table 2.

Table 2. Schedule of assessments.

Assessment	First screening	Week[a]										
		0	1	2	3	4	5	6	7	8	12	16
Screening (Web)	X											
Screening (face-to-face interview)		X										
Informed consent		X										
Randomization		X										
Mindfulness-based cognitive therapy (MBCT) class			X	X	X	X	X	X	X	X	X	X
Demographics	X	X										
Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (SCID)		X										
Satisfaction With Life Scale (SWLS)		X				X				X		X
Flourishing Scale (FS)		X				X				X		X
Scale of Positive and Negative Experience (SPANE)		X				X				X		X
Rosenberg Self-Esteem Scale (RSES)		X				X				X		X
Five Facet Mindfulness Questionnaire (FFMQ)		X				X				X		X
Connor-Davidson Resilience Scale (CD-RISC)		X				X				X		X
Self-Compassion Scale (SCS)		X				X				X		X
16-item Quick Inventory of Depressive Symptomatology (QIDS)		X				X				X		X
Generalized Anxiety Disorder 7-item scale (GAD-7)		X				X				X		X
Perceived Stress Scale (PSS)		X				X				X		X
World Health Organization Heath and Work Performance Questionnaire (WHO-HPQ)		X				X				X		X
Multidimensional Assessment of Interoceptive Awareness (MAIA)		X				X				X		X
European Quality of Life Five-Dimension Five-Level Scale (EQ-5D-5L)		X				X				X		X

[a]Psychological self-reporting measures will be completed at baseline (week 0), the intervention midpoint (week 4), postintervention (week 8), and 2 months after the completion of the intervention (week 16).

Sample Size

We performed sample size calculation based on the results of a previous feasibility study that we had conducted, which assessed the feasibility, safety, and effectiveness of MBCT for improving subjective well-being with a single arm. The pre-post difference in the mean score of the SWLS in the study was 3.1 (SD 3.4). With a statistical power of at least 80% and a two-sided 5% significance level, the sample size was calculated to be 20 participants for each arm. Allowing for a dropout rate of approximately 20%, we determined that each arm would need 25 participants, for a total of 50 participants.

Statistical Analysis

A 5% significance level will be used for all statistical analyses. To compare differences in the baseline demographics and clinical characteristics of the two groups, unpaired *t* tests will be used for the continuous variables and chi-square tests for the categorical variables. The primary and secondary outcomes will be analyzed using an intent-to-treat approach and a mixed-effect model repeat measurement, a method of handling dropouts in longitudinal clinical trials. Stata 14 (StataCorp) will be used to carry out statistical analysis.

Adverse Events

When we notice serious adverse events, we will report them to the Ethics Review Committee of the Keio University School of Medicine.

Ethics

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All procedures involving human participants and patients were approved by the Ethics Review Committee of the Keio University School of Medicine (reference number: 20170258). The study has been registered in the University Hospital Medical Information Network (UMIN) Clinical Trials Registry (UMIN 000031885).

Dissemination

The results of the study will be disseminated at several academic conferences and as published articles in peer-reviewed journals. The study will be implemented and reported in line with the CONSORT (Consolidated Standards Of Reporting Trials) statement.

Availability of Data and Materials

The datasets are available from the corresponding author upon reasonable request.

Results

This study began recruiting participants in July 2018 and recruitment was completed at the end of September 2019. Data collection and dataset construction was completed by the end of March 2020.

Discussion

This study aims to investigate the effectiveness of MBCT in the improvement of subjective well-being for healthy individuals in the community. It will attempt to detect meaningful differences in the target outcomes. When we use psychological scales that were developed in a different culture, their validity can become a critical issue because the constructs that the study measures investigate tend to be strongly affected by culture. Therefore, we decided to adopt only scales validated in a Japanese setting. The limitation of this study is that we set the wait-list group as a control group. Of course, we were aware that allocating an attention placebo (eg, relaxation or other form of psychotherapy) would have been an option for detecting the specific effect attributable to MBCT. However, we judged our choice to be acceptable because our aim is to evaluate clinical effectiveness of augmenting typical daily life with MBCT rather than to assess the efficacy of MBCT.

This study is novel in terms of its assessment of all three aspects of subjective well-being (ie, cognitive, affective, and eudemonic aspects) in the absence of other such existing works. Subjective well-being has attracted attention because there are indications that better subjective well-being works as a protective factor for better health status, including mental health. Therefore, we believe this study will generate fruitful knowledge for future research in the field.

Acknowledgments

We would like to thank Dr Yasunori Sato for advice on statistical analysis and Editage for English-language editing. This study was funded by Grant-in-Aid for Scientific Research of the Japanese Ministry of Education, Culture, Sport, Science, and Technology (KAKENHI grant number: 16K08881). The funding source has no role in developing the study design, data collection, analysis and interpretation, the writing of the report, or the decision to submit the paper for publication.

Authors' Contributions

MS drafted the grant proposal and is responsible for study implementation, study management, collecting data, and supervision. MS, TK, and AN designed the study. MS drafted the manuscript. TK, AN, MN, SP, DF, JS, and MM refined the study protocol. All authors critically reviewed the manuscript for content and approved the final version.

Conflicts of Interest

None declared.

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Abbreviations

CD-RISC: Connor-Davidson Resilience Scale
DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, Fourth edition
EQ-5D-5L: European Quality of Life Five-Dimension Five-Level Scale
FFMQ: Five Facet Mindfulness Questionnaire
FS: Flourishing Scale
GAD-7: Generalized Anxiety Disorder 7-item scale
GDP: gross domestic product
Keio CSR: Center for Stress Research at Keio University
MAIA: Multidimensional Assessment of Interoceptive Awareness
MBCT: mindfulness-based cognitive therapy
MBI: mindfulness-based intervention
MBSR: mindfulness-based stress reduction
OECD: Organisation of Economic Co-operation and Development
PSS: Perceived Stress Scale
PSS-10: 10-item version of the Perceived Stress Scale
PSS-14: 14-item version of the Perceived Stress Scale
QIDS: 16-item Quick Inventory of Depressive Symptomatology
RSES: Rosenberg Self-Esteem Scale
SCS: Self-Compassion Scale
SPANE: Scale of Positive and Negative Experience
SWLS: Satisfaction With Life Scale
UMIN: University Hospital Medical Information Network
WHO-HPQ: World Health Organization Health and Work Performance Questionnaire

Edited by G Eysenbach; submitted 16.08.19; peer-reviewed by K Sanada, P Nilsson, S Kolovos; comments to author 04.11.19; revised version received 26.12.19; accepted 30.01.20; published 08.05.20.

Please cite as:
Sado M, Kosugi T, Ninomiya A, Nagaoka M, Park S, Fujisawa D, Shirahase J, Mimura M
Mindfulness-Based Cognitive Therapy for Improving Subjective Well-Being Among Healthy Individuals: Protocol for a Randomized Controlled Trial
JMIR Res Protoc 2020;9(5):e15892
URL: https://www.researchprotocols.org/2020/5/e15892
doi:10.2196/15892
PMID:32005642

Protocol

Effectiveness of Group Cognitive Behavioral Therapy and Exercise in the Management of Major Depressive Disorder: Protocol for a Pilot Randomized Controlled Trial

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Abstract

Background: Despite evidence in scientific literature indicating the effectiveness of both cognitive behavioral therapy (CBT) and physical exercise in the management of major depressive disorder (MDD), few studies have directly compared them.

Objective: This study aims to evaluate and compare the effectiveness of group CBT, physical exercise, and only wait-listing to receive treatment-as-usual (TAU) in the management of MDD. The investigators hypothesize that participants with MDD assigned to the group CBT or exercise arms of the study will achieve superior outcomes compared with participants wait-listed to receive TAU only.

Methods: This prospective rater-blinded randomized controlled trial assesses the benefits of group CBT and exercise for participants with MDD. A total of 120 patients with MDD referred to addiction and mental health clinics in Edmonton, Canada, will be randomly assigned to one of the three equal-sized arms of the study to receive either weekly sessions of group CBT plus TAU, group exercise three times a week plus TAU, or only TAU for 14 weeks. Participants will be assessed at enrollment, 3 and 6 months post enrollment, midtreatment, and upon treatment completion for primary (functional and symptom variables) and secondary outcomes (service variables and health care utilization). In addition, participants in the intervention groups would be evaluated weekly with one functional measure. The data will be analyzed using repeated measures and effect size analyses, and correlational analyses will be completed between measures at each time point.

Results: The study will be conducted in accordance with the Declaration of Helsinki (Hong Kong amendment) and Good Clinical Practice (Canadian guidelines). Written informed consent will be obtained from each subject. The study received ethical clearance from the Health Ethics Research Board of the University of Alberta on September 7, 2018 (Pro 00080975) and operational approval from the provincial health authority (Alberta Health Services 43638). As of October 13, 2019, we have enrolled 32 participants. The results will be disseminated at several levels, including patients, practitioners, academics, researchers, and health care organizations.

Conclusions: The results of the pilot trial may inform the implementation of a multicenter clinical trial and provide useful information for administrators and clinicians who are interested in incorporating group CBT and group exercise interventions into existing care.

Trial Registration: ClinicalTrials.gov NCT03731728; https://clinicaltrials.gov/ct2/show/NCT03731728

International Registered Report Identifier (IRRID): PRR1-10.2196/14309

(JMIR Res Protoc 2020;9(5):e14309) doi:10.2196/14309

KEYWORDS

depression; major depressive disorder; cognitive behavioral therapy; group CBT; exercise

Introduction

Background and Rationale

Depressive disorders are a major public health problem. For example, the global prevalence of depressive disorders is over 4%, and depression is the single largest contributor to nonfatal health loss [1]. There is a need to identify interventions that are relatively cost-efficient, scalable, and can be offered to many people. Treatment for depressive disorders typically includes antidepressant medication and or counseling and psychotherapy.

Exercise as a form of treatment for depressive disorders, especially of mild-to-moderate severity, has evidence of benefit [2-5]. In fact, the magnitude of the effect of exercise as a treatment for depression is reported to be comparable with the magnitude of the effect of conventional treatment [6,7]. An umbrella review of systematic reviews and meta-analyses of the use of exercise to treat depressive symptoms in older adults, for example, concluded that “exercise is safe and efficacious in reducing depressive symptoms in older people” and that exercise “should be considered as a core intervention in the multidisciplinary treatment of older adults experiencing depression” [8]. A meta-analysis adjusting for publication bias concluded that “exercise has a large and significant antidepressant effect in people with depression” [9]. The mechanisms by which exercise decreases depressive symptoms may include biological mechanisms such as anti-inflammatory effects [10] or increasing neurotransmitter levels implicated in depression [11]. Other mechanisms may include increase in self-efficacy [10] or enhanced social interaction [12].

Despite this strong evidence base, few studies have incorporated multiple treatment conditions in a randomized controlled trial design, and few studies appear to have assessed the effect of group cognitive behavioral therapy (CBT) in comparison with exercise. A randomized clinical trial that assigned 54 mild-to-moderately depressed patients to a combined CBT plus exercise condition vs a CBT-only condition [13] found superior outcomes in suicidal ideation, depression, and activities of daily living in the combined condition group compared with the group receiving CBT only. However, few studies compared group CBT, group exercise, and wait-listing for treatment-as-usual (TAU) conditions. This is important in further delineating the effective components of treatment for mild-to-moderate depression, and the results have implications for service delivery and clinical recommendations in the treatment of depression within health care organizations in Alberta and beyond. Specifically, patients with major depressive disorder (MDD) referred to addiction and mental health clinics in Edmonton Zone may wait for weeks before receiving individual treatment. Thus, group treatment conditions examined in this study may serve as an expedient treatment avenue to decrease waiting list times for patients with MDD and improve outcomes.

Aim and Objectives

The aim of this project is to conduct a randomized pilot trial to evaluate the feasibility and effectiveness of group CBT and group exercise on depressive symptom scores and functioning. The client outcomes will be organized according to functional variables (relationships, well-being, and physical activity), symptom variables (change in depressive symptoms scores), and service variables (patient compliance, retention in treatment, and patient satisfaction).

Given the aim, one objective of the project is to compare the mean changes in functioning, clinical symptoms, and service satisfaction variables from enrollment baseline to 12 weeks post enrollment for (1) participants receiving group CBT plus wait-listed to receive TAU, (2) participants receiving scheduled exercise plus wait-listed to receive TAU, and (3) participants only wait-listed to receive TAU. Another objective of the study is to compare the mean changes in functioning, clinical symptoms, and service satisfaction variables from treatment baseline to 7 and 14 weeks post treatment commencement for (1) participants receiving group CBT plus wait-listed to receive TAU and (2) participants receiving scheduled exercise plus wait-listed to receive TAU.

Hypothesis

The investigators hypothesize that participants enrolled in the group CBT or group exercise treatments while wait-listed to receive TAU will achieve significantly lower symptom outcome measures scores at 12 weeks and 6 months post enrollment compared with participants only wait-listed to receive TAU on each outcome measure used. We expect that participants enrolled in the group CBT plus TAU arm will have outcomes comparable with those enrolled in the group exercise plus TAU arm of the study at 7 and 14 weeks post treatment commencement.

Methods

Overview of Study Design, Timeline, and Participant Selection

This study will be a longitudinal, prospective, parallel-design, three-arm, rater-blinded randomized clinical trial with a recruitment period of 6 months and an observation period of 14

weeks (plus waiting time) for each participant. The study will be conducted according to the timelines specified in the Gantt chart in Multimedia Appendix 1.

The research will be conducted in a municipal recreational center as well as addiction and mental health clinics in Edmonton, a large, sociodemographically diverse city in western Canada [14]. Potential participants will be recruited from the Addiction and Mental Health Intake Clinic in Edmonton. Patients with depression during the intake assessment who are presumed to meet the inclusion criteria of the study will be invited to enroll.

To confirm the diagnosis of MDD using Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) criteria, potential participants will be sent to the mood and anxiety clinic or urgent clinics in Edmonton, where they will be assessed by a psychiatrist or psychiatry resident who is independent from the study team. The psychiatrist or resident may or may not initiate, continue, or adjust pharmacotherapy. The diagnosis will be communicated to the study coordinator and clinic nurse. Participants with MDD will be informed of their eligibility to participate in the study and will be considered for randomization after providing informed consent, whereas patients with other diagnoses will be informed of their exclusion from the study and will be directed to receive an appropriate treatment for their condition.

After the diagnostic confirmation by a psychiatrist, a research assistant who is trained in study procedures will provide the potential participants with an information leaflet about the study and answer any related questions they may have. All potential participants who agree to take part in the study will provide written informed consent before the completion of the baseline assessment measures and randomization.

Patients who are aged between 18 and 65 years, have been referred by a primary care provider or self-referred to the Addiction and Mental Health Intake Clinic in Edmonton, have received a primary diagnosis of MDD from a consultant psychiatrist based on DSM-5 criteria, and have provided written informed consent will be included in the study. Patients will be ineligible if they do not meet the above inclusion criteria; have not provided informed consent; or have a diagnosis of bipolar disorder, schizophrenia, or schizoaffective disorder.

At baseline, demographic and contact information will be collected. Participants' name and contact information will be collected only for use in future communication or for the arrangement of treatment, assessment, and follow-up sessions.

Participants' medical records will also be reviewed at two points, at enrollment and 6 months after enrollment in the study, to gather information about participants' use of health services in the past 6 months to compare service utilization among the groups and to determine if participation in the intervention groups impacts the use of other health services in the short term. These data can also be used for any economic analyses (ie, cost-effectiveness) that will be conducted.

All the data will be stored for a minimum of 7 years before destruction as per the research ethics board's requirements, and the research ethics board's requirements pertaining to the collection and storage of information will be followed.

Multimedia Appendix 1 illustrates the Gantt chart for group CBT and exercise project.

Interventions

Participants enrolled in the group CBT plus TAU condition will be wait-listed to receive TAU and will receive a 2-hour session of group CBT every week for 14 weeks. Participants enrolled in the group exercise plus TAU arm of the study will be wait-listed for TAU and will receive 60 min of scheduled and facilitated exercises three times a week for 14 weeks. Participants in the TAU-only arm of the study will be wait-listed to receive individual therapy or counseling from a therapist as per current standard protocol for managing patients with MDD in addiction and mental health clinics in Edmonton Zone. All above participants may or may not receive pharmacotherapy as prescribed by a psychiatrist who is independent from the study team.

Group Cognitive Behavioral Therapy

The group CBT will be offered at 3 addiction and mental health clinics in Edmonton: Edmonton Community Mental Health Clinic, Edmonton Hope and Wellness Centre, and Alberta Health Services (AHS) Clinical Psychology Service. All therapists will use a manualized CBT protocol with the same handouts and schedule developed based on the book *Mind Over Mood* [15]. The group CBT will be provided to a group of maximum 10 participants. Each session will be 2 hours long and will be conducted by certified therapists with special training to deliver group CBT. The structure of the session will be agenda setting, check-in, review of homework, new concepts or skills, homework assignment, and feedback.

Group Exercise

For scheduled group exercise, the research team will follow the current recommendations based on a literature review for the use of exercise for the treatment of depression and the Canadian Physical Activity Guide [16] recommendations. Scheduled group exercises incorporate the following parameters:

- Type: Aerobic or strength training exercises.
- Dose: Three times per week.
- Intensity: Moderate (participant's self-rated physical activity of a 6 or 7 on the Borg Perceived Exertion Scale of 10 relative to the individual's personal capacity). Moderate heart rate level will be calculated (65%-75% of maximum heart rate) for each participant at the beginning of the study, and participants will have access to heart rate monitors (worn on the wrist) to gain an understanding of what moderate intensity feels like.
- Time: 60 min in moderate heart rate zone per session, with three sessions per week (180 min per week).
- Duration: 14 weeks.
- Others with supervision: Physical exercise sessions will be run by CanFit Pro- or Alberta Fitness Leadership Certification Association–certified recreational therapists who will assess the safety of patients' involvement in physical activity using the 2018 Physical Activity Readiness Questionnaire (PAR-Q+) before the initiation of the study and address any physical problems to minimize the risk of any adverse events happening during the sessions. The

PAR-Q+ is a screening tool to determine safe participation in exercise. Participants identified as potentially at risk with physical activity will require clearance to participate by their medical doctor.

Participants will have an opportunity to choose from a variety of physical activities to facilitate a meaningful physical activity experience that is important for long-term maintenance. Participants will have the opportunity to engage in three of the following fitness programs per week for 14 weeks:

- Monday: individual fitness for 60 min
- Tuesday: group exercise or individual fitness for 60 min
- Wednesday: aqua or swimming for 60 min
- Thursday: track walking and group exercise for 60 min
- Friday: pole walking or hiking according to the season for 60 min.

All participants must consent to participate in the study-facilitated exercise groups to be considered in the study because supervision and guidance are required for safety and ensuring consistent results. During the trial, participants are encouraged to participate in the exercise options offered. If the participant engages in the exercise independently, it will be counted as one of their sessions. Once the trial is completed, they will be supported to continue with the exercise options in the community. Participants will be provided with fitness passes and equipment as needed. It will be explained to the participant that although the expense of the equipment is subsidized by the study team to facilitate their participation, they do not have to participate because of this supportive act. They may keep the equipment should they decide to withdraw from the study at any point.

For each session, 2 recreation therapists will provide programming to a maximum of 20 participants. During the sessions, the recreation therapists will provide participants with information regarding health, wellness, fitness training, and understanding exertion levels within exercise. Participants will be encouraged to participate at a moderate level of perceived exertion for the best results (6-7 on a 10-point scale). While engaging in the exercise programs, the participants will be self-reporting intensity using a rating of the perceived exertion scale to the facilitators. Each participant must attend at least 75% of programs (32 sessions out of 42 sessions) during the 14-week period to be considered as having completed the program and for data analysis purposes.

Sample Size

As this is a pilot study, the research will utilize data that can be elicited from participants who can be enrolled within the existing operational resources and time frames. This method is acceptable for pilot studies with limited data on effect size and has been described by Haynes et al [17] as using “the patients I can get”. The study will therefore be limited to a sample size of 120, with about 40 patients recruited into each arm of the study.

Outcome Measures

We will implement and evaluate the project using the Alberta Quality Matrix for Health [18].

The outcome measures are detailed in Multimedia Appendix 2. The primary outcomes include functional variables (relationships, well-being, and physical activity) and symptom variables (depression and risk). The secondary client outcomes include service variables (satisfaction and health utilization).

Randomization and Blinding

Randomization will be enacted via randomly generated codes. Each study participant will receive a randomization code. As it will not be possible for participants to be blinded, treatment allocation will be made explicit to them as soon as randomization is concluded. The outcome assessors will be blinded to treatment group allocation by not involving them in discussions about the study participants and not granting them access to the database that contains the randomization code. In addition, study participants will self-complete all outcome assessments with the assessor facilitating procedural aspects if needed. Moreover, these assessors will not be involved in data analysis. After data collection is complete, all data will undergo a blind review for the purpose of finalizing the planned analysis.

Follow-Up Assessment

Moreover, 12 and 24 weeks after baseline assessments, a blinded researcher will contact the study participants in all three arms of the study and assist them in the completion of a range of assessment tools related to the outcome measures. The number of treatment sessions (group CBT, group exercise, or individual therapy) received by the participants at each time point would be recorded for participants in all treatment arms. In addition, participants in the group CBT and exercise arms of the study would complete the assessment tools weekly during the sessions and also at midtreatment (7 weeks after starting treatment) and at the end of the treatment (14 weeks after the treatment commencement). These self-rated assessments would be coordinated by the group facilitators.

Statistical Methods

The primary goal of the statistical analysis will be to produce summary descriptive statistics for the longitudinal data, which will provide estimates for future sample size calculations and enable calculation of effect size. For the three-arm trial, we will compare the mean change in scores for primary and secondary outcome measures from enrollment baseline to 12 weeks and 24 weeks post enrollment into the study, whereas for the two-arm trial, we will compare the mean change in scores for primary and secondary outcome measures from treatment baseline to 7 and 14 weeks post enrollment into treatment, in addition to comparing the trends in weekly change in scores on the Clinical Outcomes in Routine Evaluation-10-Outcome Measure between the 2 intervention groups. The data will be analyzed using repeated measures and effect size analyses, and correlational analyses will be completed between measures at each time point. The results of this study will guide the design for a future, more highly powered, study.

Patient and Public Involvement

The study was designed and finalized based on the nonsystematic and informal feedback from the representative patients. This randomized trial also offers patients the

opportunity to provide feedback via the patient satisfaction survey.

Results

The study will be conducted in accordance with the Declaration of Helsinki (Hong Kong amendment) [1] and Good Clinical Practice (Canadian guidelines) [2]. Written informed consent will be obtained from each subject. The study has received ethical clearance from Health Ethics Research Board of the University of Alberta on September 7, 2018 (Pro 00080975) and operational approval from the provincial health authority, AHS, on September 12, 2018 (AHS 43638). The study is registered with ClinicalTrials.gov on October 21, 2018 (registration number NCT03731728). As of October 13, 2019, we had enrolled 32 participants. The results will be disseminated at several levels, including patients, practitioners, academics, researchers, and health care organizations.

The team of investigators will plan an organizational engagement strategy to advance discussions about feasibility and effectiveness before the conclusion of the trial. This will help ensure that the findings are a relevant part of the decision-making processes in a way that is aligned with the study findings as they emerge. This may facilitate the planning of a larger study that is endorsed at both leadership and operational levels so that the potential benefits of the interventions can reach patients in a more timely fashion.

Discussion

Expected Results

The results of the study will provide important information about the effectiveness of group CBT and or group exercise in the treatment of MDD. This will augment the literature in this area and also provide practical examination to see if benefits can be derived from the addition group treatment modalities to TAU. Currently, patients with MDD referred to addiction and mental health clinics in Edmonton Zone may wait for weeks before receiving care from a health care professional in a one-to-one setting. Long wait may negatively impact patients' well-being, personal and occupational function, and satisfaction with care, and a group-based treatment may serve as an alternative for patients with MDD, which can be more expediently accessed.

The results of the pilot trial may inform the implementation of a multicenter clinical trial and provide useful information for administrators and clinicians who are interested in incorporating these interventions into existing care. The investigators expect that the pilot findings will inform and support administrative decision making with regard to further scaling and studying the intervention within the province of Alberta and beyond.

Strengths of This Study

The following are the strengths of this study:

- Randomization of participants will ensure that patients in the three treatment arms have fairly similar psychiatric morbidity at baseline.
- Blinding of the outcome assessors and the use of self-rating scales for the primary outcome measures will ensure the elimination of bias in the outcome measures.

Limitation of This Study

The rather small sample size may reduce the power of the study, which will limit the ability of the study to detect differences in outcome measures among participants in the three treatment arms.

Acknowledgments

The study team thanks Cathy McAlear for her initial contribution to the exercise component of the trial design. This work was supported by a Pfizer Depression grant (via the Department of Psychiatry, University of Alberta), and support was received from AHS.

Authors' Contributions

The study was conceived and designed by VA who also contributed to drafting the initial and final drafts of the manuscript. MY, MH, and LU contributed to the study design and drafting the initial and final drafts of the manuscript. PC, MS, JM, RS, DP, KD, LL, DT, JK, PC, DS, JC, JB, KH, DL, LF, AD, SD, SS, and AA contributed to the study design and revising the initial draft of the manuscript. All authors approved the final draft of the manuscript before submission.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Gantt chart for group cognitive behavioral therapy and exercise project.
[DOCX File , 15 KB - resprot_v9i5e14309_app1.docx]

Multimedia Appendix 2
Outcome measures.
[DOCX File , 17 KB - resprot_v9i5e14309_app2.docx]

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Abbreviations

AHS: Alberta Health Services
CBT: cognitive behavioral therapy
DSM-5: Diagnostic and Statistical Manual of Mental Disorders, 5th Edition
MDD: major depressive disorder
PAR-Q: Physical Activity Readiness Questionnaire
TAU: treatment-as-usual

Edited by G Eysenbach; submitted 28.04.19; peer-reviewed by E Kleiman, A Parks, N Van-Zalk; comments to author 29.09.19; revised version received 13.10.19; accepted 15.10.19; published 25.05.20.

Please cite as:
Yekrang Safakar M, Hrabok M, Urichuk L, Juhas M, Shalaby R, Parmar D, Chue P, Snaterse M, Mason J, Tchida D, Kelland J, Coulson P, Sosdjan D, Brown J, Hay K, Lesage D, Paulsen L, Delday A, Duiker S, Surood S, Abba-Aji A, Agyapong VIO
Effectiveness of Group Cognitive Behavioral Therapy and Exercise in the Management of Major Depressive Disorder: Protocol for a Pilot Randomized Controlled Trial
JMIR Res Protoc 2020;9(5):e14309
URL: https://www.researchprotocols.org/2020/5/e14309
doi:10.2196/14309
PMID:32449684

Protocol

A Smartphone App–Based Mindfulness Intervention for Cancer Survivors: Protocol for a Randomized Controlled Trial

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Abstract

Background: Cancer patients transitioning to survivorship after completing cancer treatments need psychosocial interventions to manage stressors such as anxiety, depression, and fear of cancer recurrence. Mindfulness-based interventions (MBIs) are effective for treating these symptoms; however, cancer survivors are often unable to participate in face-to-face interventions because of difficulties such as work and family commitments, treatment-related side-effects, scheduling conflicts, and geography. Smartphone app–based MBIs are an innovative way to deliver psychosocial cancer care and can overcome several such difficulties, since patients can participate at their own convenience.

Objective: The SEAMLESS (Smartphone App–Based Mindfulness Intervention for Cancer Survivors) study aims to evaluate the efficacy of a tailored app-based mindfulness intervention for cancer survivors (the *Am* Mindfulness-Based Cancer Survivorship—MBCS—Journey) for treating (1) symptoms of stress (primary outcome), as well as (2) fear of cancer recurrence, anxiety, depression, fatigue, and overall physical functioning (secondary outcomes). This is the first Canadian efficacy trial of a tailored mindfulness app intervention in cancer survivors.

Methods: This is a randomized waitlist-controlled trial, which will evaluate the effectiveness of *Am* MBCS for impacting the primary and secondary outcomes in cancer survivors who have completed all their cancer treatments. Outcomes will be assessed using web-based surveys with validated psychometric instruments at (1) baseline, (2) mid-intervention (2 weeks later), (3) immediately postintervention (4 weeks), (4) 3 months postbaseline, (5) 6 months postbaseline, and (6) 12 months postbaseline. The waitlist group will complete all assessments and will cross over to the intervention condition after the 3-month assessment. In addition, data will be obtained by the smartphone app itself, which includes users' engagement with the app-based intervention, their emotional state (eg, angry and elated) from a user-inputted digital emotion-mapping board, and psychobiometric data using photoplethysmography technology.

Results: The study received ethics approval in September 2018 and recruitment commenced in January 2019. Participants are being recruited through a provincial cancer registry, and the majority of participants currently enrolled are breast (44/83, 53%) or colorectal (17/83, 20%) cancer survivors, although some survivors of other cancer are also present. Data collection for analysis of the primary outcome time-point will be complete by September 2019, and the follow-up data will be collected and analyzed by September 2020. Data will be analyzed to determine group differences using linear mixed modelling statistical techniques.

Conclusions: Cancer care providers are uncertain about the efficacy of app-based mindfulness interventions for patients, which are available in great supply in today's digital world. This study will provide rigorously evaluated efficacy data for an app-based

mindfulness intervention for cancer survivors, which if helpful, could be made available for psychosocial care at cancer centers worldwide.

Trial Registration: ClinicalTrials.gov NCT03484000; https://clinicaltrials.gov/ct2/show/NCT03484000

International Registered Report Identifier (IRRID): DERR1-10.2196/15178

(JMIR Res Protoc 2020;9(5):e15178) doi:10.2196/15178

KEYWORDS

mobile health; psycho-oncology; mindfulness; mind-body therapies

Introduction

Background

Previous research suggests that cancer survivors in Canada have several unmet psychosocial needs after completing treatments, which differ from patients newly diagnosed or undergoing treatment [1]. Almost half of all cancer survivors experience symptoms from late and long-term effects of treatments such as fatigue, pain, and distress [2]. Concurrently, they must deal with psychosocial stressors such as anxiety, depression, uncertainty about the future, and fear of cancer recurrence as they transition back to their previous roles and responsibilities at home and in the workplace; these factors can impair their quality of life, performance at work, and their ability to contribute to society [3,4]. Furthermore, the number of cancer survivors in Canada continues to rise due to rapid advances in early detection and treatments for cancer in an aging population. The most recent data suggest there are over 800,000 Canadians living with a history of cancer diagnosed in the previous 10 years [5]. Moreover, these numbers are expected to increase since survival data indicate 60% of Canadians with the top 4 most common cancer diagnoses are expected to survive at least 5 years postdiagnosis [6].

Similar trends of rising numbers of cancer survivors have been reported in the United States, and the world over [2]. Thus, cancer survivors globally can benefit from innovative interventions that address their unique psychosocial needs during survivorship. A growing body of evidence supports the efficacy of a range of mind-body therapies in alleviating these and other symptoms in cancer patients and survivors [7]. Among these therapies, mindfulness-based interventions (MBIs) have demonstrated significant efficacy in impacting psychosocial and physical health in the cancer population, such as the Mindfulness-Based Cancer Recovery (MBCR) program, a 9-week group behavioral treatment program that trains participants in mindfulness techniques through meditation and gentle movement practices [8].

The investigators on this research team LC and MS have studied MBCR for the past three decades and have tested its efficacy in a range of studies and groups of people with cancer, with success in impacting a range of biological and psychosocial outcomes including, but not limited to, symptoms of stress, quality of life, and mood disturbance [8-10]. This body of work on MBCR has spanned basic mechanistic research to clinical trials and implementation science. Most research studies of this nature have tested MBIs such as MBCR when delivered face to face in a group-based setting, although a variety of online-based and digitally adapted MBIs are now available to patients through smartphone apps [11]. Mobile app–based MBIs for cancer patients and survivors allow for considerable flexibility and appeal, especially since they eliminate the need for travel time and problems due to scheduling conflicts [11,12].

Digital Health Interventions in Cancer Care

One of the most significant social and economic changes in the modern world has been the use of computer technology and the internet. Recent data indicate that 76% of Canadians now own a smartphone device with data connection across all demographic groups, and the numbers are projected to increase consistently [13,14]. The popularity of this medium is of great interest for health practitioners, researchers, and policy makers considering the wide-ranging capabilities of smartphone devices. In the field of cancer care, reviews of internet and smartphone app–based interventions for cancer patients and survivors have suggested that cancer patients find these interventions to be highly acceptable and feasible [15,16]. Furthermore, psycho-oncology researchers have advocated for more research with psychosocial interventions that can be delivered using the internet and smartphone apps in the cancer population [15-17].

Benefits of App-Based and Online Mindfulness Interventions

App-based and online mindfulness-based interventions circumvent problems with traditional face-to-face delivery of MBCR such as work schedules, conflicts with other appointments, lack of childcare, and residing far from treatment centers in remote locations. Another potential benefit of app-based and online mindfulness interventions in cancer care is the considerable cost savings for the health care system without compromising on the quality of care, as online and artificial intelligence technologies can simulate the real-world experiences; in addition, studies have shown these interventions to be highly feasible and acceptable. For example, authors LC and MS conducted a feasibility trial of online MBCR, which found that more than 80% of participants completed the online MBCR program, and a 10% response rate to recruitment letters was achieved (the target was 5%) [18]. Also, recent systematic reviews and meta-analyses of app-based mindfulness interventions in the cancer population report high feasibility and acceptability; albeit engagement is an important variable to consider for intervention success [16,19,20].

However, while there are hundreds of commercially available mindfulness training apps, eg, *Headspace*, *Calm*, and *10% Happier* [21,22], only *Headspace* has been customized for cancer patients and been scientifically evaluated [21]. Data from

a randomized waitlist-controlled trial and a prospective cohort study of *Headspace* have demonstrated good overall efficacy for improving outcomes such as quality of life and anxiety in women diagnosed with breast cancer [21,23]. However, the overall science of app-based MBIs is still in its early stages and far from achieving consensus about efficacy of intervention platforms, as well as understanding mechanisms of action [12,17]. For example, this is demonstrated by a randomized trial of *Headspace* with college students that reported no effects for the mindfulness component of *Headspace's* app-based program [24].

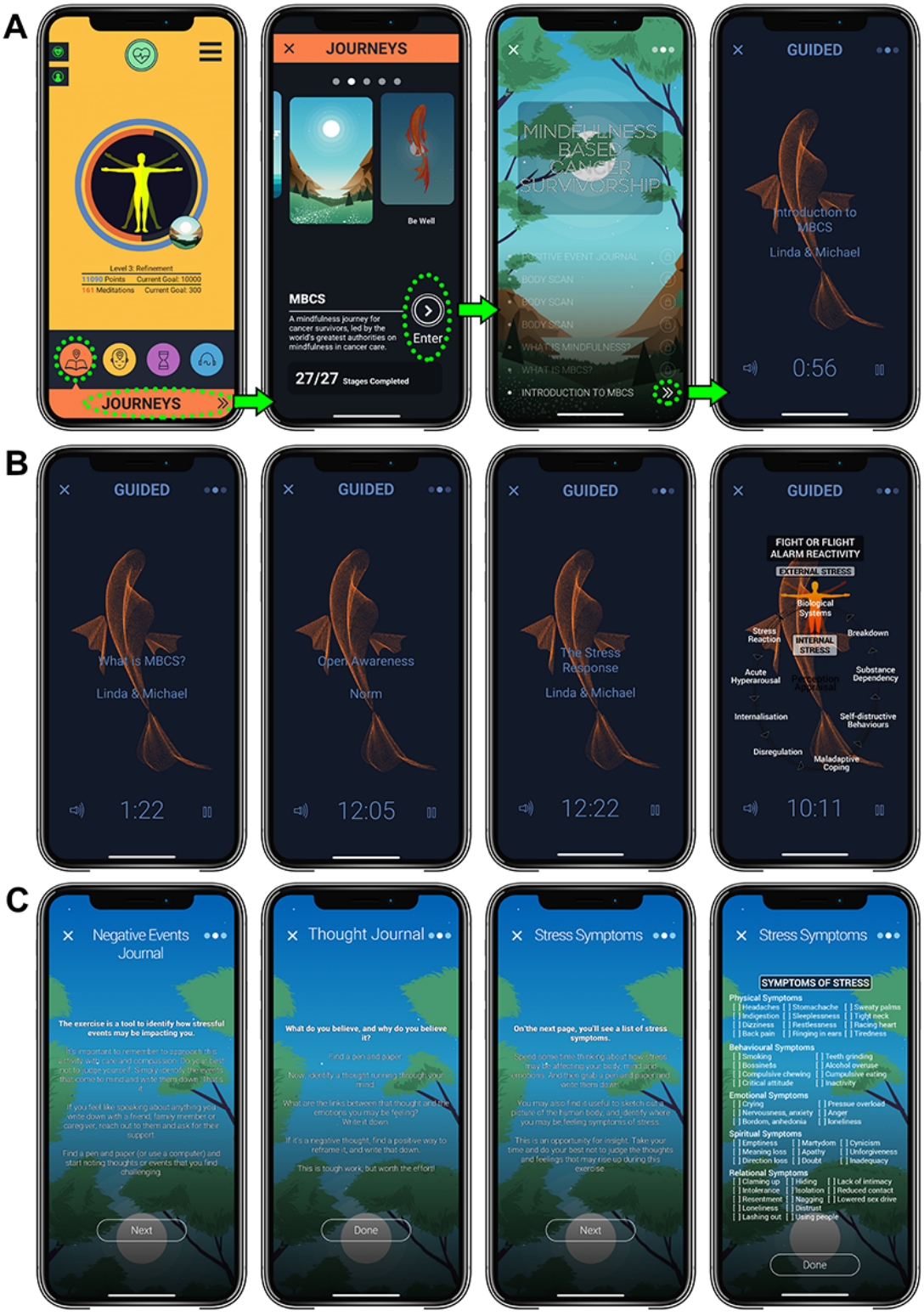
Furthermore, *Headspace's* audio content is exclusively voiced and delivered by the app's founder in a monologue format [25]. This approach may not connect with all cancer patients and survivors, considering the importance of the patient-psychotherapist relationship in determining the success of any psychotherapeutic practice [26,27]. Also, cancer patients and survivors are more inclined to accept and utilize content created and delivered by clinical experts, for reasons such as source credibility and condition-specific content [28-30]. The research team for this study was interested in developing an app-based MBI for cancer survivors that simulated the interactive dialogic approach used in the MBCR program. The research team chose to evaluate the *Am Mindfulness* app as it could potentially address the gaps in the design and delivery of app-based MBIs for the cancer population.

Am Mindfulness is a readily editable digital platform with audio and visual capabilities and its content can be updated and modified with automatic app updates. *Am Mindfulness* was developed and is maintained by Mobio Interactive (MI) Inc. [31], a Canadian technology company based in Toronto, Canada, cofounded by MT and BS; user data are maintained on secure servers in Canada and meet security and Health Insurance Portability and Accountability Act privacy standards required for medical data. The name for *Am Mindfulness*, referred to simply as, *Am*, and pronounced "ahm" was chosen by MI for several reasons. First, "am" is the present tense of the verb "to be," which is a linguistic embodiment of mindfulness given the high emphasis that mindfulness practices place on observing the present moment. Second, because of how "Am" is pronounced, it sounds similar to both the word for "soul" in French ("âme") and the chant "ohm" used in ancient meditative practices from India. Finally, the name "Am" is relatively simple and less likely to bias individuals on the app's purpose or offering in the way that names for other meditation-focused apps such as "Calm" or "Smiling Mind" may.

The design of *Am Mindfulness* allows for considerable flexibility with delivering content in real time through the "Journeys" app feature. Each app-based "Journey" involves a sequence of custom audio tracks, visuals with text and in-app exercises designed with a particular objective, eg, mindful survivorship. The content of a "Journey" can be seamlessly introduced and refined for a patient population in real time. MI describes their major motivation for creating the "Journeys" feature in *Am Mindfulness* as their commitment to create and deliver diverse content voiced over by clinical experts, in addition to mindfulness practitioners, to address the needs of specific patient populations [32]. Evidence from a recent randomized trial with a prerelease version of the *Am Mindfulness* app (called *Wildflowers*) has demonstrated efficacy evidence for reducing anxiety in college students before a stressful event of an examination [33].

In this project, the *Am* Mindfulness-Based Cancer Survivorship (MBCS) journey was developed and recorded in the voices of MBCR program facilitators LC and MS. Several audio tracks in the *Am* MBCS journey have a dialogue and interaction between LC and MS, who are clinical psychologists and leading experts on mindfulness-based cancer recovery, having developed and scientifically evaluated the MBCR program together for over 20 years. Details of the *Am* MBCS journey are described in the *Intervention* section and illustrated in Figure 1. In this study, we intend to test the efficacy of the *Am* MBCS Journey, referred to hereon as *Am* MBCS, to reduce stress in cancer survivors. As secondary objectives, we will investigate the feasibility of recruitment as well as the usability of the app and in-app data on specific usage patterns.

Figure 1. The Mindfulness Based Cancer Survivorship (MBCS) Journey Contained within *Am*. (A) Navigation menu. (B) Core audio content (C) In-app exercises.

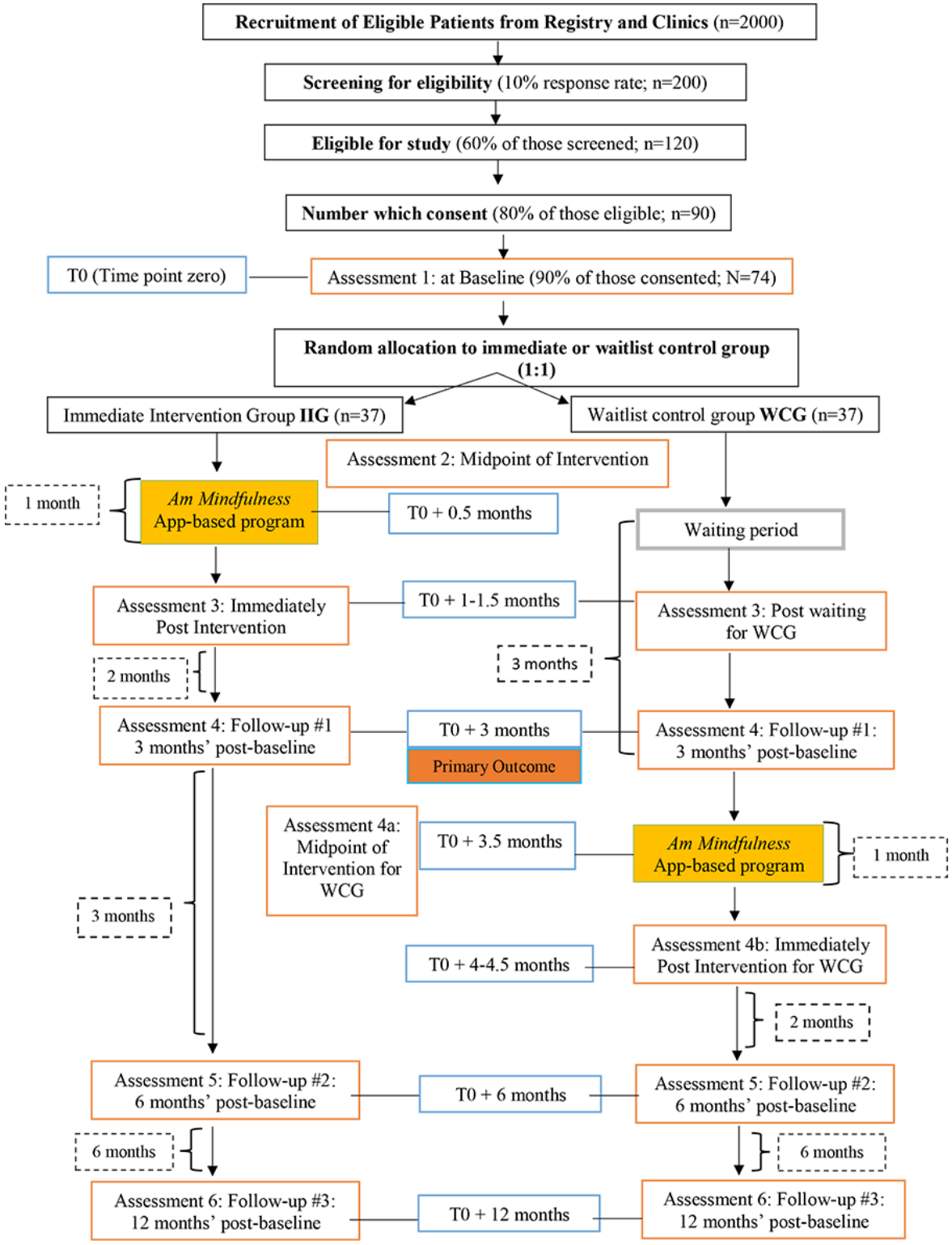


Methods

Study Design

The study is a two-armed randomized waitlist-controlled design with 1:1 allocation to treatment (immediate *Am* MBCS app group) or control (waitlist usual care) arms, with assessments at six time points: (1) baseline, (2) mid-intervention (2 weeks later), (3) immediately postintervention (4 weeks), (4) 3 months postbaseline, (5) 6 months postbaseline, and (6) 12 months postbaseline. A detailed study flowchart is shown in Figure 2. This is an open-label trial, as blinding to interventions is most often not possible in psychosocial intervention research.

Figure 2. SEAMLESS Study Flow Chart. Includes study design, stage, and all time points of data collection for study assessments.



Participants

Cancer survivors with any type of cancer who have completed their active treatments at least 2 weeks before recruitment in this study will be included. Inclusion criteria are intentionally broad to be pragmatic and improve generalizability to the real world. Refer to Table 1 for detailed rationale for each inclusion and exclusion criterion.

Table 1. Inclusion and exclusion criteria.

Criteria	Rationale and notes
Inclusion	
(1) Men and women over the age of 18 years	Both men and women are included to broaden the generalizability of results and allow sex comparisons. All participants must be adults.
(2) Completed all cancer treatments 2 weeks before enrollment	A brief period of time is required for patients to recuperate after their last treatment, before starting a new intervention.
(3) Access to a smartphone with data connection	Patients will require access to a smartphone to participate. The study team will communicate primarily by phone, text message, and email. In case some patients' do not have a data plan or an insufficient data plan with their smart phone, we will pay for their data connection (up to 0.5 GB/month).
(4) Willing to give time for mindfulness practice	Patients need to have the motivation to devote approximately 20 to 30 min daily, which is equal to 5 to 7 sessions a week over the course of 1 month to do the mindfulness meditations and practices.
(5) Sufficient ability to speak and read English	The audio lectures and meditations and assessments will be conducted in English, so participants must be able to understand the audio and fill out the questionnaires.
(6) Willingness to be randomized into immediate or waitlist groups and complete all assessments	People must be comfortable with potentially having to wait to get access to the app-based program for another 3 months, as well as be motivated to give 30 to 40 min of their time to complete the online survey assessments.
Exclusion	
(1) Suffering from current major depressive disorder, or other psychiatric disorder (self-reported) that would interfere with the ability to participate	Evidence indicates that participants with active psychological disorders should be first treated for these problems individually, before engaging in experimental mental health and meditation programs of this nature, which are not intended to treat these disorders.
(2) Currently engaging in mindfulness meditation one or more times per week	To ensure sample homogeneity, the study will include participants who are NOT currently practicing mindfulness, using an app or otherwise. However, this would not exclude everyone who may have casually experimented with the aforementioned interventions in the past.
(3) Cognitive impairment that would interfere with completing questionnaires or the intervention; <6 on the Brief Screen for Cognitive Impairment (BSCI) [3]	People require enough cognitive capacity to complete the questionnaires, navigate and listen to the app and complete homework independently. The BSCI only rules out those with significant cognitive impairment and will not exclude those with the milder cognitive impairment associated with cancer-related "brain fog."

Recruitment

Potential participants will be recruited at a comprehensive cancer center in Western Canada from a Provincial Cancer Registry.

Alberta Cancer Registry

The Alberta Cancer Registry (ACR) is a population-based registry, established in 1942, that records and maintains data on all new cancer cases and cancer-related deaths occurring in the province of Alberta. The registry records information about the type of cancer and cancer treatments, as well as personal information, such as name, date of birth, sex, provincial health care number, and postal code. The ACR will contact all potential participants on behalf of the research team with a study information letter with the research team's contact information. Potential participants will include patients diagnosed with any type of cancer, who completed their treatments at least 2 weeks prior and who reside outside the Calgary metropolitan region. The geographical criteria were chosen to access cancer survivors in urban and rural areas of Alberta that are distant from the University Health Center, as most mindfulness-based programs and studies have been mainly accessible for residents of the Calgary metropolitan region due to its proximity to the University Health Center. The ACR's method of contact ensures patient privacy and provides patients the choice to participate in the study. Interested participants will then contact the research team, and then are further screened for inclusion criteria.

Sample Size

In previous studies with face-to-face group MBCR, we have observed medium effects for symptoms of stress (measured by the Calgary Symptoms of Stress Inventory [C-SOSI]) as the primary outcome and expect similar effects in this study. Also, recent meta-analyses of MBIs and psychosocial stress outcomes have demonstrated a similar medium standardized effect size of Cohen d=0.5 for stress [34]; also, most MBI studies collect their primary outcome at 3 months postbaseline as most mindfulness interventions span 6 to 10 weeks [7,34]. For this study, we therefore used a medium effect size (f=0.25) to conduct an a priori sample size calculation using the software G*Power 3.1.9.3 developed and maintained by researchers at Heinrich Heine University Düsseldorf [35]. The other parameters for estimating the sample size included, a standard type-1 error rate, α=.05, and a low risk of type-2 error, power (1-β)=.95, to detect interaction effects between time points (baseline and 3 months postbaseline) and group (intervention and control) using a repeated measures analysis of variance with correlation among repeated measures assumed to be 0.5 and nonsphericity correction ε=1. The total required sample size reported by G*Power was 54 participants to detect such an interaction effect.

In addition, based on our previous experience with online and in-person MBI trials and previous app-based studies

[10,18,20,34,36], we assumed approximately 20% attrition and 10% to 15% probability of missing data. Therefore, we oversampled for this study accordingly. Hence, the final total sample size we aim to recruit in this study is N=74, with n=37 in the immediate intervention arm and n=37 in the waitlist control arm. Please refer to Figure 2 for the study flowchart that describes estimated sample size calculations at each assessment.

Randomization

Participants will be randomized by the study statistician, by generating participant ID numbers and group allocations for the entire study in advance using a random number generator program in SPSS. Block lists of randomized participant IDs will then be uploaded to the Research Electronic Data Capture (REDCap) randomization module, which will allow the study staff to provide immediate group allocation to participants after completion of consent procedures. Only the study statistician will develop the group assignments, which are locked by REDCap after upload, to prevent selection bias. Randomization will occur after the baseline assessment, and those in the immediate *Am* MBCS intervention group will get a text message and email containing the link to download the *Am Mindfulness* app, from the Android or Apple app store. The waitlist control group will be informed that they will need to wait for the intervention and will be contacted when they can download the *AmMindfulness* app and start the intervention.

Informed Consent Procedures

Informed consent will be obtained electronically through the secure, web-based app designed to support data capture for research studies, REDCap, which is supported by the technology team at the University of Calgary, Canada, where this research is being conducted. REDCap's web-based app uses secure two-factor web authentication, data logging, and secure sockets layer encryption that ensures the security and confidentiality of private information for obtaining informed consent [37]. An email with a survey link will be sent to the participant. After the participant clicks on the link for the study from their email client, the first page of the REDCap survey for this study will open in a new window or tab and will contain the details of the informed consent form. Participants will check the box "Yes" that asks them whether they completely understood the terms of their voluntary participation in the study.

Participants will then actively provide electronic consent to the study by clicking on the "Agree" button, which will be preceded by stating that, "Clicking on the 'Agree' button below indicates that (1) you have read the informed consent information, (2) you voluntarily agree to participate, and (3) you are at least 18 years of age." Participants will also have the option to opt out of the study by clicking the "Disagree" button, which will be followed by the statement, "If you do not wish to participate in the research study, please decline participation by clicking on the 'Disagree' button."

Only those participants that click on "Agree" will be able to proceed with completing the rest of the questionnaires. Participants will be able to download and save a PDF version of the consent form for their records. Participants will enter their name, email, and cellphone number after completing the form. After participants provide their online consent, they will be asked to complete the baseline measures online on REDCap. Subsequently, participants will be sent a study welcome email, which will contain orientation material and instructional pictures and videos about how to use the *Am* app, and instructions for the 4-week intervention. In addition, the study staff will also conduct a study orientation phone call to guide participants to using the app with ease.

Intervention

The Am Mindfulness-Based Cancer Survivorship Journey

Am Mindfulness ("Am"; second generation of the app, *Wildflowers Mindfulness*) supports a personalized mindfulness practice through guided meditations, audio lectures and discourses, reminders, a timer to facilitate self-guided meditation, journaling features, and psychobiometric recordings and feedback. The *Am* app is currently available in four languages (English, Mandarin, Dutch, and German) and can be viewed and downloaded from the Android and Apple app stores with the platform-agnostic link [38]. Within *Am*, study participants will be instructed to access the *Am* MBCS journey. *Am* MBCS has a total of 27 steps that include, audio-recorded lectures, guided meditations such as body scans, and writing an events journal; see Figure 1 to screenshots of the *Am* MBCS journey contents. The curriculum is based on our previous experience with the evidence-based MBCR program and related meditations, which is described under 5 discrete units of learning in Table 2. The content of the audio instruction by LC and MS is similar to that delivered in the in-person classes on these units, with examples specific to situations and symptoms common for people living with cancer. Common topics such as coping with pain, insomnia and fear of cancer recurrence are included.

Participants will be encouraged to participate in the app-based activities for 20 to 30 min every day, with a minimum of 4 days in a week, over a period of 4 weeks. To promote engagement with the app-based program, user data will be tracked confidentially (see the section on *Feasibility, Acceptability, Adherence, and Contamination*) and users with low engagement will be sent text messages to promote app usage, eg, "Please remember to listen to your *Am* MBCS mindfulness recordings for today." Text messages will be delivered using the secure communications platform, Twilio [39]. Also, the research team will monitor participant engagement metrics on a daily basis, and low or nonengaged users will receive a phone call with support for problem solving. In addition, *Am Mindfulness* also sends users regular push notifications, which appear as motivational messages on the user's mobile screen that may also promote engagement.

Patients using the app can also access the meditations on *Am* through the app's "Library" feature, which contains all the meditations on the app indexed by author and name. Although some meditations are perpetually free, users need to pay for the full selection of guided sessions and biofeedback technology; therefore, participants in this study will be provided with a 12-month paid subscription to the *Am* app.

Table 2. App-based mindfulness-based cancer survivorship curriculum.

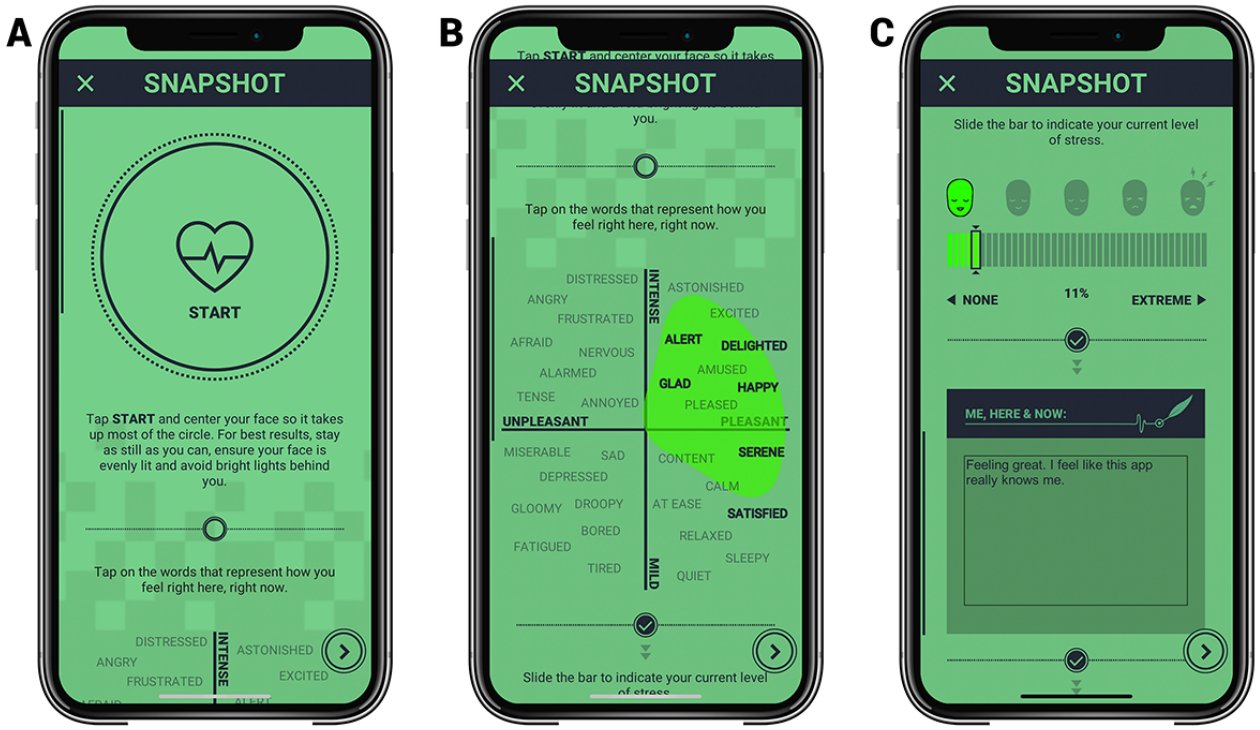
Unit #	Topics or focus of module	Meditation	Exercise
1	What is mindfulness; why mindfulness for cancer?; belly breathing exercise; introduction to Body Scan with focus on cancer-related changes in the body.	Body Scan (short)	Positive events journal
2	Mindful attitudes (nonjudgment, acceptance, nonattachment) in the context of cancer.	Mindfulness of breath and mindful movement	Negative events journal
3	Stress response; biology of stress, stress and cancer; link between inner narrative and chronic stress; sleeping well exercise.	Mini breathing exercises, mindful movement, and walking meditation	Symptoms of stress checklist or mapping stress on the body
4	Stinkin' Thinkin'; maladaptive stories we tell ourselves; common cognitive distortions with cancer-related examples; coping with thoughts and fears of cancer recurrence.	Open awareness	Thought log
5	Introduction to guided imagery; using imagery to cultivate loving kindness toward the suffering of self and others.	Mountain meditation and compassion meditation Body Scan (long)	Intention or plan moving forward

Am's App-Based Stress Measurement

The *Am* app also has four innovative stress measurement features that serve as exploratory outcomes for this trial. First, cognitive stress is objectively quantified via a 30-second "selfie" video that uses an algorithm to extract heart rate and heart rate variability from the biosignals inherent to the human face using photoplethysmographic imaging principles [40]. The amount of cognitive stress is determined via deep neural networks trained on tens of thousands of video and stress pairings and has reported 86% accuracy for determining an individual's stress as "very low," "medium low," "medium high," and "very high" [41]. Second, emotional stress levels are obtained via a digital 4-quadrant emotion mapping board (mood board) that lists emotions such as "happy," "sad," and "tense" ranging on one axis from unpleasant to pleasant, and along another axis from mild to intense; see Figure 3 for screenshots of the in-app stress assessments. Each emotion listed within the mood board is associated with a score that is not disclosed to the user and used to calculate mood. Third, subjective stress is obtained via a slider ranging from "none" to "extreme." Fourth, personal notes are input using an open field text box. The output of the mood board and stress slider provides data that have been benchmarked to standard psychological surveys [33].

The *Am* app uses secure web authentication, data logging, and encryption that ensures security and confidentiality of any personal identifiable information and in-app data. *Am* and its previous version *Wildflowers* have together received approximately 100,000 downloads and *Am* is rated 4.8 stars from 23 reviews in the Canadian Apple app store as of July 30, 2019.

Figure 3. In-App Psychobiometric Assessments within *Am*. (A) "Selfie" video using photoplethysmography technology to quantify stress; (B) "Mood board" containing 32 emotion words and "stress slider" for stress self-assessment; and (C) "Journaling" feature to input experiences.



Procedures

Experimental Group

Participants will be provided a 12-month paid subscription to *Am*. The first month of this *Am* subscription is dedicated to the study intervention. Users will be encouraged to participate in the app-based activities for 20 to 30 min every day, with a minimum of 4 days in a week, after which they will get reminder notifications.

Waitlist Control Group

Participants will receive treatment as usual, followed by a delayed (waitlist) intervention of the same *Am* MBCS app-based intervention after the 3-month postbaseline assessment of the *Am* app intervention group (see Figure 2). Control group participants will get access to the *Am* app only after completing their 3-month waiting period.

Trial Registration and Reporting

This trial has been registered at the ClinicalTrials.gov database of privately and publicly funded clinical studies [42]. The results will be reported as per the updated Consolidated Standards of Reporting Trials (CONSORT) eHealth checklist [43] version 1.6.1. and will follow guidelines and the flow diagram for reporting nonpharmacological treatments [44].

Outcome Measures

The outcome measures employed in this study include a series of well-validated psychometric instruments for assessing a variety of psychosocial constructs. See Table 3 for a detailed description of outcomes. We will also use the standardized outcome measures available from the Patient-Reported Outcomes Measurement Information System (PROMIS), which is a set of person-centered measures that evaluate physical and psychosocial health in adults and children [45]. The advantage of using PROMIS measures is that they are psychometrically sound and have been created to be relevant across all conditions for the assessment of symptoms and functions [45]. Finally, we are also going to obtain and analyze the data from the *Am* app with regard to the user's self-report, biometrics, and engagement. The entire battery of questionnaires will be completed securely online and requires approximately 30 to 45 min.

Table 3. Outcome measures.

Construct	Measure (abbreviation)	Description
Screening measures		
Cognitive function	Brief Screen for Cognitive Impairment (BSCI) [46]	The BSCI consists of 3 items which are asked to the patient over the phone. The first item on the BSCI consists of a memory recall question, and the other 2 items ask about ability to carry out daily tasks without help. The scores obtained from the 3 items are then weighted and summed to arrive at the final BSCI score wherein >6 is significant impairment.
Background measures		
Demographics and medical history	Age, sex, marital status, education, other medical conditions, and medications	Age, sex, marital status, education, other medical conditions, and medications. All these constructs will be assessed using standardized self-report items.
Primary outcome		
Symptoms of stress	Calgary Symptoms of Stress Inventory (C-SOSI) [47]	The C-SOSI is a 56-item scale, derived from exploratory factor analysis on the 95-item Symptom of Stress Inventory (SOSI) collected from cancer patients who attended our MBCS program. A 5-point scale ("never" to "very frequently") is used to rate the frequency of stress-related symptoms in the past week. There is a total score and 8 subscales (depression, anger, muscle tension, cardiopulmonary arousal, sympathetic arousal, neurological or GI, cognitive disorganization, and upper respiratory symptoms), all of which have high internal consistency (0.80 to 0.95), and the total score has good convergent and divergent validity with other well-validated measures.
Secondary outcomes		
Fear of cancer recurrence	Fear of Cancer Recurrence Inventory (FCRI) [48]	FCRI contains 42 items, evaluating 7 components associated with the fear of cancer recurrence: triggers, severity, psychological distress and functioning impairments, insight scale, reassurance, and coping strategies. Each item is measure one a Likert scale ranging from 0 (not at all or never) to 4 (a great deal or all the time). Total score can be obtained from each subscale and a total FCRI score can be obtained by adding the total scores of all subscales, higher scores indicate higher levels of fear of cancer recurrence.
Mindfulness	Mindfulness Attention Awareness Scale (MAAS) [49]	MAAS is a 15-item scale, designed to assess characteristics associated with mindfulness, such as open or receptive awareness of and attention to what is taking place in the present. Participants use a scale from 1 to 6 (almost always to almost never), to indicate how frequently or infrequently they have each experience. Higher scores reflect higher levels of dispositional mindfulness. A thorough validation process has demonstrated the reliability and validity of the MAAS with high internal consistency, α=.86.
Rumination	Rumination-Reflection Questionnaire (RRQ) [50]	The RRQ is a 24-item, 5-point Likert Scale. The rumination subscale of the RRQ assesses recurrent, primarily past-oriented thinking about the self, which is prompted by threats, losses, or injustices to the self. The scale correlates with mindfulness in expected directions and has demonstrated high internal consistency of α=.92.
Experiential avoidance	Acceptance and Action Questionnaire (AAQ) [51]	The AAQ was developed to measure experiential avoidance, the tendency to negatively evaluate internal experiences. (eg, emotions and body sensations), unwillingness to be in contact with such experiences, and the need to control or alter them or the contexts that engender them [51]. The psychometric properties of versions of the AAQ have been well established in clinical (eg, anxiety disorder) and nonclinical samples. The 16-item AAQ that will be used in this study produces a single factor, with acceptable internal consistency, α=.77.
Anxiety	Patient-Reported Outcomes Measurement Information System (PROMIS)-Cancer Bank v 1.0–Anxiety [52]	PROMIS-Anxiety questionnaire assesses the anxiety domains of self-reported fear (fearfulness, panic), anxious misery (worry, dread), hyperarousal (tension, nervousness, restlessness), and somatic symptoms related to arousal (racing heart, dizziness). All PROMIS-Cancer instruments were developed for use with any cancer patient. The PROMIS-Cancer Anxiety item bank contains a total of 22 items, 20 of which are also in the PROMIS-Anxiety item bank, so it can be correlated with studies of other clinical populations. The PROMIS-Cancer Anxiety item bank will be delivered to patients in this study. The PROMIS-Cancer Anxiety has demonstrated high internal consistency (Cronbach α>.9).

Construct	Measure (abbreviation)	Description
Depression	PROMIS-Cancer Bank v1.0–Depression [53]	PROMIS-Depression questionnaire for cancer patients assesses the domains of depression, which include self-reported negative mood (sadness, guilt), views of self (self-criticism, worthlessness), and social cognition (loneliness, interpersonal alienation), as well as decreased positive affect and engagement (loss of interest, meaning, and purpose). Somatic symptoms (changes in appetite, sleeping patterns) are not included. The PROMIS-Cancer Depression item bank contains a total of 30 items, 23 of which are also in the PROMIS-Depression item bank, so it can be correlated with studies of other clinical populations. The PROMIS-Cancer Depression item bank will be delivered to patients in this study. The PROMIS-Cancer Depression has demonstrated high internal consistency (Cronbach α>.9).
Fatigue	PROMIS-Cancer Bank v1.0–Fatigue [54]	PROMIS-Cancer Fatigue measure assesses a range of self-reported symptoms from mild subjective feelings of tiredness to an overwhelming, debilitating, and sustained sense of exhaustion that likely decreases one's ability to execute daily activities and function normally in family or social roles. Fatigue is divided into the experience of fatigue (frequency, duration, and intensity) and the impact of fatigue on physical, mental, and social activities. The PROMIS-Cancer Fatigue item bank contains a total of 54 items, all of which are also in the PROMIS-Fatigue item bank and will be delivered to patients in this study. The PROMIS-Ca Fatigue has demonstrated high internal consistency (Cronbach α>.9) in numerous studies within cancer and other clinical populations [54].
Physical Function	PROMIS-Cancer Bank v1–Physical Function [55]	PROMIS-Physical Function instruments measure self-reported capability rather than actual performance of physical activities. This includes the physical functioning, mobility as well as instrumental activities of daily living, such as running errands. The PROMIS-Cancer Physical Function has items specific to cancer patients and survivors. The PROMIS-Cancer Physical Function item bank contains a total of 45 items, 33 of which are also in the PROMIS-Physical Function item bank [55], and will be delivered to patients in this study. The PROMIS-Cancer Physical Function has demonstrated high internal consistency (Cronbach α>.9).
Return to work	Employment, hours of paid work, ability to work, and rate of return-to-work at 12-months	Self-reported work status will be assessed at each time point including (1) current working status (working full-time; part-time; retired; short- and long-term disability; unpaid homemaker); (2) weekly hours of paid work; and (3) job type using a well-established job classification system. If applicable, participants will be asked at follow-up on what date they returned to paid work.
Exploratory measures		
User self-report	Mood, stress, and intent for mindfulness	Stress: Adjusting a dynamic slider between the minimum score "no stress" and the maximum score "max stress." Mood Board: Participant can select between 1 and 24 "mood words" that indicate how they are feeling, eg, angry, happy, elated, and sad.
User biometrics	Heart rate, respiratory rate, and relative blood oxygen saturation	Photoplethysmographic imaging, which is the measurement of volumetric change observed via the selfie camera of the smartphone, provides data that can be used to infer user biometrics, such as heart rate, respiratory rate, and relative blood oxygen saturation.

Feasibility, Acceptability, Adherence, and Contamination

Feasibility of Intervention

The ACR provides the specific number of potential participants contacted for the study across the province. The number of participants who were invited through the registry, those who contact the team showing interest, as well those screened for eligibility, completion of intervention, and each assessment point will be tracked (see Figure 2). Intervention response rate and overall completion rate will be calculated from the aforementioned data points.

Acceptability, Adherence, and Engagement

The app usage of patients will be tracked through the engagement data from the app, which include session length, identity, type and frequency, points and badges earned, number of page and screen views, mindful activities in the app, total time spent on the mindfulness audio tracks, and number of daily visits to the app. *Am* also records which lessons and meditations participants accessed frequently. Participants with low engagement during the *Am* MBCS intervention period, defined as less than 4 times a week, will get reminder notifications through text message and phone calls with resources for problem solving. Acceptability and adherence to the intervention will be estimated from the engagement obtained from the app and completion rate of outcome assessments

Contamination

A standardized form assessing the use of a range of complementary therapies will be administered at each time point. We will also ask the waitlist control group if they used any other mindfulness or meditation apps during their 3-month waiting period.

Objectives and Hypotheses

Objective 1: Primary Outcome

The first objective is to evaluate the efficacy of the *Am* app–based MBCS program to relieve symptoms of stress (primary outcome).

Hypothesis 1: Compared with controls, the *Am* app–based MBCS program participants will report significantly less symptoms of stress at 3 months postbaseline (primary outcome) assessment.

Objective 2: Secondary Outcomes

The second objective is to evaluate the efficacy of the *Am* app–based MBCS program to decrease the fear of cancer recurrence, anxiety, depression, and fatigue, and to improve overall physical functioning (secondary outcomes) at 3 months postbaseline assessment.

Hypothesis 2: Compared with controls, the *Am* app–based MBCS program participants will report significantly less fear of cancer recurrence, rumination, experiential avoidance, anxiety, depression, and fatigue, and increased mindfulness and overall physical functioning at 3 months postbaseline (secondary outcomes).

Objective 3: Exploratory Outcomes

This includes the exploratory aims as follows: (1) to explore correlations between the self-reported outcome data and the psychobiometric data collected by the *Am* app, (2) to determine changes over time between the *Am* app–based MBCS program and the waitlist control group.

Hypothesis 3: Self-reported data obtained from all participants will significantly correlate with the app-based self-reported stress data and biometric stress data.

Hypothesis 4: To determine the short-term, medium-term, and long-term effects of the *Am* app–based MBCS program with regard to the primary and secondary outcomes collected at all time points.

Data Analysis

Participants will enter data from their home computers or smartphones using the secure REDCap data collection and management system (approved by the University of Calgary and Alberta Health Services). Data will then be transferred into SPSS and or SAS for analysis. Data analyses will utilize linear mixed models (LMM) and intent-to-treat (ITT) principles to assess several planned comparisons across the groups based on identified aims and hypotheses.

Intent-to-Treat Analysis

Data related to recruitment, participation, and dropout rates will be reported according to the guidelines given by the CONSORT-eHealth statement [43]. All participants that entered our study will be included in our analyses and will be retained in the arm (treatment or control) to which they were originally randomly allocated. This study will employ an ITT analysis design, wherein participants who were nonadherent to the protocol will be included in statistical analyses, regardless of their alignment with the inclusion criteria, the treatment they received, and if they withdrew from the intervention protocol (attrition) completely or deviated from the protocol (nonadherence).

Descriptive Statistics

Data will be cleaned, the descriptive statistics of the sample will be assessed, and all variables will be checked for normality of distribution. Descriptive statistics of our sample will be calculated to summarize demographic and disease-related characteristics and check for group differences between groups using Chi-squared and *t* tests. In case data are nonnormal, the Kenward-Roger correction for degrees of freedom will be applied to the LMM. Potential treatment moderators of age, sex, cancer type, cancer stage, and chemotherapy regimen will also be included as possible covariates. We will also conduct correlation and regression analyses to determine correlations between scores of the primary and secondary outcome measures, eg, correlation between C-SOSI and PROMIS-Cancer Anxiety scores, and between secondary outcome measures, eg, correlation between PROMIS-Cancer Fatigue scores and mood words selected by the participant in the *Am* app.

Hypothesis Testing

Hypothesis 1

LMM is a suitable statistical method for this study because of the ability to perform sophisticated statistical imputation of data missing at random in a longitudinal study design. In addition, the LMM also includes mixed effect methods with a random intercept model, which can account for the variances between participants and within participants. Therefore, we plan to use the LMM analyses for testing hypotheses 1 and 2, wherein the LMM will estimate differences between the immediate group and waitlist control group by conducting a group × time interaction analysis with a significance level of $\alpha<.05$. Each of the LMMs will include fixed effects for time (within-subjects factor) and group (between-subjects factor) and a random effect for the participant. Also, the restricted maximum likelihood estimate method in the LMM will be used to estimate the model parameters and standard errors with a compound symmetry covariance structure to account for the correlation between measurements. Data for testing hypothesis 1 will be C-SOSI total scores and subscale scores for 3 months postbaseline. Within- and between-group differences for the immediate and waitlist groups revealed by the LMMs will be reported with respective *P* values and the specific model effects, *F* (*df*).

Hypothesis 2

Similar to hypothesis 1, for hypothesis 2, we will use the same LMMs to test for within- and between-group differences for the secondary outcomes.

Hypothesis 3

For hypothesis 3, linear and curvilinear multiple regression models will be used, along with simple Pearson correlations to detect associations between the primary and secondary self-reported outcomes and the exploratory outcomes obtained from the app data.

Hypothesis 4

The short-term (2 weeks and 1 month postbaseline), medium-term (3 and 6 month postbaseline), and long-term (6 and 12 month postbaseline) longitudinal changes in the primary and secondary outcomes will be determined using the LMM quadratic model regressions. To account for the correlation between measurements, the restricted maximum likelihood estimate method in LMM will be used to estimate the model parameters and standard errors with a compound symmetry covariance structure. In addition, analyses with data nesting within participants will also be conducted that will control for the invariant part of each participant's scores. The LMM regression weights (β) as well LMM regression coefficients will be reported along with a quadratic regression graph including all time points of data collection.

Results

Recruitment commenced in January of 2019 and the target sample for enrollment was reached on May 2, 2019. Currently 83 patients have consented and enrolled in the study and are in various stages of their assessments and programs. Anticipated date for the completion of primary outcome data collection is August 1, 2019. Also, data collection for the entire trial is expected to be completed by May 2020.

Discussion

Limitations

Considering app-based mindfulness interventions in cancer care are still in the early stages of design and testing, this study has certain design- and intervention-related limitations. First, regarding study design–related limitations, this trial included survivors of all cancer types and stages, which results in high levels of variability of symptoms and cancer-related side effects, which may impact the internal validity of the trial and mask treatment-related effects because of the intervention. However, as the ultimate aim of this research is to reach all cancer survivors regardless of geography, the inclusion criteria were intentionally kept broad to mirror the real-world usage. Second, in terms of the intervention, we selected a 4-week duration for the app-based mindfulness program based on a similar app-based study of a previous version of *Am Mindfulness*, called *Wildflowers*, with anxious college students [33]. This 4-week length of the app-based program may not be long enough for cancer survivors, especially those who are completely new to mindfulness meditation and related stress management techniques. Indeed, in-person mindfulness programs for cancer survivors have been between 6 and 9 weeks [8,11,56]. Future research into dose-response efficacy of app-based mindfulness interventions in the cancer population is needed to provide an evidence-based duration for app-based mindfulness programs in cancer care.

Conclusions

This study has the potential to provide a large-scale delivery tool for mind-body therapies to effectively reach cancer patients and survivors the world over. Cancer patients are often unable to successfully participate in face-to-face group programs for a variety of reasons. A smartphone app–based mindfulness program can overcome several difficulties faced by cancer survivors with participating in mindfulness interventions. Patients can participate from home in real time without the added burden of travel, parking, and walking to classes. If effective, this type of low-cost, mobile app–based intervention would be readily welcomed by patients and could easily be translated into clinical practice to reach a large number of patients and survivors, no matter where they reside, including those in remote locations.

Acknowledgments

This study is funded by the Enbridge Research Chair in Psychosocial Oncology and a Canadian Institutes of Health Research, Strategy for Patient Orientated Research Mentorship Chair in Innovative Clinical Trials, awarded to LEC.

Conflicts of Interest

Two coinvestigators on this project, MT and BJS, are the cofounders of MI and are majority shareholders of the company at approximately 40% each. One coinvestigator, NASF, is an advisor for MI and holds <1% of the company's stock. The remaining authors declare no conflicts of interest.

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Abbreviations

ACR: Alberta Cancer Registry
CONSORT: Consolidated Standards of Reporting Trials
C-SOSI: Calgary Symptoms of Stress Inventory
ITT: intent to treat
LMM: linear mixed model
MBCR: Mindfulness-Based Cancer Recovery
MBCS: Mindfulness-Based Cancer Survivorship
MBI: mindfulness-based interventions
MI: Mobio Interactive Inc
PROMIS: Patient-Reported Outcome Information System
REDCap: Research Electronic Data Capture

Edited by G Eysenbach; submitted 19.08.19; peer-reviewed by E Kent, C Roos; comments to author 15.10.19; revised version received 27.11.19; accepted 04.02.20; published 11.05.20.

Please cite as:
Subnis UB, Farb NAS, Piedalue KAL, Speca M, Lupichuk S, Tang PA, Faris P, Thoburn M, Saab BJ, Carlson LE
A Smartphone App–Based Mindfulness Intervention for Cancer Survivors: Protocol for a Randomized Controlled Trial
JMIR Res Protoc 2020;9(5):e15178
URL: https://www.researchprotocols.org/2020/5/e15178
doi:10.2196/15178
PMID:32390591

Protocol

Optimization of Upper Extremity Rehabilitation by Combining Telerehabilitation With an Exergame in People With Chronic Stroke: Protocol for a Mixed Methods Study

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Abstract

Background: Exergames have the potential to provide an accessible, remote approach for poststroke upper extremity (UE) rehabilitation. However, the use of exergames without any follow-up by a health professional could lead to compensatory movements during the exercises, inadequate choice of difficulty level, exercises not being completed, and lack of motivation to pursue exercise programs, thereby decreasing their benefits. Combining telerehabilitation with exergames could allow continuous adjustment of the exercises and monitoring of the participant's completion and adherence. At present, there is limited evidence regarding the feasibility or efficacy of combining telerehabilitation and exergames for stroke rehabilitation.

Objective: This study aims to (1) determine the preliminary efficacy of using telerehabilitation combined with exergames on UE motor recovery, function, quality of life, and motivation in participants with chronic stroke, compared with conventional therapy (the graded repetitive arm supplementary program; GRASP); (2) examine the feasibility of using the technology with participants diagnosed with stroke at home; and (3) identify the obstacles and facilitators for its use by participants diagnosed with stroke and stroke therapists and understand the shared decision-making process.

Methods: A mixed methods study protocol is proposed, including a randomized, blinded feasibility trial with an embedded multiple case study. The intervention consists of the provision of a remote rehabilitation program, during which participants will use the Jintronix exergame for UE training and the Reacts Application to conduct videoconferenced sessions with the therapists (physical or occupational therapists). We plan to recruit 52 participants diagnosed with stroke, randomly assigned to a control group (n=26; 2-month on-paper home exercise program: the GRASP with no supervision) and an experimental group (n=26; 2-month home program using the technology). The primary outcome is the Fugl-Meyer UE Assessment, a performance-based measure of UE impairment. The secondary outcomes are self-reported questionnaires and include the Motor Activity Log-28 (quality and frequency of use of the UE), Stroke Impact Scale-16 (the quality of life), and Treatment Self-Regulation Questionnaire (motivation). Feasibility data include process, resources, management, and scientific outcomes. Qualitative data will be collected by interviews with both participants and therapists.

Results: At present, data collection was ongoing with one participant who had completed the exergame- telerehabilitation based intervention. We expect to collect preliminary efficacy data of this technology on the functional and motor recovery of the UE,

following a stroke; collect feasibility data with users at home (adherence, safety, and technical difficulties); and identify the obstacles and facilitators for the technology use and understand the shared decision-making process.

Conclusions: This paper describes the protocol underlying the study of a telerehabilitation-exergame technology to contribute to understanding its feasibility and preliminary efficacy for UE stroke rehabilitation.

Trial Registration: ClinicalTrials.gov NCT03759106; http://clinicaltrials.gov/show/NCT03759106.

International Registered Report Identifier (IRRID): DERR1-10.2196/14629

(JMIR Res Protoc 2020;9(5):e14629) doi:10.2196/14629

KEYWORDS

stroke; rehabilitation; virtual reality; telerehabilitation; upper extremity; motivation

Introduction

Background

In up to 85% of stroke survivors, sequelae persist in the upper extremity (UE) [1], resulting in a long-term impact on daily living activities [2,3]. To stimulate neuroplastic changes that promote motor recovery, stroke survivors should follow an intensive, task-specific, stimulating, and, above all, repetitive exercise program [4]. However, the programs offered by conventional therapies, in particular, during chronic stage, are not sufficient for people to achieve the level of repetition and intensity required for recovery [4]. In Canada, patients diagnosed with stroke receive the Graded Repetitive Arm Supplementary Program (GRASP) [5] as a home exercise program after discharge from traditional rehabilitation services [3]. The GRASP is recommended by the Canadian Best Practice Recommendations for Stroke Care [3] to provide training and increase the use of the impaired arm in daily life activities [5]. However, patients must be motivated enough to do the exercises on their own and to perform enough repetitions to achieve improvement. A minimum of 15 hours is suggested for an intervention to result in a moderate improvement in daily living activities following a stroke [6]. Numerous studies offering an intensive exercise program, in chronic stroke, reported significant improvements in UE impairment (P=.05) [7,8] and even maintenance of these changes over a period of 6 months after treatment [8].

Increasing Training Intensity in Stroke Rehabilitation

An interesting alternative that has been proposed to exercise intensity and exploit neuroplastic properties involves the use of virtual reality. For every 30 repetitions performed in a standard rehabilitation session, the same person can perform 600 to 800 repetitions within a 1-hour session in a virtual environment [4]. This is an important difference between the two approaches that highlights the potential of virtual reality. Thanks to its design, a virtual environment can simulate the real world while maintaining total control over the parameters of the tasks to be executed within it to foster motor learning [4]. In the context of rehabilitation, virtual reality has been integrated in the form of *exergames* because the gaming goal is to enhance activity through various types of exercises. Among these exergames, some have been specifically designed for stroke rehabilitation, including for balance training as well as for training for both lower and upper limb deficits (eg, Caren system, Lokomat, Armeo, and Jintronix [4,6,9,10]). The nature of the exergame interface makes it possible to modify the difficulty level of the exercises via various parameters such as intensity (time and repetition), visual feedback, speed, strength, and range of motion [4]. Progressing the exercise to ensure it remains challenging may motivate the user to complete the exercises [4]. However, there is no way to ensure that the movements made in the virtual environment are performed correspond to what is being trained. When performed in clinic, a health professional can ensure that the exercises are adjusted, and the movements are executed appropriately. However, at home, monitoring by a health professional needs to be considered to prevent compensatory movements during the exercises, inadequate choice of difficulty level, inappropriate completion of the exercises, and lack of motivation to pursue exercise program. The interfaces of the exergames do not allow automatic adjustment adapted to the person's abilities and do not sufficiently detect compensations [4,6,9,10]. Thus, the follow-up by a therapist would make it possible to optimize the exergames' benefits for the user (such as by adapting the difficulty parameters and by choosing games that are relevant for the user) and to help transfer motor learning from the virtual environment to activities of daily living.

To increase monitoring, a telerehabilitation system could allow such a follow-up through videoconferencing sessions between the user and the therapist. Such systems are increasingly used to provide remote rehabilitation services [11]. Its efficiency, compared with the standard treatment (face-to-face interventions), has been demonstrated, resulting in similar clinical results among participants diagnosed with stroke [12], therefore increasing accessibility to stroke rehabilitation services. Combining telerehabilitation with virtual reality (VirTele) could allow live sessions in which the therapist can observe the user playing and follow the game screen, at the same time, to assess how the user manages to complete the movements requested through the exercises (detect compensations, correct pathological patterns, and directly modify the difficulty setting necessary for the smooth running of the exercise). Therefore, the VirTele technology could allow continuous adjustment to the exercises and monitoring of the user completion to create a more personalized, tailored training program. Furthermore, in the long term, the VirTele exercise program could empower users to integrate the use of their impaired UE in their daily activities, through shared decisions made with the therapist.

Study Objectives

Given the evidence for the efficacy of exergames as well as telerehabilitation for stroke rehabilitation, but the limited evidence of combining these technologies, such as in the VirTele program, the overall goals of this study are to explore its preliminary efficacy for UE rehabilitation and examine its feasibility for use with stroke survivors at home. More specifically, the objectives of this study are to (1) determine the preliminary efficacy of VirTele on UE motor recovery, function, quality of life, and motivation in participants with chronic stroke, compared with conventional therapy (GRASP); (2) examine the feasibility of using VirTele with participants diagnosed with chronic stroke at home; and (3) identify the obstacles and facilitators for the technology use by participants diagnosed with stroke and stroke therapists and understand the shared decision-making process.

It is hypothesized that the exergame-telerehabilitation program will lead to greater UE motor recovery than usual care (GRASP) in participants with chronic stroke. We also hypothesize that the exergame-telerehabilitation program will have a greater impact on function, quality of life, and motivation in participants with chronic stroke.

Methods

Study Design

This is a mixed method study design consisting of a randomized, blinded feasibility trial with an embedded multiple case study that will take place in Montreal, Canada. The randomized feasibility trial is a two-arm, single-blind trial design in which eligible participants will be randomly allocated to an experimental (VirTele for 8 weeks) or control, usual care group (GRASP for 8 weeks). The feasibility trial captures both feasibility and preliminary efficacy outcomes. Publishing the feasibility results would provide a better understanding of the context in which the efficacy data were collected and a better interpretation of the final results [13,14].

Outcome measures will be assessed for both groups on four occasions: at baseline (T1), at the end of 2-month intervention (T2), after a 1-month follow-up period (T3), and after a 2-month follow-up period (T4; Figure 1).

Figure 1. Description of the outcome measurement time. GRASP: Graded Repetitive Arm Supplementary Program; VirTele: program that combines virtual reality exergame and telerehabilitation application.

Randomization and evaluations will be performed by research assistants who are not involved in the study. All participants will provide informed written consent before enrollment. This study is registered at clinicaltrials.gov (NCT03759106) and has received ethics approval from the Research Ethics Boards of Centre for Interdisciplinary Research in Rehabilitation of Greater Montreal (June 28, 2018).

Participant Selection and Recruitment Strategy

At study entry, we will administer the Chedoke-McMaster arm component [15] to get evidence of UE impairment. Only participants with a score of 2 to 6 will be eligible. We will also verify balance maintenance during sitting position and detect any UE mobility restrictions limiting the ability to play (restricted shoulder movements because of pain) through active and passive mobilizations.

Stroke survivors who have residual UE deficits and are no longer receiving rehabilitation services will be eligible for study participation if they fulfill the eligibility criteria. The inclusion criteria are as follows: first-time unilateral ischemic or hemorrhagic stroke or no residual deficits from a previous stroke and able to use the Jintronix system (eg, able to move the game avatar with impaired limb). The exclusion criteria are as follows: being medically unstable (eg, uncontrolled cardiac condition), severe cognitive or communication deficits, visual impairments limiting the ability to use the games, and UE mobility restrictions limiting the ability to play (eg, restricted shoulder movements because of pain).

We intend to recruit participants from the community and from the archives of rehabilitation centers (offline) situated in the Montreal, Sherbrooke, and Laval areas (Quebec, Canada).

Study therapists (physical therapists or occupational therapists) from the different participating sites will also be included in the study to explore their experiences with the technology and comprehend the shared decision-making process underlying their choice of games and difficulty levels.

Sampling

To date, no studies have reported on the use of combining such technologies, such as in the VirTele program so that this randomized, blinded feasibility trial will provide evidence for the effect size. However, as the first estimate of effect size, a sample size of 52 participants has been calculated using the Fugl-Meyer Upper Extremity Assessment as a primary outcome and G*Power 3.1 [16]. We assumed a medium effect size of 0.2, which was reported in a study with chronic stroke survivors

with a 2-arm randomized clinical trial [17] and accounting for 20% retention issues (alpha=.05 and power=80%). This sample size corresponds to recommendations for pilot efficacy and feasibility trials [18] and is realistic, given time and budgetary constraints as well as recruitment potential. Thus, for the randomized, blinded feasibility trial, 52 participants will be recruited and randomly allocated to the experimental (n=26) or control group (n=26). A block randomization with a block size of six will be used, given time and material constraints.

For the multiple case study component, four therapists and the first 10 participants from the experimental group will be invited to participate in interviews. However, the final sample size of the participants diagnosed with stroke will be adjusted depending on the qualitative data saturation [19].

Description of Interventions

Experimental Group

The participants in the experimental group will receive the VirTele program. VirTele is an 8-week home program during which participants will use the Jintronix exergame [10] for UE training and the Reacts telerehabilitation application [20] to conduct videoconferenced sessions with the therapists (physical therapists or occupational therapists). All the equipment necessary for the proper functioning of the VirTele program, including the computer, the Kinect camera, the Reacts, and Jintronix software as well as a constant internet accessibility (USB internet key), will be provided for free to the participants. A technician will oversee the transport and the installation.

Telerehabilitation Component

The Reacts application is an interactive audio-video platform that allows secure communication between therapists and participants using standard computer or tablet technologies [20]. The application enables a live game access when it is used in combination with Jintronix. Thus, the therapist will be able to see the participant doing exercises and see the exergame platform while it is being used. The access to the live game platform allows the therapist to track the tasks or movements required by the game and see how the participant manages to accomplish them to adjust the difficulty level of the game according to the participant's motor skills and interest. The Web sessions with Reacts will take place three times a week for 2 weeks, twice a week for 2 weeks, and then once a week for the remaining 4 weeks.

Reacts can also be used alone, making it possible for the participant to interact with the therapist when finishing the exercises. These sessions provide an opportunity to discuss difficulties regarding playing games and to subsequently modify the rehabilitation program according to the participant's abilities and preferences. This shared decision-making process can help foster motivation to make health-related decisions (eg, setting goals weekly with the therapist, determine the optimal level of difficulty of the exercises, and choosing the games) and specially to continue rehabilitation after the end of the intervention. This shared decision-making process will aim to increase the empowerment of the participant, facilitating subsequently the transfer of the functional gains acquired in the context of the study into real life. This transfer occurs by identifying ways of reproducing the tasks of the game in activities of the daily life and increasing the use of the affected UE in the long term. Participant empowerment will be further encouraged by using motivational interviewing based on self-determination theory (SDT) principles during telerehabilitation sessions [21,22]. This theory states that humans naturally tend to achieve changes that respect and enable the satisfaction of their three basic psychological needs, namely, (1) autonomy, (2) connectivity, and (3) competence [22,23]. There are two regulation processes predicting behavioral engagement and maintenance: the behavior emanating from intrinsic motivation and the internalization of extrinsic motivation [23].

Virtual Reality Component

The Jintronix exergame consists of six UE games played for varying amounts of time and at different difficulty levels (speed, precision, and range of movements), which can be tracked remotely by the therapist asynchronously through the data provided in Jintronix Web-based portal. The therapist is also able to modify the difficulty parameters according to the performance data recorded on the portal. This exergame uses a Kinect camera, which captures the person's body movements without wearing sensors. Participants will be invited to use Jintronix at least five times a week for 8 weeks, for 30-min sessions, performing a total of 20 hours of exercise. A minimum of 15 hours is suggested for an intervention to result in a moderate improvement in activities related to daily living following a stroke [6].

Jintronix includes an automated log system, which records the active time spent by participants in each game and the score achieved. The therapist can access the exergame interface at any time to monitor the participant's progress and adherence to the exercise program and modify the difficulty level.

Before starting the intervention, therapists will receive training in motivational interviewing [24] to ensure a client-centered rehabilitation program that aligns with the SDT [21]. We used SDT [23] as a conceptual framework to guide the VirTele intervention to empower the participant and solicit their interest and motivation for the treatment plan that the therapist and participant will decide on together. The combination of the telerehabilitation system (Reacts) and the Jintronix exergaming system aims to foster participant-therapist interaction throughout the rehabilitation program and to develop a partnership relationship based on information sharing and trust. It is in this perspective that SDT was integrated. Its constructs were used as a basis for a discussion plan which the therapist refers to during videoconferenced sessions.

All participants in the experimental group will participate in a 30-min training session with the technician responsible for the installation of the technology to learn to use the VirTele technology.

Control Group

The participants in the control group will receive GRASP based on their UE function. It includes strengthening exercises of arm and hand, range of motion, and functional arm activities [5]. The program includes some equipment such as a ball, a bean bag, or paper clips. The participants will be invited to carry out

the GRASP exercises over the 8 weeks, 5 days a week for 30 min each day, performing 20 hours of exercises in total (same as experimental group). A paper log journal will be provided to track the amount of time spent on the exercises and the number of sessions as well as any adverse events (fatigue and pain). The control group will not receive any follow-up with the therapist, but at the end of the study, the participants will be offered one session with the therapist to discuss strategies for improving long-term UE function. Before starting the intervention with GRASP, the participants will receive a 30-min training session for using the program equipment by one of the therapists included in the study.

Data Collection

Quantitative Data

At study entry, the participant's sociodemographic information (gender, age, civil status, language, number of years of education completed, primary occupation, and stroke characteristics) will be collected for descriptive purposes.

For the randomized, blinded feasibility trial, several outcomes measures will be used to address the different objectives. The first objective of the trial is to determine the preliminary efficacy of VirTele on UE motor recovery, function, quality of life, and motivation, in participants with chronic stroke, compared with conventional therapy (GRASP).

The Fugl-Meyer Upper Extremity Assessment will be the primary outcome to determine the efficacy of the technology for UE motor control recovery. This is a performance-based measure of UE impairment [25,26]. It includes 13 items scored on a 3-point ordinal scale of 0 to 2 [26]. The Fugl-Meyer Upper Extremity Assessment has been shown to have good internal consistency (alpha=.82-.84) and good concurrent validity (r=0.74) [25].

The secondary outcomes are self-reported questionnaires and include the Motor Activity log 28 [27,28], the Stroke Impact Scale-16 [29,30], and the Treatment Self-Regulation Questionnaire-13 [31].

The Motor Activity log 28 is a self-reported measure of UE use [27,28]. This rates the quality and frequency of use of the UE in 28 everyday tasks and is administered by interview [27,28]. The Motor Activity log 28 demonstrated high reliability (r=0.82) and high validity, with excellent concurrent correlation with Stroke Impact Scale hand function scores (r=0.72) [32]. The impact on quality of life will be determined using the Stroke Impact Scale-16, a stroke-specific, self-reported, health status measure consisting of 16 items concerning daily activities [29,30]. The Stroke Impact Scale-16 has been shown to have good internal consistency (alpha=.87) and a good convergent and discriminant validity [33]. Motivation will be measured using the Treatment Self-Regulation Questionnaire-13 [31], a 13-item questionnaire that has been developed to measure treatment motivation, aligned with SDT. The Treatment Self-Regulation Questionnaire has been shown to be reliable with a high internal consistency (alpha=.73-.95) and valid across health care contexts and has been used in rehabilitation [34]. The two regulation processes of the SDT (intrinsic and extrinsic motivation) are targeted in the form of subscales in the Treatment Self-Regulation Questionnaire-13 [31]. The use of this questionnaire allows us to investigate the impact that the motivation could have on adherence to the program and its effectiveness.

The second objective of the randomized, blinded feasibility trial is to assess the feasibility of using VirTele with participants diagnosed with stroke at home. Feasibility data include indicators of process, resources, management, and scientific feasibility [35]. In Table 1, we describe all the outcomes that will be used for each indicator. These data will also provide evidence to examine the validity of the research protocol to inform the planning of a larger clinical trial.

A trained assessor who is not involved in the delivery of interventions and blinded to group assignment will be responsible for the face-to-face administration of the outcome measures.

Table 1. Description of feasibility indicators outcomes.

Feasibility indicators	Outcomes
Process	
Recruitment rate	• Percentage of participants who meet the eligibility criteria and accept to participate (20%) • Rate of participants per month • Duration of recruitment
Retention rate	• Percentage of participants who complete the 2-month intervention with telerehabilitation with virtual reality
Resources	
Exercise adherence rate	• Percentage of participants who complete 150 min of Jintronix exercises per week
Number and duration of sessions	• These data will be obtained from the Jintronix exergame and Reacts app system
Frequency and time spent by the therapist assisting for real-time sessions with Jintronix	• Logs completed by the therapist at the end of each session
Resources utilization	• Logs completed and time spent by therapists and technical staff
Management	
Technical problems with the technology	• Obtained from a log maintained by the study therapists and technical team
The role of the shared decision making and empowerment in achieving task goals	• Encourage participants to report new task goals every week • Percentage of participants who achieved the goals set with the therapist • Percentage of task goals achieved per participant
Scientific	
Safety	• Occurrence of adverse events (pain, falls, motion sickness, dizziness, exertion, fatigue, and headaches) will be documented by a computerized participant log
Satisfaction	• With the technology: the Modified Short Feedback Questionnaire [36] • With the interaction between the therapist and the participant: Health Care Climate Questionnaire (Perceived Autonomy Support) [37]
Size of sample	• The calculation will be done from the size of the treatment effect or the variance of the treatment effect

Qualitative Data

Individual semistructured interviews of 30 min will be conducted with the first 10 participants from the experimental group (n=10) after the end of 8-week intervention. The interview guide will be developed based on the Unified Theory of Acceptance and Use of Technology (UTAUT) conceptual framework [38]. This theory includes four essential constructs (expected performance, expected effort, social influence, and facilitating conditions), which are considered as direct determinants of the intention and behavior of adoption and the use of new technologies by stakeholders [38]. Therefore, semistructured interviews will be used to inform not only the intention and behavior of adoption and use of VirTele by participants diagnosed with stroke and therapists but also of UE use in the future (through UTAUT constructs). When combined with SDT constructs, the interview will inform the participants' empowerment and the shared decision-making process underlying the therapist choice of games and difficulty levels.

The study therapists will also be interviewed to describe their experience with VirTele (obstacles and facilitators), explore their behavior to see if they align with SDT, and investigate the shared decision-making process underlying their choice of games and difficulty levels. Individual semistructured interviews of 30 min will be used. The UTAUT and the SDT will serve as basis for the interview guide development.

All interviews will be voice recorded and transcribed verbatim. A logbook and reflective notes will also be taken.

Data Analysis

Quantitative Data Analyses

Statistical analysis of the quantitative data will be performed using the Statistica software. Descriptive statistics will be used to report sociodemographic characteristics of participants (age, gender, handedness, and stroke characteristics) in both groups (experimental vs control). To address the first objective of the randomized, blinded feasibility trial, a mixed model approach will be applied for primary and secondary outcomes measure. Each model will contain one between-subject effect factor (group: control vs experimental), one within-subject effect factor (time: T1, T2, T3, and T4), and two covariates (gender and age)

factors, which may impact exergame use. For each outcome measures, residual plots will be examined to verify normality and identify the best covariance structure. All the outcomes measure changes will be compared with the minimal clinically important differences. The effect size of the comparison between experimental and control groups will be calculated to estimate the final sample size. To address the second objective of the randomized, blinded feasibility trial, descriptive statistics (frequencies, means, and standard deviations) will be used to highlight the amount of exercise performed, the occurrence of adverse events, and participant and therapist satisfaction level in the experimental and control groups.

Qualitative Data Analyses

For the qualitative data, thematic analysis will be conducted for each case group. Transcripts will be coded using a predetermined coding scheme (Multimedia Appendix 1) based on the conceptual frameworks as well as other codes emerging from the data using NVivo software, and then codes will be grouped into overarching themes. To ensure the scientific rigor of qualitative data, the principles of Lincoln and Guba [39] will be applied. Audit trail and verification by members will be done to respect confirmability. A debriefing (external verification) will be applied to ensure credibility. Reliability will be achieved with verification by two coders of a part of the data. Transferability will be assured by taking reflexive notes and a detailed description of the context of the intervention. During the analysis, the results of the qualitative and quantitative data will be compared to help explain findings.

Results

We expect to (1) collect preliminary efficacy data of this technology on the functional and motor recovery of the UE, following a stroke; (2) collect feasibility data with users at home (adherence, safety, and technical difficulties); and (3) identify the obstacles and facilitators for the technology use and understand the shared decision-making process during the VirTele program.

At the time of this manuscript submission, data collection was ongoing with one participant who had completed the study (experimental group) and used VirTele for 2 months [40] (Multimedia Appendix 2). At this stage of the study, we have not yet started the data analysis.

Discussion

Study Design

This paper describes the research protocol for a mixed method study, including a randomized, blinded feasibility trial with an embedded multiple case study. The aims of this study are to (1) determine the preliminary efficacy of VirTele on UE motor recovery, function, quality of life, and motivation in participants with chronic stroke, compared with conventional therapy (GRASP); (2) examine the feasibility of using VirTele with participants diagnosed with chronic stroke at home; and (3) identify the obstacles and facilitators for the technology use by participants diagnosed with stroke and stroke therapists and understand the shared decision-making process.

We have chosen a mixed study design because the use of both qualitative and quantitative approaches makes it possible to construct a more complete image of the studied phenomenon. The combination of the two methodologies should be approached not from the point of view of their differences but from the complementarities they can bring to the study [41]. If the feasibility trial examines the content of the intervention to see if it is effective and feasible, the qualitative approach examines the context of the intervention to see if it can be accepted and applied in clinical practice and explain some of the quantitative findings [42]. Feasibility trials are important to ensure that larger randomized clinical trials are rigorous and feasible and economically justifiable [13].

Data Collection

Participants will be recruited from different sites to increase the representativeness of the target population in the region. The control group will not receive any motivational interviewing or follow-up to keep the standard aspect of therapy that corresponds most to the clinical reality. This will enable us to identify the added value of the VirTele program compared with GRASP. After outcome measures collection in T1 and T2, to compare the effect of each intervention within and between groups, we will collect additional measures at T3 and T4 to evaluate the retention of gains.

The multiple case study provides an in-depth description of stakeholders use experience and potential use of VirTele program. In this study, we will have two case groups: participants diagnosed with stroke and study therapists (physical therapists or occupational therapist). Each of these cases experiences the intervention differently, and it is therefore essential to report them through interviews. The variation of the cases makes it possible to increase the variation of the experiences and thus to increase the robustness of the qualitative results [19]. UTAUT and SDT will serve as a basis for establishing certain links between the concepts that will emerge (Multimedia Appendix 1).

The results of this study will allow to verify if all elements of the protocol work well together to conduct a broader future study. We have tried to provide as much detail as possible about the various processes and steps of the protocol to facilitate its reproduction by other studies that seek to develop tools for the remote management of chronic diseases.

This project will also provide preliminary evidence of the efficacy of VirTele on motor and functional recovery of the UE following chronic stroke for future guidelines review, although studies caution us about solely using results from feasibility studies to establish intervention efficacy [35].

Conclusions

Extending rehabilitation following a stroke with remote services may be a promising strategy to overcome the limited resources in the health system. The VirTele program is a new approach that may provide stroke survivors continuous and remote access to rehabilitation services. This paper describes the protocol underlying the study of this technology to better understand how it can be used among different stakeholders and explore its preliminary efficacy in a chronic stroke population.

Acknowledgments

This work was supported by the Canadian Institutes of Health Research (385297, 2017) and a scholarship of the Mission Universitaire de Tunisie. The funding source had no involvement in the conduct of the research or the preparation of the article.

Conflicts of Interest

None declared.

Multimedia Appendix 1
The predetermined qualitative coding scheme.
[PDF File (Adobe PDF File), 25 KB - resprot_v9i5e14629_app1.pdf]

Multimedia Appendix 2
A screenshot of the combined use of Jintronix and Reacts.
[PNG File , 1747 KB - resprot_v9i5e14629_app2.png]

Multimedia Appendix 3
Peer-review reports from the Canadian Institutes of Health Research - Part 1.
[PDF File (Adobe PDF File), 73 KB - resprot_v9i5e14629_app3.pdf]

Multimedia Appendix 4
Peer-review reports from the Canadian Institutes of Health Research - Part 2.
[PDF File (Adobe PDF File), 75 KB - resprot_v9i5e14629_app4.pdf]

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Abbreviations

GRASP: Graded Repetitive Arm Supplementary Program
SDT: self-determination theory
T1: at baseline
T2: at the end of 2-month intervention
T3: after a 1-month follow-up period
T4: after a 2-month follow-up period
UE: upper extremity
UTAUT: Unified Theory of Acceptance and Use of Technology
VirTele: program that combines virtual reality exergame and telerehabilitation application

Edited by G Eysenbach; submitted 07.05.19; peer-reviewed by E Dove, M Rosly; comments to author 03.10.19; revised version received 28.11.19; accepted 07.02.20; published 21.05.20.

Please cite as:
Allegue DR, Kairy D, Higgins J, Archambault P, Michaud F, Miller W, Sweet SN, Tousignant M
Optimization of Upper Extremity Rehabilitation by Combining Telerehabilitation With an Exergame in People With Chronic Stroke: Protocol for a Mixed Methods Study
JMIR Res Protoc 2020;9(5):e14629
URL: http://www.researchprotocols.org/2020/5/e14629/
doi:10.2196/14629
PMID:32097119

Protocol

A Web-Based, Positive Emotion Skills Intervention for Enhancing Posttreatment Psychological Well-Being in Young Adult Cancer Survivors (EMPOWER): Protocol for a Single-Arm Feasibility Trial

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Abstract

Background: Adolescent and young adult cancer survivors (AYAs) experience clinically significant distress and have limited access to supportive care services. Interventions to enhance psychological well-being have improved positive affect and reduced depression in clinical and healthy populations but have not been routinely tested in AYAs.

Objective: The aim of this protocol is to (1) test the feasibility and acceptability of a Web-based positive emotion skills intervention for posttreatment AYAs called Enhancing Management of Psychological Outcomes With Emotion Regulation (EMPOWER) and (2) examine proof of concept for reducing psychological distress and enhancing psychological well-being.

Methods: The intervention development and testing are taking place in 3 phases. In phase 1, we adapted the content of an existing, Web-based positive emotion intervention so that it would be suitable for AYAs. EMPOWER targets 8 skills (noticing positive events, capitalizing, gratitude, mindfulness, positive reappraisal, goal setting, personal strengths, and acts of kindness) and is delivered remotely as a 5-week, Web-based intervention. Phase 2 consisted of a pilot test of EMPOWER in a single-arm trial to evaluate feasibility, acceptability, retention, and adherence and to collect data on psychosocial outcomes for proof of concept. In phase 3, we are refining study procedures and conducting a second pilot test.

Results: The project was part of a career development award. Pilot work began in June 2015, and data collection was completed in March 2019. The analysis is ongoing, and results will be submitted for publication by May 2020.

Conclusions: If this intervention proves feasible and acceptable, EMPOWER will be primed for a subsequent large, multisite randomized controlled trial. As a scalable intervention, it will be ideally suited for AYA survivors who would otherwise not have access to supportive care interventions to help manage posttreatment distress and enhance well-being.

Trial Registration: ClinicalTrials.gov NCT02832154, https://clinicaltrials.gov/ct2/show/NCT02832154.

International Registered Report Identifier (IRRID): DERR1-10.2196/17078

(JMIR Res Protoc 2020;9(5):e17078) doi:10.2196/17078

KEYWORDS

emotions; telemedicine; happiness; eHealth; cancer; young adult; internet; mobile phone

Introduction

Background

Adolescent and young adult cancer survivors (AYAs) are an important underserved group at risk for significant psychological distress. There are approximately 70,000 new diagnoses of cancer annually in AYAs (aged 18-39 years) [1]. Currently, nearly 2 million people in the United States are living with or have survived being diagnosed with cancer as an AYA. Five-year survival rates of AYAs are high (>80%) [2], and AYAs have approximately 35 to 59 years of life expectancy remaining [3], underscoring the importance of posttreatment survivorship care. AYAs face unique challenges, given the physical, cognitive, and psychosocial developmental milestones disrupted as a result of cancer [4,5]. Notably, the prevalence of clinically significant depression or anxiety is much higher compared with older adults [6-12]. For older adults, cancer is a distressing event but a more normative experience in an aging population. In addition, older adults typically have greater experience in coping with major life events. For AYAs, a cancer diagnosis is routinely unexpected, considerably disruptive, and frequently socially isolating, factors that contribute to higher rates of psychological distress. Moreover, AYAs may have inadequate insurance coverage, limited financial assets, and experience significant work interruption, leading to greater financial strain and contributing to elevated distress [13,14]. Accordingly, AYAs can benefit from targeted, supportive care interventions to decrease distress and enhance well-being as they navigate posttreatment survivorship.

The National Cancer Institute has called for supportive care interventions in AYAs to address psychological health deficits [15]. Although a modest but growing number of psychosocial interventions have been developed for AYAs [16,17], including those that use electronic health (eHealth) modalities [18-20], none have included a focus on enhancing psychological well-being through positive emotions. eHealth interventions represent promising options for patient engagement, especially with *digital natives* such as AYAs, and provide opportunities for fostering user engagement, which is positively associated with intervention efficacy [21]. The vast majority of AYAs access the internet (94%-99%) [22] and own smartphones (92%-96%) [23]. As AYAs have shown that they prefer remotely delivered, on-demand interventions [24], there is a clear need and opportunity for eHealth interventions to positively impact AYAs' psychological well-being. Moreover, although the deleterious effects of psychological distress are well researched, comparatively less attention has been focused on the benefits of psychological well-being. Psychological well-being is significantly associated with better health outcomes (better physical health [25] and lower risk of mortality in healthy and chronically ill samples [26-30]), is unique from the influence of distress, and includes domains that are inherently valued by patients (better relationships, more creativity, and better work quality [31]).

Objectives

In this protocol paper, we describe the development and pilot testing of a Web-based positive emotion skills intervention for posttreatment AYAs, Enhancing Management of Psychological Outcomes With Emotion Regulation (EMPOWER). We are adapting an existing multicomponent positive emotion skills intervention [32-36] and tailoring it for AYAs. EMPOWER is a 5-session intervention designed to teach participants 8 skills for increasing positive emotion in their daily lives.

The objectives of this investigation are to (1) test the feasibility and acceptability of a Web-based positive emotion skills intervention tailored for AYAs posttreatment and (2) examine proof of concept of the positive emotion skills intervention for reducing psychological distress (depression, anxiety, and anger) and enhancing psychological well-being (positive affect, life satisfaction, meaning and purpose, and general self-efficacy). In addition, exploratory analysis will examine associations with other indicators of health-related quality of life (HRQOL; fatigue, pain interference, sleep disturbance, physical functioning, and social functioning) and health behaviors (diet, exercise, alcohol use, and smoking). Ultimately, this research seeks to develop an optimized Web-based positive emotion skills intervention for posttreatment AYAs, which will be tested in a future randomized controlled trial (RCT).

Methods

Overview

The intervention development and testing were planned for 3 phases. Phase 1 aimed to adapt a Web-based positive emotion skills intervention to maximize the acceptability and relevance of the intervention content for posttreatment AYAs. Phase 2 aimed to conduct a pilot test of EMPOWER in a single-arm trial to evaluate feasibility, acceptability, retention, adherence, and collect data on psychosocial outcomes for proof of concept. In phase 3, we incorporate any suggested modifications from the phase 2 pilot to address any potential challenges encountered from the first round of pilot testing and to ensure that we are maximizing our ability to recruit, retain, and support AYAs. These changes are followed by a second round of pilot testing. Planned accrual was 20 for phase 2 and 20 for phase 3.

Participants were recruited through 2 comprehensive cancer centers (the Robert H Lurie Comprehensive Cancer Center [RHLCCC], and the Wake Forest Baptist Comprehensive Cancer Center [WFBCCC]) and supplemented by recruitment over social media. All participants were asked to provide daily emotion reports over the course of the 5-week intervention and received self-paced Web-based instruction and practice in skills for increasing their daily experience of positive emotion. Participants were assessed at baseline, at 8 weeks (immediately postintervention), and at 12 weeks. To minimize participant burden, we used brief and well-validated National Institutes of Health (NIH) Patient-Reported Outcomes Measurement

Information System (PROMIS) and NIH Toolbox measures to assess most study outcomes.

Phase 1: Intervention Adaptation

As the first step in this phase, the study principal investigator (PI: JS) reviewed candidate interventions for potential adaptation and testing among AYA posttreatment survivors. The MARIGOLD intervention, developed by a lead collaborator (JM) for individuals with elevated depressive symptoms, provided the constellation of skills to promote positive emotions through emotion regulation and was tailored for Web-based delivery [35,36]. MARIGOLD is a 5-session intervention that teaches participants 8 empirically-based skills (ie, positive events, savoring, gratitude, attainable goals, mindfulness, positive reappraisal, personal strengths, and acts of kindness) to increase the frequency of positive emotions experienced in their lives. As AYAs are digital natives, having access to and comfort with digital technologies [22,23], this mode of intervention delivery was well suited for them.

In the second step of this process, the study team reviewed the intervention content with a particular focus on ensuring that the appropriate coping skills were represented, and the language used was applicable for posttreatment AYAs. As a third step in this process, we solicited stakeholder input from AYAs and their providers. Stakeholders reviewed the intervention content and provided feedback on the quality of advice (eg, *Does this sound like something you can do*?), their affective response (eg, *Talk about how reading it made you feel*.), and the appropriateness of images used in the lessons (eg, *Some pages have a photo or video. Give your comments on that*.). All feedback was reviewed and discussed by the full study team to finalize the intervention content before pilot testing.

Phase 2: Initial Pilot Testing

Study Population

Participant eligibility inclusion criteria included (1) able to read and understand English, (2) able to provide informed consent, (3) past history of a cancer diagnosis (excluding basal cell skin carcinoma), (4) 18 to 39 years of age at diagnosis, (5) currently within 0 to 5 years post active treatment, and (6) wireless internet connection or a home computer that is connected to the internet. Exclusion criteria included (1) evidence of cancer recurrence or a history of multiple primary cancers, (2) currently receiving palliative or hospice care, or (3) a significant psychiatric history. Our past work with posttreatment AYAs underscores the psychologically vulnerable posttreatment, *reentry* period, as they navigate new and sometimes recurring challenges to their psychological well-being [6,37-39]. Providing a Web-based, self-guided, well-being intervention during this critical transition phase helps address some of these unmet needs.

Study Procedures

Recruitment and Enrollment

With prior approval from the medical oncologists, study staff identified potential RHLCCC and WFBCCC patients from the electronic medical record. Potentially eligible patients were recruited through a direct in-clinic approach and mailed letters, followed by a phone call from a study team member. The recruitment call was followed by an email outlining the details discussed during the phone call and instructions on the next steps and a link to the screening questionnaire. The patients were then screened for eligibility using Qualtrics, a Web-based data collection tool that enables researchers to create study-specific websites for capturing participant data securely. Those who were ineligible were shown a message thanking them for their interest but informing them that they were not eligible for the study. Patients who were eligible were navigated to the consent form and initial study questionnaire on Qualtrics. On completion of the baseline questionnaire, all participants were asked to begin daily emotion reporting for 2 weeks before beginning the intervention.

Intervention Content

The EMPOWER intervention is a 5-session Web-based intervention that teaches 8 skills for increasing the frequency of positive emotions: (1) *noting daily positive events* [40-43], (2) *capitalizing* on or savoring positive events [44,45], (3) *gratitude* [46-48], (4) *mindfulness* [49-52], (5) *positive reappraisal* [53-58], (6) focusing on *personal strengths* [59-61], (7) setting and working toward *attainable goals* [57,58,62-64], and (8) small *acts of kindness* [65-69] (see Table 1). The skills are presented over 5 weeks. A week consists of 1 to 2 days of didactic material and several days of brief, real-life skills practice and reporting, with each day's *home practice* taking approximately 20 to 30 min to complete. Participants cannot skip ahead, but they can return to old lessons or exercises if they choose. Most exercises are in *diary* format in which participants' past responses are displayed next to their new ones so that every time the participant visits that exercise, they see their growing list of past positive experiences. All aspects of the intervention, including the didactics and skills practice, are self-guided and interactive. Additional details of the development of the intervention are published elsewhere [35,36].

Table 1. Overview of the skills and content of the Enhancing Management of Psychological Outcomes With Emotion Regulation intervention.

Session and skills	Session content
Week 1	
Positive events	Learning to recognize positive events (eg, a good conversation with a friend, a good cup of coffee) and the associated positive affect.
Capitalizing	Practicing ways to amplify the experience of positive events (eg, taking an extra moment to savor the experience as it is happening, reliving the positive experience, telling someone else about the positive experience).
Gratitude	Taking a moment to feel thankful or appreciative of the things you have in life (eg, family, a sunny day, a good night's rest).
Week 2	
Mindfulness	Learn and practice the awareness and nonjudgment components of mindfulness.
Week 3	
Positive reappraisal	Understanding positive reappraisal and the idea that different forms of positive reappraisal can all lead to increased positive affect in the face of stress (eg, seeing the *silver lining*, finding out things were not as bad as they could have been, identifying good things that came out of the event).
Week 4	
Personal strengths	Participant lists his or her personal strengths and notes how they may have used these strengths recently (eg, having a good sense of humor, being artistic).
Achievable goals	Understanding the characteristics of attainable goals and setting some goals for the week.
Week 5	
Acts of kindness	Understanding that small acts of kindness can have a big impact on positive emotions (eg, buying the person behind you in line a cup of coffee).

Intervention Platform

Our Web intervention is delivered via a customized website built on Moodle, a courseware platform that is used by schools and universities worldwide. Moodle allows the delivery of text or video instruction as well as interactive activities such as journals and adaptive quizzes. Moodle is recognized as secure and well-tested software, and Health Insurance Portability and Accountability Act-compliant hosting is provided by the Northwestern University. All communications with the website use industry-standard transport layer security or secure sockets layer encryption. Another layer of security is provided by avoiding any use of personally identifiable information, medical information, or other sensitive information in the context of the intervention. Participants' Moodle accounts are not linked to their real name or email address. Email and text message reminders are handled by a smartphone Ecological Momentary Assessment text messaging system that does use the participant's name and email address, but that cannot be linked to their Moodle account. The design of our intervention website has been refined through a number of iterations based on user testing and feedback from study participants (eg, simplifying the interface and clearly labeling new material and exercises). We have also ensured that material is viewable on handheld, tablet, and laptop devices.

Acceptability Interview

Research staff conduct a 30-min audio-recorded, postintervention phone interview with all participants approximately 1 week after the intervention is complete to gather acceptability data. Participants are asked to rank order their favorite intervention skills, their intentions to practice each of the skills, and their plans for continued practice. In addition, they are asked whether or not they would recommend the intervention to a friend or someone newly diagnosed with cancer.

Participant Incentives

Each participant is paid US $10 for each completed assessment for a maximum of US $30. In addition, participants are paid US $0.25 for each of three daily emotion assessments over the two separate 2-week reporting periods (4 weeks; 28 possible daily reports, up to US $21 per participant). In total, participants are compensated a maximum of US $51 for their participation in the study and are paid in full on completion of the study via a virtual gift card.

Fidelity Monitoring

We record how frequently participants visit the website and how many times they complete the daily practice exercises for each skill. This information can be used in *dose-response* analyses to determine if greater exposure to the exercises leads to stronger intervention effects. We monitor participant progress during the study and contact participants who appear to be having trouble or disengaging from the intervention. Our experience indicates that even very brief human contact can increase participants' commitment to the intervention. Participants receive an email or phone call from a study staff member if they fail to visit the website for more than 3 days in a week. Participants who cannot be reached or who do not resume visiting the website but also do not ask to leave the study are recontacted once per week for 3 weeks. After that time, they are counted as noncompleters, although we still try to contact them to obtain postintervention measures. Participants who do not reach the final lesson at the end of 10 weeks are also

considered noncompleters and asked to take the postintervention measures at that time.

Measures

Patients complete self-report questionnaires throughout the intervention designed to evaluate state and mood-based aspects of psychological well-being as well as related patient-reported outcomes that may be impacted (ie, HRQOL and health behaviors) as a result of changes in psychological well-being. Psychological well-being includes both negative and positive aspects and is assessed by daily emotion reports (ie, run-in period before the intervention, end of day recall during the intervention, and run-out period after the intervention) and by weekly recall measures at baseline (pretest), approximately 8 weeks after baseline (posttest), then at 12 weeks (follow-up). The HRQOL and health behavior measures are also administered at baseline/pretest, posttest, and then follow-up (see Multimedia Appendix 1). All measures are completed from home via participants' PCs. In addition to the measures listed below, we assess key demographics (race/ethnicity, education, household income, and insurance status), cancer type, time since diagnosis, type of treatment, and time since treatment.

Daily Emotion Reports

Daily frequency of positive and negative affect is assessed using modified versions of the NIH Toolbox positive affect short form [70] and the NIH PROMIS depression and anxiety short forms [71]. Participants are asked to respond to each item in terms of how they feel *today*. During the 2-week *run-in*/*run-out* period (weeks 1 and 2 and weeks 11 and 12), all participants complete the daily emotion reports 3 times per day with respect to their emotions at that moment. The purpose of the run-in period is to address any technical issues that participants experience, to ensure participants are comfortable reporting their emotions, to evaluate compliance with completing these reports, and to provide a pre- and postcomparison of state-based affective experiences. Furthermore, the study is designed with a relatively intensive engagement process, and we sought to identify participants who were willing and able to comply with the modest but frequent assessments, didactics, and skills practice that are part of EMPOWER. If participants do not complete at least nine daily reports in a week's time, they are excluded from further participation in the study. In this circumstance, the participant is notified by email. One week before the 12-week assessment point, participants are contacted and asked to provide the last 2 weeks of daily emotion reporting in time to complete the final assessment. During the 5-week intervention, participants complete the end of day recall at the end of each day with respect to their emotions that day.

Psychological Well-Being

Psychological well-being is assessed with NIH Toolbox short forms, capturing 3 common components: positive affect, life satisfaction, and meaning and purpose [70]. In addition, the NIH PROMIS general self-efficacy short form [72] is administered, as it is a closely related construct to psychological well-being and positively associated with better health-related outcomes.

Health-Related Quality of Life

We use the PROMIS global health items to assess overall HRQOL [73] and the PROMIS-29 [74,75] to assess domain-specific aspects of HRQOL. The PROMIS global scale consists of 10 items that assess general health, including overall physical and mental health. The PROMIS-29 consists of 29 items that assess physical functioning, anxiety, depression, fatigue, sleep disturbance, social functioning, pain interference, and pain intensity. These PROMIS measures are supplemented with additional items from the PROMIS physical function short form [76] and the PROMIS anger short form [71]. These measures were included to identify potential *signal relationships* for psychological well-being and HRQOL.

Health Behaviors

Healthy behaviors often associated with enhanced coping and better psychological adjustment are assessed [77]. Physical health behaviors include diet [78], exercise [79], alcohol consumption [78], and cigarette smoking [78].

Phase 3: Subsequent Pilot Testing

Primary outcomes will be reviewed and evaluated by the study team. If any outcomes are suboptimal (poor adherence, retention, and accrual), modifications to study procedures will be discussed by the team and implemented to attempt to improve these primary outcomes. A second round of pilot testing will then be conducted to evaluate the same primary and secondary outcomes with a new sample of AYA survivors. Study population, measures, and analytic plans are expected to remain largely unchanged.

Analysis Plan

Analysis of Primary Objectives

Accrual will be estimated as the number of patients accrued divided by the number of months of accrual. A 95% CI for the monthly accrual rate will be calculated based on the Poisson distribution. The refusal rate will be estimated as the number of patients who refuse to participate divided by the number eligible. Retention will be primarily defined as the proportion of patients who provide 8-week and 12-week data. Patients who discontinue the intervention (refuse phone calls) but complete the outcome assessments will be counted in the numerator for calculating retention. Retention estimates will be calculated overall and by site. Adherence to the intervention will be calculated as the number of intervention sessions completed, the frequency of completing exercises, and the number of website visits. We will calculate and report the mean adherence across all individuals as well as the proportion of patients who completed 3 or more sessions. Several measures will be used to quantify acceptability, including quantitative measures and interviews. Means and the proportion responding affirmatively to the highest 2 responses for each question will be combined, and exact 95% CIs will be calculated for these estimates.

Analysis of Secondary Objective

Quantitative outcomes will be assessed by a covariance pattern model for repeated measures to examine the change in patient-reported outcomes over time.

Power and Sample Size

Although this is a pilot study, and we will not be testing the efficacy of the intervention, we want to estimate feasibility, acceptability, and changes in patient-reported outcomes with a fair degree of precision. With a total of 40 patients, we can estimate CIs around means within SD 0.31 and proportions within SD 15.5%, with 95% CI. Assuming 20% of the patients may drop out, we could estimate CIs for means within SD 0.35 and proportions within SD 17.3% for measures evaluated at the end of the study.

Results

Phase 1: Intervention Adaptation

The project was part of a career development award, funded in September 2011, and the pilot work began in June 2015 with intervention adaptation efforts. We first reviewed the MARIGOLD Web-based protocol in detail, and skills that were too narrowly focused on the protocol's prior target of treating depression were removed (ie, behavioral activation). The skills sequence remained the same with the exception of mindfulness, which was substituted for behavioral activation in week 2. Next, the study team reviewed the content language of the intervention and changed terms or phrases to reflect the experiences of having had cancer. For example, content language for the skill of positive reappraisal was changed to reflect commonly experienced feelings and cognitions of cancer survivors. Finally, 4 AYA stakeholders (a pediatric oncologist and AYA Medical Director, a clinical psychologist and Director of AYA Oncology, and 2 posttreatment AYA survivors) reviewed the EMPOWER intervention and provided feedback. All stakeholder input was reviewed and discussed by the study team, and minor modifications were made to content language (eg, adding *fear* as a commonly experienced unpleasant emotion among cancer survivors) and images (eg, substituting an image in the Strengths lesson for one that is more broadly applicable to cancer survivors who may have physical limitations) to finalize the intervention before pilot testing.

Phases 2 and 3: Pilot Testing

Recruitment began for phase 2 in October 2015, and recruitment began for phase 3 in April 2017. Data collection was completed in March 2019. Data analysis is currently ongoing, and the first results are expected to be submitted for publication in May 2020.

Discussion

Principal Findings

This paper describes the study protocol for adapting and pilot testing the EMPOWER intervention, a Web-based positive emotion skills intervention for AYA cancer survivors. In this study, we are tailoring an existing positive emotions intervention to align with the needs and preferences of posttreatment AYAs and then piloting the intervention over two waves of data collection to refine study procedures. Our short-term goal for this work is to produce a multicomponent, emotion regulation intervention that is feasible and acceptable to AYA cancer survivors for future testing as part of a larger RCT.

Strengths and Limitations

There are a number of strengths to this research study. First, psychosocial interventions to promote psychological well-being are infrequently tested in cancer survivorship despite their potential beneficial effects. In a meta-analysis of interventions that impact well-being outcomes in cancer, 28 RCTs with positive affect outcomes were identified, yielding an overall increase in positive affect (g=0.35) [80]. However, only 36% (10/28) of those RCTs were specifically designed to target positive affect, and only 11% (3/28) of those interventions were focused on posttreatment cancer survivors [81-83]. Our dual approach will allow us to impact psychological well-being by reducing and shortening psychological distress as well as increasing and sustaining psychological well-being.

Second, EMPOWER uses a Web-based eHealth strategy that is accessible via desktop PC, tablet PC, or smartphone (both iPhone and Android systems). As already noted, AYAs are *digital natives* and leveraging their technological aptitude for multicomponent, tailored intervention delivery allows us to match their needs and preferences to supportive care content. Moreover, because EMPOWER is scalable, it can be simultaneously delivered to a limitless number of AYAs at multiple and geographically diverse sites. Treatment integrity and fidelity to EMPOWER remain fully intact, reducing threats to internal validity. Thus, there is great long-term potential to reach AYAs who are underserved and might not typically have access to psychosocial services through community-based practices where a majority receive care [84,85].

Third, our approach uses state-of-the-art systems in the measurement of patient-reported outcomes by including emotional, physical, and social health measures from the NIH Toolbox [70,86,87] and NIH PROMIS [88-90]. These psychometrically robust measurement systems have been systematically created through rigorous qualitative and quantitative science methodologies, yielding measures that are reliable, valid, and responsive. Moreover, the static short forms were created by selecting the best performing items that provide coverage to a range of constructs, which helps to minimize respondent burden without sacrificing measurement precision. Thus, we can assess more content-relevant domains with fewer questions.

Despite these strengths, it is worth noting the potential limitations to our work. First, we are conducting a single-arm trial for this pilot study and not randomizing participants to a control arm. Although an RCT is indeed the *gold standard* of intervention research, the single-arm approach is a defensible strategy when examining primary outcomes of feasibility and acceptability for a small pilot study. As part of a future strategy with this research, we are planning to conduct a large RCT. Second, we are not screening participants into the study based on moderate to high distress scores as some emotional well-being interventions typically do. Although such an approach might result in larger effect sizes for our psychological outcomes (both distress and well-being), this would prevent us from exploring the potential benefits of this intervention for those who may not have clinically significant levels of distress but could benefit from improved emotional well-being

nonetheless. That said, we are screening out noncompliant participants with our run-in period, and this may result in a selection bias toward a highly motivated and compliant sample. Third, AYA cancer survivors have some of the poorest participation rates in cancer clinical trials (both therapeutic and supportive care) [91-94]. Recruiting AYAs involves significant time and resources. As there is a clear need for interventions that can help improve their psychological well-being, our work is a necessary first step.

Finally, our emphasis on interventions to enhance psychological well-being is not intended to deny, minimize, or otherwise ignore the significant stress of being diagnosed with and treated for cancer as an AYA or the deleterious impact it has on patients' psychological and physical health. Nor is it advocating a superficial *don't worry, be happy* approach to dealing with their illness. Rather, we are suggesting that if we broaden our focus to include a wider range of coping strategies, including interventions to promote psychological well-being, we will better equip AYAs to manage the deleterious effects of stress [95].

Conclusions

The goal of this work is to adapt and pilot test a Web-based, emotion regulation intervention designed to enhance positive emotions among AYA posttreatment cancer survivors. If EMPOWER proves feasible and acceptable, it will be primed for a subsequent large, multisite RCT. As a scalable intervention, it will be ideally suited for AYA survivors who would otherwise not have access to supportive care interventions to help manage posttreatment distress and enhance well-being.

Acknowledgments

The research reported in this publication was supported by the National Cancer Institute of the NIH under award number K07CA158008 (PI: JS). LM was supported by NCI R25 CA122061 (PI: Nancy Avis).

Conflicts of Interest

None declared.

Multimedia Appendix 1
Study timeline.
[DOCX File , 14 KB - resprot_v9i5e17078_app1.docx]

Multimedia Appendix 2
Peer-reviewer report from NIH.
[PDF File (Adobe PDF File), 135 KB - resprot_v9i5e17078_app2.pdf]

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Abbreviations

AYA: adolescent and young adult cancer survivor
eHealth: electronic health
EMPOWER: Enhancing Management of Psychological Outcomes With Emotion Regulation
HRQOL: health-related quality of life
NIH: National Institutes of Health
PI: principal investigator
PROMIS: Patient-Reported Outcomes Measurement Information System
RCT: randomized controlled trial
RHLCCC: Robert H Lurie Comprehensive Cancer Center
WFBCCC: Wake Forest Baptist Comprehensive Cancer Center

Edited by G Eysenbach; submitted 15.11.19; peer-reviewed by Y Kim, K Schmeelk-Cone; comments to author 13.01.20; revised version received 10.02.20; accepted 27.02.20; published 28.05.20.

Please cite as:
Salsman JM, McLouth LE, Cohn M, Tooze JA, Sorkin M, Moskowitz JT
A Web-Based, Positive Emotion Skills Intervention for Enhancing Posttreatment Psychological Well-Being in Young Adult Cancer Survivors (EMPOWER): Protocol for a Single-Arm Feasibility Trial
JMIR Res Protoc 2020;9(5):e17078
URL: http://www.researchprotocols.org/2020/5/e17078/
doi:10.2196/17078
PMID:32463014

Protocol

Improving Hand Hygiene Compliance in Nursing Homes: Protocol for a Cluster Randomized Controlled Trial (HANDSOME Study)

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Abstract

Background: Hand hygiene compliance is considered the most (cost-)effective measure for preventing health care–associated infections. While hand hygiene interventions have frequently been implemented and assessed in hospitals, there is limited knowledge about hand hygiene compliance in other health care settings and which interventions and implementation methods are effective.

Objective: This study aims to evaluate the effect of a multimodal intervention to increase hand hygiene compliance of nurses in nursing homes through a cluster randomized controlled trial (HANDSOME study).

Methods: Nursing homes were randomly allocated to 1 of 3 trial arms: receiving the intervention at a predetermined date, receiving the identical intervention after an infectious disease outbreak, or serving as a control arm. Hand hygiene was evaluated in nursing homes by direct observation at 4 timepoints. We documented compliance with the World Health Organization's 5 moments of hand hygiene, specifically before touching a patient, before a clean/aseptic procedure, after body fluid exposure risk, after touching a patient, and after touching patient surroundings. The primary outcome is hand hygiene compliance of the nurses to the standards of the World Health Organization. The secondary outcome is infectious disease incidence among residents. Infectious disease incidence was documented by a staff member at each nursing home unit. Outcomes will be compared with the presence of norovirus, rhinovirus, and Escherichia coli on surfaces in the nursing homes, as measured using quantitative polymerase chain reaction.

Results: The study was funded in September 2015. Data collection started in October 2016 and was completed in October 2017. Data analysis will be completed in 2020.

Conclusions: HANDSOME studies the effectiveness of a hand hygiene intervention specifically for the nursing home environment. Nurses were taught the World Health Organization's 5 moments of hand hygiene guidelines using the slogan "Room In, Room Out, Before Clean, After Dirty," which was developed for nursing staff to better understand and remember the hygiene guidelines. HANDSOME should contribute to improved hand hygiene practice and a reduction in infectious disease rates and related mortality.

Trial Registration: Netherlands Trial Register (NTR6188) NL6049; https://www.trialregister.nl/trial/6049

International Registered Report Identifier (IRRID): DERR1-10.2196/17419

(JMIR Res Protoc 2020;9(5):e17419) doi:10.2196/17419

KEYWORDS

hand hygiene; protocol; nurse; nursing home; randomized controlled trial; intervention

Introduction

Health care–associated infections (HAI) are a significant source of morbidity in nursing home residents. If we include urinary tract infections, we see on average more than one HAI per resident per year in European nursing homes [1]. Not only do residents become ill from HAI but HAI may also affect staff due to their own illness and increased workload, further disrupting care. Hand hygiene (HH) can play a role in an infection prevention strategy.

Most studies focus on hand hygiene compliance (HHC) in hospitals, ignoring other settings with vulnerable populations, such as nursing homes [2]. The few published studies that recorded HHC in nursing homes according to the World Health Organization (WHO) standards show estimates of 6% to 27% HHC before an intervention [3-7]. There is some evidence that infectious disease rates and mortality rates decrease in nursing homes when HHC increases through HH interventions [4,8-10]. While most HH intervention studies document HHC rates in hospitals, there are a few published studies showing that interventions can significantly influence HHC in a nursing home [4,8,11]. For example, 2 studies in long-term care facilities in Hong Kong showed significant increases in HHC in intervention arms (27% to 61%, $P<.001$; 22% to 49%, $P<.001$; and 26% to 33%, $P=.10$), no significant changes in control arms after implementing multifaceted HH interventions involving the provision of hand sanitizer, reminder materials, education, and, in one case, performance feedback [4,8]. In Taiwan, nursing assistants showed significantly better HHC (from 9% to 30%, $P<.001$) 3 months after participating in a 1-hour class and 30 minutes of hands-on training [11].

Due to a paucity of HH studies in nursing home settings using the WHO hand hygiene standards, we designed a trial to evaluate the impact of an intervention package tailored to the specific context of nursing homes. HH interventions developed for hospitals are not necessarily appropriate for nursing homes. First, the 5 HH moments of the WHO are difficult to interpret and use in the nursing home setting. The 5 moments of the WHO dictate that HH should be done before touching a patient, before a clean/aseptic procedure, after body fluid exposure risk, after touching a patient, and after touching patient surroundings. At the same time, a patient's surroundings in a nursing home is a fluid concept. Nursing home residents are generally mobile, sharing communal areas. For example, should touching a resident's walking frame in the living room be considered touching a resident's environment (after which HH is indicated)? Is a section of a table in a living room a particular "resident's environment" because that resident is sitting there at that moment? Second, interventions should minimally disturb the homelike setting. For example, hanging hand sanitizer dispensers on beds could be perceived as transforming the homelike environment to a medicalized one. Another difference is that nurses in nursing homes generally have less education than nurses who work in hospitals. The intervention should therefore be adapted to their educational level by using simple language and hands-on exercises [12].

The HANDSOME study was developed to evaluate the effectiveness of an intervention to improve HHC in nursing homes. An additional goal of the study is to determine if an intervention is more effective when implemented following an outbreak. In this paper, we describe the study design and protocol details of the HANDSOME study.

Methods

Overview

The HANDSOME intervention is based on our experience with developing HH interventions in hospital and childcare settings. We performed a randomized controlled HH study in 15 hospitals throughout the Netherlands [13]. Underlying determinants for HHC were addressed through various means, including making changes to the physical environment (eg, adding dispensers), creating new social norms, and implementing an HH e-Learning program. While the control and intervention arms did not differ in HHC at baseline, there was a statistically significant difference in HHC during the follow-up between the control arm (24.9% HHC) and intervention arm (35.4% HHC) [14]. In childcare settings, we conducted a cluster randomized controlled trial including providing HH products, providing HH training to childcare workers, organizing team sessions to promote goal setting, and providing stickers and posters for caregivers and children as cues to action. This led to a statistically significant increase in HHC in the intervention arm, even 6 months after the intervention [15]. Considering the significant increases in HH in these settings, we adapted these interventions for the current study.

Trial Design

HANDSOME is a parallel-group, observer-blinded, and observed-blinded cluster randomized controlled trial to increase nurses' HHC. For the purpose of this study, nurses were defined as those who have completed a 3-year or 4-year degree in nursing. The study has 3 study arms: 2 intervention arms and 1 control arm. Nursing homes were randomized to one of the 3 trial arms: fixed intervention, conditional intervention, and control. The nursing homes in the 2 intervention arms received the same intervention, while the control nursing homes did not receive the intervention. The nursing homes in the fixed intervention arm received the intervention at a predetermined date, while the nursing homes in the conditional intervention arm received the same intervention as the fixed intervention arm, but only after an infectious disease outbreak. The conditional intervention arm was conceived with the idea that an outbreak would cause an increased sense of infection risk and urgency, leading towards a better and/or more sustained HH performance. The control locations were free to implement any other infection prevention intervention, since this is

"business as usual" and it is unethical to withhold care improvements from residents. Nursing homes were observed several times for HHC, required to complete illness incidence reports, and subjected to microbiological surface sampling.

Background information about the nursing homes was collected through a structured interview. This was followed by a baseline observation in every nursing home unit. Next, nursing homes were randomized into 1 of the 3 study arms. Randomization was at the level of the nursing home rather than the individual nurse or ward, since the intervention was available to an entire nursing home. The aim was to include a minimum of 55 nursing homes: 15 fixed intervention nursing homes, 25 conditional intervention nursing homes, and 15 control nursing homes (see Sample Size Calculations).

A tablet-based app was used to document compliance. Results from background interviews, pilot observations, and the pilot intervention were used to refine the observation app and intervention. Since we were able to determine which types of HH opportunities (submoments) are the most common, these were added to the app to get more insight into HHC. We also used this extra information to address specific HH issues during the intervention, such as how to handle laundry or use a telephone, tablet, or hand brace. We were also able to specifically incorporate the most common invasive procedures in the intervention lessons. The pilot intervention allowed us to revise the materials so that they were easier to use.

Trial Aim

We aimed to increase compliance with the WHO's 5 moments of HH [16], which was measured during repeated observations over a period of 12 months.

Study Setting

All data were collected in nursing homes in the Netherlands. To capture diversity, these nursing homes are situated throughout the country in areas with differing degrees of urbanization.

Recruitment

Recruitment of nursing homes began by sending printed flyers with information about the study to large nursing home organizations listed on a website that lists most health care providers in the Netherlands (*ZorgkaartNederland*). Digital flyers were also sent to health care associations so they could inform their members about the study. In addition to the nursing homes recruited for the study, 3 nursing homes from 3 distinct organizations were recruited as pilot locations to train observers and test the intervention. After the distribution of the flyers, organizations were contacted by phone to discuss willingness, eligibility, and conditions for participation. Interested nursing homes were visited personally to further discuss participation. Enrollment began April 25, 2016. Participants are no longer being recruited.

Eligibility Criteria

Eligibility criteria were identified to foster homogeneity between nursing home units. First, only publicly funded organizations willing to commit 3 or 4 nursing homes to the study were eligible. By allocating different nursing homes within the same organization to different study arms, we aimed to minimize variation between the study arms. Each nursing home committed a minimum of 2 eligible units. Nursing home wards were considered eligible as a unit if they had 3 or more nurses working between 8:00 am and 2:00 pm on weekdays so that we could observe a minimum of 3 nurses during one observation session. If there were not enough nurses employed during those hours in one ward, multiple wards were combined and considered 1 unit for purpose of this study. If a nursing home could only supply 1 unit, it was coupled with a unit from another nursing home from the same organization. All wards primarily provided somatic or psychogeriatric residential care. Nursing homes were allowed to perform other infection prevention improvements, provided they did not simultaneously participate in other HH trials.

Allocation

The randomization process was accomplished through a stepwise procedure after baseline observations. The primary investigator first drew (computer-generated) one nursing home per organization at random for the fixed intervention arm. After this, one nursing home per organization was randomly drawn for the conditional intervention arm. The remaining nursing homes were randomly assigned to the conditional intervention arm or the control arm. This method allowed for random allocation while minimizing the variation between the study arms.

Intervention

Studies have shown that using multiple strategies that address multiple determinants (eg, a multimodal approach) is the most effective in increasing HHC [17]. Another key determinant for good HHC is repetition [17-19]. These were the cornerstones of our intervention.

For the purpose of the current trial, we scanned literature for determinants that influence HH [18,20,21], in particular for determinants that we had not considered in our earlier interventions. Additionally, 5 interviews were held at nursing homes for a better understanding of obstacles to HH. Next, intervention mapping principles were used to further recognize applicable determinants, methods, and strategies for the development of this intervention [22] (Table 1). The intervention was further refined after informal discussions with members of more than 20 nursing home organizations during the recruitment period. The intervention continued to be adjusted as an iterative process.

Table 1. Intervention mapping for HANDSOME: using determinants and methods to develop the strategy for intervention components.

Intervention element	Determinant(s)	Method(s)/strategy(s)
Meeting with management		
Present the average HHC[a] in nursing homes. Show there is room for improvement.	Knowledge	Reporting
Talk about costs (time and money) and harm (illness of residents and staff) associated with a methicillin-resistant *Staphylococcus aureus* or norovirus outbreak.	Perceived threat, acknowledging importance	Consciousness raising, persuasive communication, anticipated regret
Use a form to structurally discuss necessary facilities and facility changes for efficient HH[b] practices. Stress that the organization, not the resident, must provide all HH materials. Help optimize where HH materials are stored and how and when they are replaced.	Environmental restructuring, rules and regulations, awareness, assistance for organizational change	Organizational diagnosis and feedback/tailoring, systems change, reduce environmental barriers, persuasive communication, participatory problem solving, structural redesign, cue altering/nudging, consciousness raising, goal setting, problem management tool
Talk about the Dutch guidelines for personal hygiene and noncompliance policies at other organizations. Talk about risk of infection. Use a form to register a (new) personal hygiene policy for the organization. Make sure that employees have a safe space for personal belongings. Offer solutions for personnel with rings.	Seeing importance, rules and regulations, professional standards	Systems change, nonfinancial incentives, mandate, anticipated regret, tailoring, organizational diagnosis tool
Let management know that they can receive a "Good hand hygiene" certification if they achieve a minimum HHC.	Motivation	Nonfinancial incentives, early commitment
Convince management that their presence at Lesson 1 will positively influence HHC results. Plan lessons and the personal hygiene presentation.	Capable leadership	Persuasive communication (with management), planning
Lesson 1		
A senior nursing home manager introduces the intervention and expresses the importance of HH.	Leadership commitment, framing	Persuasive communication, public commitment, introduce systems change
Show an HH video. Present health care–associated infection statistics for nursing homes and explain health risk to self and others. Help employees visualize HH from the perspective of the resident.	Create urgency, framing	Persuasive communication, consciousness raising, anticipated regret, shifting perspective
Teach using a presentation. Teach "Room In, Room Out, Before Clean, After Dirty." Teach and discuss HH when handling pills, food, and laundry. Teach when to use hand sanitizer or soap and the proper use of gloves.	Knowledge	Chunking, using imagery, personal feedback
Team creates a group HH goal.	Self-efficacy, sense of ownership	Implementation intentions/goal setting, social influence, team commitment
Introduce the e-Learning and show the nurse's watch they can earn by completing the e-Learning.	Facilitate learning, nonfinancial incentives	Structural redesign, beginning of repeated exposure
Show posters and ask where they want to see the posters. Hand out small bottles of hand sanitizer for use in the e-Learning,	Nonfinancial incentives, self-efficacy, sense of ownership	Cue altering
Presentation of the personal hygiene policy		
A senior nursing home manager presents the personal hygiene policy (no long nails, nail polish, rings, bracelets, watches, braces, or long sleeves). Make consequences known for noncompliance.	Mandate, perceptions of norms, leadership commitment	Punishment, persuasive communication, role models
Lesson 2		
Make an inventory of barriers to good HH.	Attitude, knowledge	Discussion
Think of solutions for barriers.	Systems change	Tailoring, organizational diagnosis, planning coping responses, group discussion, structural redesign, systems change
Lesson 3		
Participants "wash" hands with paint and see where they miss.	Attitude, knowledge	Participation
Participants learn how to disinfect their hands.	Knowledge, self-efficacy	Guided practice

Intervention element	Determinant(s)	Method(s)/strategy(s)
Participants see that they get paint on hands after glove removal and that the paint represents invisible bacteria/viruses.	Knowledge	Anticipated regret, rationalize risk
Remind participants that they can earn a watch by completing the e-Learning.	Non-financial incentives	Persuasive communication
E-Learning		
Show playback squelching excuses not to do HH. Show films from the perspective of the resident.	Professional behavior standards, attitude	Using imagery, shifting perspective
Explain when to use hand sanitizer or soap. Practice using hand sanitizer with participants.	Knowledge, skills, self-efficacy	Advance organizers, modelling, guided practice
Use videos with correct and incorrect behavior to teach HH moments and common HH actions. Teach how to perform HH when preparing food and pills.	Knowledge	Chunking, modelling, active learning
Teach how to work efficiently to avoid unnecessary HH using videos with correct and incorrect behaviors.	Clinical work process flow	Systems change
Teach the proper use of gloves with still images and videos with correct and incorrect behaviors.	Perceived norms, knowledge	Active learning, imagery, modelling, persuasive communication
Show that HH does not inhibit other tasks or social contact with the resident.	Self-efficacy	Modelling
Give a quiz after every module.	Knowledge	Reinforcement through testing, feedback, monitoring
Promise a nurse's watch when the e-Learning is completed. Use dripped learning so that the e-Learning is completed in small modules over 14 weeks. Send reminders.	Curiosity, information system, knowledge, non-financial incentive	Facilitation, anticipated regret, reminders, repetition
Poster		
Multiple copies of a new poster are hung throughout the nursing home every month.	Social influence, perceived norms	Visuals, repeated exposure, cue to action
Photo competition		
Let nursing home employees know they can win a prize for the best photo of hands.	Nonfinancial incentives	Providing cues
Arts and crafts project		
Residents are informed about HH and the organization's HH goals.	Knowledge	Consciousness raising
Residents perform an activity involving hands. Nursing home displays artwork.	Perceived norms	Participation, cues to action

[a]HHC: hand hygiene compliance.

[b]HH: hand hygiene.

The intervention has 4 main components: a meeting with the management, 3 live group lessons, e-Learning, and posters. Additionally, there is a photo competition and an arts and crafts project. All components were published on a website after completion of the intervention [23].

Meeting With Management

A meeting at the nursing home took place 1-2 months after the baseline compliance measurement. A senior nursing home manager, infection prevention specialist, and facilities manager were asked to attend the meeting. The meeting started with consciousness raising about the cost of a methicillin-resistant *Staphylococcus aureus* (MRSA) outbreak so the participants would anticipate regret if they did not implement necessary changes. Next, information about the intervention and necessary facilities for HH were presented. Removing environmental barriers and adding cues to action were discussed, including the strategic placement of hand sanitizer and posters. Tailored system changes were advised to encourage better HH, such as how to hygienically dispose of dirty laundry.

The Dutch guidelines for (hand-related) personal hygiene dictate that staff members providing care do not wear rings, nail polish, artificial nails, long nails, bracelets, watches, a brace, or long sleeves [24]. Policy changes for personal hygiene noncompliance were discussed, including disciplinary consequences. Management was also asked to give a personal hygiene presentation between the first and second lesson. Although personal hygiene is broader than hand-related personal hygiene, we stressed the need to address hand-related personal hygiene.

Nursing homes were also promised a nonfinancial incentive. If they had a higher than average HHC, they would receive a certificate of good HH. At the end of the meeting, an

intervention implementation schedule was discussed. While the compliance measurements were only completed at certain wards, all nurses and nurses' aides from the entire nursing home were welcome to participate in the intervention.

Lessons

A member of the study team provided 3 lessons lasting a half hour each. The lessons were generally given multiple times on one day to a maximum of 18 participants per session.

The first lesson began with an introduction by a senior nursing home manager, showing leadership commitment to systems change. The first goal of the lesson was to create awareness about the necessity of HH. Still images, video, and a persuasive live presentation promoted consciousness raising and anticipated regret. The second goal was to teach the participants when they needed to perform HH. They were taught using a novel description of the 5 HH moments of the WHO [25], namely "Room In, Room Out, Before Clean, After Dirty" ("Kamer in, Kamer uit, Voor schoon, Na vies"). "Room In" corresponds to the WHO Moment 1 (before touching a patient). "Room Out" corresponds to WHO Moment 4 (after touching a patient) and Moment 5 (after touching patient surroundings). "Before Clean" corresponds to WHO Moment 2 (before a clean/aseptic procedure), and "After Dirty" corresponds to WHO Moment 3 (after body fluid exposure risk). This method comprises the same HH moments as the WHO standard, is more adapted to the nursing home setting, is easier to remember (one slogan), and is easier to visualize.

After explanation of the HH moments and reiteration that the participants are now expected to follow the rules for HH, the participants had time to ask questions. The next step was to ask the participants to pick a HH goal that would receive extra attention. This group goal was a moment that they thought was attainable and immediately implementable. The main reasons for creating a goal were to reflect upon what was just learned, create a sense of ownership, and create team commitment. All goals mentioned during the day's session were printed on a small poster and hung in the nurses' office to act as a reminder.

A larger, colorful poster was presented. Participants were told that different posters would come every month and asked where they would like the posters to hang so that they felt ownership of the project.

To encourage e-Learning participation, participants received a nurse's watch (which you can pin on your clothing) after completion of the e-Learning. They also left the meeting with an immediate reward, since they left with a small bottle of hand sanitizer to be used during the e-Learning. This was done to create a positive association with HH. After Lesson 1, the management-level contact(s) were informed in person and by mail of any pertinent staff comments so that they could consider making system or facility changes.

Between Lesson 1 and Lesson 2, a senior nursing home manager presented the newest rules for personal hygiene to the nurses and nurses' aides. Materials were made available to assist the manager with the presentation, including a picture of an agar with bacterial growth caused by a ring and a poster displaying personal hygiene rules. Nurses and nurses' aides were informed of their organization's disciplinary consequences if they did not adhere to the personal hygiene rules.

Lesson 2 lasted 30 minutes and was usually combined with Lesson 3 to create one lesson of 50 minutes. The main goal of the second lesson was to remove the barriers that nurses experience when trying to perform HH. Each participant was given a sheet with 28 stickers representing 13 different barriers. There were 2 blank stickers, allowing participants to write down any additional barriers. The stickers represented 4 themes, namely facilities, forgetting, choosing not to do HH, and the telephone. The barriers were identified through literature, interviews, and observations.

Sheets of paper were hung on the walls, one sheet for each of the 4 elements of the slogan (Room In, Room Out, Before Clean, After Dirty). Participants were asked to place one sticker on each piece of paper representing the main reason that he or she did not perform HH at that moment. This system facilitates an organizational diagnosis of HH impediments. Once the stickers were placed, the most prevalent barriers were discussed. Group discussions resolved barriers by designing new coping strategies, cues to action, and environmental changes. The barrier analysis with solutions was in turn discussed with the nursing home manager so that any necessary system or facility changes could take place.

During Lesson 3, participants learned the correct execution of HH through active participation. Using gloves and paint, participants saw which parts of their hands they missed when washing them incorrectly and that fluids, bacteria, and viruses can get on hands during glove removal. They also learned the correct HH procedure. Although the WHO promotes a 6-step method [25], wrist rubbing was added since this area can easily be contaminated when removing gloves. After the third lesson, management was informed of any participant feedback that could influence HHC.

E-Learning

The e-Learning served two purposes: It allowed nurses and nurses' aides who were unable to attend the live lessons to gain HH knowledge, and it provided reinforcement of these lessons. The e-Learning consisted of an introduction and 7 lessons. The themes of the lessons were the resident's perspective, how to wash and disinfect your hands, when to execute HH, HH in combination with sterile activities, time-saving work habits, glove use, and social aspects of HH. Videos modelled knowledge, guided practice, and promoted active learning by encouraging participants to scrutinize videos.

After viewing the introduction, the participant was invited every other week to complete the next lesson. This method provided participants with regular reminders to perform HH. Each lesson lasted 5-10 minutes and ended with a quiz to reinforce the message. After completing the entire e-Learning, the participant received a certificate and a nurse's watch.

Posters, Photo Competition, and an Arts and Crafts Project

To reinforce the message, 3 supplementary components were developed, namely posters, a photo competition, and an arts

and crafts project. The posters acted as reminders and included large pictures of hands and the text: “Did you remember to wash your hands?” (*Vergeet je niet je handen te wassen?*). The posters were designed to be visually appealing with a cheery image so that they could be placed in living areas. New posters were distributed monthly over a 10-month period so that the message would repeatedly capture attention. Of these posters, 5 came from the photo competition and the arts and crafts project.

Participants were invited to submit a photo for the photo competition. The idea behind this activity was to get nurses to think about HH in diverse situations, including outside the workplace. The photo submission needed to contain pictures of hands. The winners of the 3 best photos received a gift certificate. Their photos were used for 3 of the monthly posters.

Additionally, nursing homes received a package of information containing instructions on implementing a hand-related arts and crafts project with the residents. This activity had 3 goals: to create a training moment for the residents to learn when to perform HH, to inform residents that the staff is paying more attention to HH, and to again remind staff to perform HH. The 2 most appealing pieces of art were turned into 2 of the monthly posters.

Strategies to Improve and Monitor Adherence to Protocols

While the researcher used persuasive communication to convince nursing home management to allow the entire nursing staff to participate in all 3 lessons, we assumed that not everyone would attend. Intervention adherence was documented. Attendance at the HH lessons and e-Learning lessons was recorded. Additionally, attendees were asked in the process evaluation if they received information about personal hygiene policy and if they saw HH posters hanging in the nursing home.

Outcomes

Primary Outcome Measure

HHC is the primary outcome measure. HHC is defined as the number of times that HH is performed at an HH opportunity (according to the WHO’s 5 moments of HH), divided by the total number of times that it should be performed, expressed as a percentage. We only documented HH as compliant if hand sanitizer or soap, water, and a paper towel were used. Compliance was measured through live observations, still considered the gold standard, even though there is a risk of observer bias and the Hawthorne effect [26,27]. There were 4 registered timepoints (Table 2).

Table 2. Timeline of the study.

	Study period									
	Recruitment	Baseline	Randomization	Post-allocation						Close-out
Timepoint	Mar-Sep 2016	Oct 2016	Nov 2016	Dec 2016	Jan 2017	Feb 2017	Mar-Apr 2017	May 2017	Oct 2017	Nov-Dec 2017
Recruitment										
Eligibility screening	X	—[a]	—	—	—	—	—	—	—	—
Signed commitment	X	—	—	—	—	—	—	—	—	—
Randomization	—	—	X	—	—	—	—	—	—	—
Intervention (fixed intervention arm)[b]										
Meeting with management	—	—	—	X	—	—	—	—	—	—
Lesson 1	—	—	—	—	X	—	—	—	—	—
Lessons 2 & 3	—	—	—	—	—	—	X	—	—	—
E-Learning[c]	—	—	—	—	X	X	X	X	X	—
Posters[c]	—	—	—	—	X	X	X	X	X	—
Assessments										
Structured interview	X	—	—	—	—	—	—	—	—	—
Compliance observations	—	X	—	—	—	X	—	X	X	—
Illness registry[c]	—	X	X	X	X	X	X	X	X	—
Microbiology samples	—	X	—	—	—	X	—	X	—	—
Process evaluation	—	—	—	—	—	—	—	—	—	X
Close-out questionnaire	—	—	—	—	—	—	—	—	—	X

[a]Not applicable.

[b]For the conditional intervention arm, the intervention timeline was dependent upon the month an outbreak occurred.

[c]Continuous intervention exposure or measurement.

Secondary Outcome Measure

The incidence of gastroenteritis, influenza, assumed pneumonia, MRSA, and urinary tract infections in the nursing home residents is the secondary outcome measure. Nursing home staff recorded these infectious diseases on a weekly basis, along with infectious disease outbreaks. The McGeer criteria were used to define the infectious diseases [28].

Additional Outcome Measures

Additional outcome measures included the presence of norovirus, rhinovirus, and *Escherichia coli* on 3 types of surfaces in the nursing home. Norovirus is a common viral gastrointestinal pathogen, rhinovirus is a common respiratory pathogen, and *E. coli* is a common bacterial indicator of fecal contamination of the physical environment. To measure the presence of these pathogens, microbiology samples were taken with wipes and sent to the laboratory for analysis. Samples were taken during the first 3 timepoints for the primary outcome.

Hand-related personal hygiene compliance was also documented as an additional outcome measure. This was measured according to Dutch guidelines [24]. A nurse was considered compliant if he or she did not have long nails, acrylic nails, or polished nails and did not wear a ring, bracelet, wristwatch, brace, or long sleeves. Personal hygiene was noted for every nurse who was observed for HHC. Compliance is defined by the percentage of personal hygiene–compliant nurses, divided by the total number of nurses observed. Hand-related personal hygiene compliance was documented at the same timepoints as the primary outcome measure.

Timeline

The recruitment period lasted from March through September 2016 (Table 2). The trial began with baseline measurements of HH, personal hygiene, and environmental sampling in October 2016 (baseline). At this point, nursing homes began submitting a weekly disease incidence report of the illnesses mentioned earlier. After the baseline measurements, nursing homes were allocated to 1 of the 3 study arms. For the fixed intervention nursing homes, this was followed by a meeting with management, the first lesson, presentation of the e-Learning, start of monthly posters, and announcement of the photo competition. After the first lesson, the first follow-up observations occurred at the fixed intervention and control nursing homes 3 months after baseline. This was followed by the second and third HH lessons and the dissemination of information about the arts and crafts project at the fixed intervention nursing homes. 6 months after baseline, both the fixed intervention and control nursing homes were observed again. The last observation occurred at the fixed intervention and control nursing homes 12 months after baseline.

After randomization, individual conditional intervention nursing homes followed the same schedule as the fixed intervention nursing homes, but only after an outbreak occurred. Preliminary analyses of the outcome measures were performed after every round of observations. All data were collected by December 2017. This study will be completed in 2020.

Sample Size Calculation

The HH intervention was expected to increase HH compliance from 35% pre-intervention to 50% post-intervention. The sample size was calculated based on 80% power with a two-sided α of .05, taking into account the clustering of observations within nursing homes and assuming a heterogeneity between nursing homes of 0.4. It was determined that a sample size of 45 nursing homes would be sufficient, with 15 nursing homes participating in each arm. Since we could not assume that all nursing homes in the conditional intervention arm would have an outbreak during the study period, the goal was to have a minimum of 25 nursing homes in this arm.

We aimed to evaluate 2 units at each nursing home and to observe 3 nurses in each unit for a maximum of 2 hours each. This equates to 12 hours of observation per nursing home per observation round, in which we expected to observe 75 HH opportunities, equally divided over the 5 moments of the WHO. We therefore expected approximately 1125 opportunities per arm per observation round.

Blinding

Blinding the researcher to the intervention arm was not possible in this trial because the researcher also taught the lessons. The nurses were blinded by giving distinct names to the lessons (The New Way of Working) and the observations (HANDSOME), so that they appeared to be different projects. Furthermore, nurses were told that the observers were registering the frequency of health care activities. HH observers were not informed which nursing homes were receiving the intervention, although they may have noticed HH posters from the intervention while observing.

Data Collection Instruments

Before the first observation, nursing home unit managers were interviewed in person or over the telephone. A baseline questionnaire was used to gain more insight into the background characteristics of each individual unit, such as the number of employees, brand of HH products, and type of care provided by the unit.

We designed a tablet-based observation app to measure HH and hand-related personal hygiene. The registration events were based on the 5 moments of HH, as determined by the WHO and Dutch guidelines for personal hygiene [16,24]. Hand-related personal hygiene was recorded once for every observed nurse per observation day.

When documenting HH, a distinction was made between the use of hand sanitizer or combination of water, soap, and paper towel. If neither method was used at an opportunity or if the water-soap-paper towel combination was missing one element, then the HH opportunity was considered “missed.” To be considered compliant, HH needed to happen in the same room in which the action occurred. The only exceptions to this rule were if a nurse brought a resident to another room, a nurse carried something soiled, or no door needed to be opened before leaving the room. In these cases, HH should have taken place at the end of the action.

Compliance to the 5 moments of the WHO was broken down into submoments, giving more insight into the frequency of and compliance at submoments (Table 3). Three additional activities that potentially facilitate pathogen transmission were registered separately, namely the preparation and serving of food and medication, taking gloves to use for non-resident related activities, and social contact. HHC related to food and medication activities was documented since this could be considered a clean procedure (Moment 2). HH before taking gloves for non-resident related activities was noted because taking gloves without first performing HH may contaminate other gloves from the same box [29]. According to the WHO guideline for long-term health care, HH is not required during social contact, even though it does involve hand contact and thus potentially facilitates pathogen transmission [16]. We therefore recorded the number of times that this occurred. We defined social contact as patting the shoulder/knee, shaking hands, patting a hand, and hugging.

Table 3. Moments and submoments for hand hygiene compliance documentation.

Moment	Submoment
Moment 1 (before touching a patient)	Washing or providing perineal care in own room, providing perineal care at the toilet, other care, and after the use of a mobile phone, tablet, or computer during resident contact (during Moment 1 activities)
Moment 2 (before clean/aseptic procedure)	Catheter care, wound care, injection, feeding tube care, colostomy care, pain pump care, eye drops, tracheostomy tube care, mucous suction, other invasive care, and after the use of a mobile phone, tablet, or computer during resident contact (during Moment 2 activities)
Moment 3 (after body fluid exposure risk)	Invasive care, removing bedding, washing/cleaning the resident in own room, helping resident at the toilet, other (body fluid of a resident), own body fluid, helping animals, and before the use of a mobile phone, tablet, or computer during resident contact (during Moment 3 activities)
Moment 4 (after touching a patient)	Resident care and before the use of a mobile phone, tablet, or computer during resident contact (during Moment 4 activities)
Moment 5 (after touching a patient's surroundings)	No submoments
Additional potential moments for pathogen transmission	
Before using gloves (not patient-related)	No submoments
Before food and pills	Preparing or administering medicine, preparing food, serving food, helping with eating, and washing the resident's hands before eating
Social contact	Pat on the shoulder, shaking hands, touching a hand, and hugging

Once the observations were finished with one nurse, the observer reset the app for the observations with the next nurse. Personal hygiene compliance was only registered one time per nurse.

The residents' infectious disease occurrence was recorded by staff. Each unit received a notebook in which a designated person (nurse, team leader, or geriatrician) recorded the weekly incidence of gastroenteritis, influenza, assumed pneumonia, MRSA, urinary tract infections, and an outbreak. The nursing home was free to decide who was responsible for the reporting. We only collected anonymized patient data. Definitions of the illnesses were given in the notebook to promote homogeneity in reporting. Weekly reports were sent to the researcher via email or WhatsApp.

Microbiology samples were collected at baseline, 3 months after baseline, and 6 months after baseline (Table 2). Samples were taken from a communal table, a communal toilet, and the computer mouse and keyboard. The qualitative molecular detection technique quantitative polymerase chain reaction was used to detect viral indicator organisms and *E. coli*. The wipes used in this process do not supply quantitative results, but they make it possible to cover a larger surface area than with swabs, enhancing the sensitivity.

A process evaluation occurred after the intervention. Every nurse who attended at least one live lesson or started the e-Learning received an email with a link to a process evaluation questionnaire. They were asked questions to measure fidelity at the unit and their opinion about different aspects of the intervention.

After the intervention was completed, a senior nursing home manager participated in a close-out questionnaire to assess system changes or infection prevention programs that may have affected HHC during the study period.

Measuring Compliance: Training and Planning

Independent observers were trained to observe HHC using an adapted training method from an HHC study in Dutch hospitals [30]. Observers were primarily nurses and doctors in training. These observers were trained over a period of 2-3 days using videos, case studies, and live observations at 2 nursing homes. The training ended with an examination using videos from Hand Hygiene Australia [31]. The observers also received training in collecting microbiological samples.

Observers documented nurses' HHC at the nursing home from 8:00 am to 2:00 pm. The objective was to observe a minimum of 3 nurses, each for a maximum of 2 hours.

Promoting Participant Retention

If a nursing home considered stopping the intervention, it was encouraged to continue the program through persuasive communication. If the nursing home refused to follow the protocol, the researcher had the option to withdraw the participant from the program. If the nursing home dropped out of the intervention, management was still asked to answer questions in the close-out questionnaire.

Data Management and Dissemination

Data were collected in different ways. Background information about the nursing homes and information from the close-out questionnaire were collected during interviews and from forms sent from the nursing homes. This information was entered in an Excel (Microsoft Corp, Redmond, WA) document. Weekly infectious disease incidence reports were similarly entered in an Excel document by a dedicated staff member. All compliance data were entered in an app and downloaded into Excel documents. Compliance data will be cleaned in SPSS version 25 (IBM Corp, Armonk, NY). The results of the microbiology samples were entered in an Excel document. Information from the process evaluation was gathered with an online survey and downloaded into SPSS. HHC and protocol adherence results were disseminated to participating nursing homes in personalized reports. The results of the study will be made available to the wider community in scientific publications. Data will be managed and archived according to the Quality Manual of the Department of Public Health, Erasmus MC, University Medical Center Rotterdam. Researchers may request access to the data from the chair of the Department of Public Health, Erasmus MC, University Medical Center Rotterdam.

Statistical Methods

The various outcomes of the trial (primary, secondary, and additional) will be analyzed separately according to the specific research hypotheses (Table 4).

Table 4. Statistical methods

Outcome	Hypothesis	Outcome measure	Methods of analysis
Primary: hand hygiene	Improvement is higher in the intervention arms than the control arm.	Hand hygiene compliance (binary)	Multilevel logistic regression
Secondary: infectious disease incidence	There will be a lower disease incidence in the intervention arms than in the control arm.	Infectious disease incidence (binary)	Multilevel logistic regression
Additional: presence of norovirus, rhinovirus, and *Escherichia coli*	There will be a lower detection rate of microorganisms on surfaces in the intervention arms than in the control arm.	Proportion of samples positive for norovirus (genogroups I and II), rhinovirus (continuous), and *Escherichia coli*	Multilevel loglinear regression
Additional: personal hygiene	Improvement is higher in the intervention arms than in the control arm.	Personal hygiene compliance (binary)	Multilevel logistic regression

Ethics Approval and Consent to Participate

Ethical approval for the study was waived by the Medical Ethics Review Committee of the Erasmus MC (no.58158). Any significant changes to the study protocol were communicated to the Medical Ethics Review Committee. All changes were communicated to the participants, steering committee, and study sponsor. Consent to participate is not relevant in this study, since we did not collect any patient information. No identifying information about the nurses was collected. All collected data will be anonymized before publication to protect the privacy of the nursing home and nursing home staff. Data sets will be anonymized according to our quality manual and data management plan.

Results

The study was funded in September 2015. Medical ethical approval was waived in August 2016. Data collection started in October 2016 and was completed in October 2017. In total, 124 nursing home units were recruited in 62 nursing homes. Of these, 116 units were allocated: 36 to the fixed intervention arm, 50 to the conditional intervention arm, and 30 to the control arm. Data analysis is ongoing, and the first results are expected to be published in 2020.

Discussion

The HANDSOME study was created to increase HHC in nursing homes. We took this opportunity to not only look at HHC but also to investigate a secondary outcome of the incidence of gastroenteritis, influenza, assumed pneumonia, MRSA, and urinary tract infections in the nursing home residents. The presence of norovirus, rhinovirus, or *E. coli* on nursing home surfaces was also documented, creating the opportunity to triangulate with HHC and infectious disease incidence. We also documented hand-related personal hygiene compliance.

The HANDSOME intervention was developed specifically for the nursing home setting. It used a blended learning model to reach as many nurses as possible. HANDSOME reframes the WHO's HH moments so that they are understandable and easily recalled in a nursing home setting. We created the slogan "Room In, Room Out, Before Clean, After Dirty," which incorporates the WHO framework for HH. It specifically takes into account that most health care actions occur in the residents' bedrooms, social contact is excluded from the HH rules in nursing homes, and it is only feasible to consider the resident's room (or that portion of the room that belongs to him or her) as the resident's surroundings.

"Room In, Room Out" is a concept that has been used before in HH policies, mostly with the terms "Wash In, Wash Out"

[32,33]. The "Wash In, Wash Out" method is problematic for various reasons. It inherently neglects HH before an aseptic procedure and after contact with bodily fluids. Additionally, as demonstrated by Sunkesula et al [34], the health care worker would often be expected to do unnecessary HH when using the "Wash In, Wash Out" method since health care workers often do not touch patients in the patient's room. Furthermore, "Wash In, Wash Out" inherently emphasizes hand washing and ignores the benefits of using hand sanitizer. We address these problems by using the terms "Room In, Room Out, Before Clean, After Dirty" and teaching participants in the lessons and e-Learning that they do not need to perform HH in a resident's room if they do not touch the resident or the resident's surroundings and they can omit "Room In" if they only touch the resident's surroundings without touching the resident.

Our observational method should also give more insight into HHC moments. Our study is one of the few that looks specifically at the separate moments and submoments of the 5 WHO moments. This way, we can gain better insight into which health care actions occur most frequently in nursing homes and which moments need the most attention to attain a higher HHC and less illness. We also expect to gain more insight into barriers for each HH moment. During the second lesson, participants were asked to specify barriers experienced during the different HH moments.

This study should add to the body of evidence that HHC is suboptimal in nursing homes and can be significantly improved through an intervention. We also expect to gain insight in personal hygiene compliance in nursing homes. Another strength of this study is that it created an aggregate register of residents' infections. Although there are some data about HAIs in nursing homes, most nursing homes only register illness in individual dossiers [1]. This study collected data about infection incidence using the same definitions as the National Institute for Public Health and the Environment in the Netherlands so that the data can be compared [35]. This could add more insight and help form the agenda to avoid unnecessary illness. We believe that this is also one of the first studies to systematically sample nursing home surfaces for various viruses and bacteria in order to study the potential added value as an alternative method to monitor HHC.

Another novel aspect of our intervention is that we may discover if an intervention is more successful at a random point in time or after an infectious disease outbreak. We should create more insight into when HH interventions should be implemented.

This study also has limitations. Since we used the gold standard of measuring HHC, observers directly observed nurses giving care. This may have caused Hawthorne or observer bias. A second limitation is that nursing homes were not required to send every nurse to the lessons, conceivably causing a significant variation in compliance to the protocol. Another limitation could be that observers were able to guess which nursing homes received the intervention, since these nursing homes had HH posters from the intervention hanging on the walls, which may unconsciously have influenced their observations. Last, we only observed HH at organizations with at least 3 nursing homes. This study therefore does not necessarily reflect HHC at smaller organizations.

Considering that there are few studies that have rigorously investigated the WHO's recommendations for HH, HANDSOME will provide needed insight into HH in nursing homes. The results from this study could help in creating more refined and successful HH interventions in the future. Future interventions can focus on the moments that are more often missed.

Acknowledgments

We would like to thank Caspar Looman for the original statistical analysis for sample size calculation and Jennifer Bloem for her assistance in this project. This work is supported by the Netherlands Organization for Health Research and Development (ZonMw) [grant number NL50-53000-98-151]. Essity Hygiene Products AB supplied non-monetary assistance (small bottles of hand sanitizer). ZonMw and Essity have no role in or authority over the design, collection, management, analysis, interpretation, and publication of data or in writing the manuscript.

Conflicts of Interest

None declared.

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Abbreviations

HAI: health care–associated infection.
HH: hand hygiene.
HHC: hand hygiene compliance.
WHO: World Health Organization.

Edited by G Eysenbach; submitted 11.12.19; peer-reviewed by C Smith, D Szinay; comments to author 13.02.20; revised version received 20.02.20; accepted 26.02.20; published 01.05.20.

Please cite as:
Teesing GR, Erasmus V, Petrignani M, Koopmans MPG, de Graaf M, Vos MC, Klaassen CHW, Verduijn-Leenman A, Schols JMGA, Richardus JH, Voeten HACM
Improving Hand Hygiene Compliance in Nursing Homes: Protocol for a Cluster Randomized Controlled Trial (HANDSOME Study)
JMIR Res Protoc 2020;9(5):e17419
URL: https://www.researchprotocols.org/2020/5/e17419
doi:10.2196/17419
PMID:32356772

Protocol

Patient-Reported Outcome Measures in Cystic Fibrosis: Protocol for a Systematic Review

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Abstract

Background: Patients with cystic fibrosis (CF) can struggle with burdensome symptoms and treatment regimens that negatively affect every aspect of their life. As physiological parameters can fail to capture these complications, the assessment of health-related quality of life (HRQOL) has gained prominence. HRQOL can be measured using standardized patient questionnaires called patient-reported outcome measures (PROMs). The Australian Cystic Fibrosis Data Registry (ACFDR) collects clinical data on adult and pediatric patients with CF. The incorporation of PROMs into the ACFDR would enable monitoring of HRQOL trends, benchmarking of HRQOL outcomes, and support of HRQOL research in CF.

Objective: Prior to incorporation of a PROM in the ACFDR, this systematic review was planned to evaluate whether any suitable PROMs are currently being used for CF.

Methods: This systematic review will be conducted in compliance with the PRISMA-P (Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols) guidelines. MEDLINE, EMBASE, Scopus, CINAHL (Cumulative Index of Nursing and Allied Health Literature), PsycINFO, and Cochrane Library databases were searched for articles published between January 2009 and February 2019 on the use of PROMs to measure HRQOL in adult and pediatric patients with CF. Study designs such as observational studies, reviews and validation studies were included. Studies describing randomized controlled trials, dissertations, books, guideline statements, and abstracts were excluded. The COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) risk of bias checklist was used to assess the methodological quality of included studies. A descriptive synthesis of the results will be undertaken in line with the outcomes of this study.

Results: As of July 2019, the search has been conducted and 4530 records were screened. After two phases of screening, 97 studies were included in the final review and subjected to data extraction. Reviewers are currently in the process of critical appraisal.

Conclusions: This review will identify any PROM(s) that may be used to measure HRQOL in the ACFDR.

Trial Registration: PROSPERO International Prospective Register of Systematic Reviews CRD42019126931; https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=126931

(JMIR Res Protoc 2020;9(5):e15467) doi:10.2196/15467

KEYWORDS

patient-reported outcome measure; PROM; cystic fibrosis; health-related quality of life

Introduction

Disease Background

Cystic fibrosis (CF) is the most common life-shortening autosomal recessive disease affecting Caucasian populations [1]. CF (ICD-10 code E84) is caused by mutations affecting the cystic fibrosis transmembrane conductance regulator (CFTR) protein, which transports chloride ions across epithelial cell membranes [2]. Changes in chloride ion concentration cause thicker exocrine secretions and increased salt concentration throughout the body [1]. In the respiratory tract, where the

disease is most detrimental, thickened mucus restricts the airway lumen [2] and impairs clearance of microorganisms, resulting in chronic cough, increased infections, and bronchiectasis [3]. Pulmonary disease can progress to respiratory failure and death [2]. Other common consequences of CFTR mutations include pancreatic insufficiency, impaired intestinal motility, impaired growth, and diabetes [2].

Although life expectancy with CF has improved significantly in the last few decades [4], patients with CF continue to struggle with symptoms that have a profound impact on all areas of life [5]. In addition, daily treatment regimens have become more complex and time-consuming and can require 2-3 hours a day [6]. Traditional physiological parameters that measure disease severity do not capture the impact of symptom and treatment burden on daily functioning. As a result, the assessment of health-related quality of life (HRQOL) in CF has gained prominence as an alternative measure of disease severity and functional limitation [7].

HRQOL has been defined as "an individual's perception of their position in life" [8]. It is a multidimensional construct that encompasses physical symptoms, daily functioning, psychological well-being, social functioning, and relationships [8]. As these domains are best understood and described by patients themselves, patient-reported outcome measures (PROMs) are commonly used to report HRQOL [6]. PROMs are standardized questionnaires filled out by patients or their proxies [9]. They capture patients' perceptions of their own well-being [9].

In CF, PROMs are currently used for a variety of purposes including the following: as outcomes in clinical trials, to evaluate the efficacy of new interventions, to measure the effects of disease on patient functioning, or to compare the cost-effectiveness of treatments [10]. However, PROMs can be used most effectively when captured prospectively and longitudinally through routine data collection [11]. Including a PROM within a pre-existing clinical registry is a cost-effective method of HRQOL data collection [11]. When PROMs have been incorporated in national [12] and international [11,13,14] registries for other diseases, they have been used to track treatment outcomes, monitor HRQOL trends, and support benchmarking and quality improvement [15].

Australian Cystic Fibrosis Data Registry

The Australian Cystic Fibrosis Data Registry (ACFDR) was established in 1998 and collects clinical data on adult and pediatric patients with CF. Information is collected multiple times a year from specialist clinics [16]. At the end of 2017, the ACFDR held data from 3151 patients [16], estimated to be over 90% of Australian patients with CF [17]. Data collected included patients' demographics, social functioning, physical health, treatments, hospitalizations, and mortality [16]. Growing interest in the incorporation of PROMs in Australian registries [18] has led to the evaluation of a HRQOL PROM in the ACFDR. This systematic review was planned as the first phase of a project to identify a PROM that would be appropriate to include in ACFDR data collection.

Objectives

Preliminary searches identified no published data on the use of PROMs in CF clinical registries and no recent systematic reviews summarizing adult and pediatric HRQOL PROMs in CF. Therefore, we planned a systematic review to examine all PROMs currently applied to CF populations to identify whether any PROMs are suitable to incorporate in the ACFDR. We require information on the populations and contexts PROMs are used, their reliability and validity in those populations, and how they are perceived by patients. Information on mode and frequency of PROMs administration is also required. We believe this systematic review will identify a suitable PROM to use in the ACFDR and the best method to implement this PROM.

The primary objective of the proposed systematic review is to identify which PROMs examining HRQOL have been used in adult and pediatric populations with CF and to summarize their psychometric properties. Secondary objectives are to identify how PROMs are administered and assess patient perceptions of PROMs.

Methods

This systematic review protocol follows the PRISMA-P (Preferred Reporting Items for Systematic Review and Meta-Analyses Protocol) guidelines [19]. A detailed description on population, intervention, comparison, and outcome of the systematic review is outlined in Textbox 1.

Inclusion and Exclusion Criteria

Inclusion and exclusion criteria for articles can be found in Textbox 2.

Textbox 1. Population, intervention, comparison, and outcome (PICO) of systematic review.

Population: Adults (aged 18 years old and above) and children (aged under 18 years old) with diagnosed cystic fibrosis (CF)

Intervention: Generic and disease-specific patient-reported outcome measures (PROMs) that evaluate health-related quality of life in patients with CF

Comparison: Studies without a comparator will be considered for inclusion.

Outcome: The primary outcome measure is the assessed or stated psychometric properties of PROMs. The secondary outcome measures are (1) contexts in which PROMs have previously been used, (2) administration methods of PROMs, and (3) acceptability of PROMs for patient population.

Textbox 2. Article inclusion and exclusion criteria.

Inclusion Criteria:

- Articles describing the use of patient-reported outcome measures (PROMs) to measure health-related quality of life in cystic fibrosis (CF)
- Study participants of all ages and genders with a prior diagnosis of CF, including cases where proxy respondents have completed PROMs on behalf of patients
- Study designs including reviews, observational studies, and validation studies
- Available in English language
- Published in the last decade (from January 2009 to February 2019)

Exclusion Criteria:

- Published before January 2009
- Describing randomized control trials
- Unpublished manuscripts, dissertations, books and book chapters, conference proceedings, meeting abstracts, and guideline statements

Study Design

Quantitative (eg, cohort, longitudinal, prospective, retrospective, validation, and case studies) and qualitative studies (eg, phenomenological, grounded theory, and case reports) exploring HRQOL outcomes in patients with CF were included. Mixed methods research articles were also included in the review.

Context

Studies conducted in clinical environments such as acute care (hospital inpatient services and emergency departments) and subacute care (primary health care and outpatient clinics) were included. Patients recruited from databases, patient support groups, and registries were also included.

Outcomes of Interest

The primary outcome of interest is to identify which PROMs are currently used in adult and pediatric populations with CF and to summarize the psychometric properties of PROMs (eg, content validity, internal consistency, responsiveness), as assessed for the study population or as stated based on previous studies.

Secondary outcome measures include (1) contexts in which HRQOL PROMs are currently used (eg, interventional studies, prevalence studies, clinical registries); (2) administration methods of PROMs (eg, paper survey, electronic, interview, use of proxy-respondents); and (3) acceptability of PROMs (eg, relevance, ease of use, clarity) as described by authors of the study.

Search Methods

Initial Ovid MEDLINE searches were undertaken to find published studies and reviews relevant to the topic. Keywords and index terms from these articles were recorded and used to develop the final search strategy. The search strategy was finalized in Ovid MEDLINE and adapted as required for other databases using the MeSH trees. The draft search strategy included the terms “patient reported outcome” OR “patient reported outcome measure” OR “self-report*” OR “questionnaire” OR “scale” OR “perception” OR “quality of life” OR “QOL” AND “cystic fibrosis.” The search was restricted to the past 10 years to only include PROMs relevant to the current population with CF.

The following databases were searched: MEDLINE, EMBASE, Scopus, CINAHL (Cumulative Index of Nursing and Allied Health Literature), PsycINFO, and Cochrane Library. A search of the gray literature was not conducted. Bibliographies of all selected studies fulfilling inclusion criteria will be scanned to identify any articles missed by the search.

Data Management

All studies identified in database searches were compiled in Endnote X7 (Clarivate Analytics). Duplicates were deleted using the Endnote “Remove Duplicates” function and a manual scan of the results. Review documentation and search results were saved and backed up in Monash University’s faculty-allocated network storage (S-drive). Data will only be accessed by the reviewers.

Selection Process

In the first stage of screening, one reviewer (IR) read the titles and abstracts of all studies identified by the search. Studies that met the inclusion criteria were included. During the second stage, two reviewers (IR and RR) read the full texts of the remaining studies and removed any that clearly met the exclusion criteria. Any disagreements that arose were resolved through discussion.

If bibliographies of selected full texts comprised any articles consistent with the inclusion criteria, the full texts of these articles were also considered for inclusion. The number of studies at each stage of the search were recorded using the PRISMA-P flow diagram.

Data Extraction

Data was extracted by one reviewer. The information that was extracted from articles is detailed in Textbox 3. Information on methods of PROMs development, target age range, and purposes for which PROMs were developed will be extracted by searching bibliographies for original studies describing PROM development.

Textbox 3. Data extracted from included articles.

- Study design (cross-sectional, longitudinal, validation, development, interventional, review)
- Study population (number of participants)
- Type of study (quantitative or qualitative)
- Age group of participants (adult, pediatric, all ages)
- Mean age of participants, where provided
- Recruitment of patients (inpatient, outpatient, database, registry, etc)
- Setting in which patient-reported outcome measure (PROM) is administered (inpatient, outpatient)
- PROM(s) used
- Type of PROM(s) (generic, specific)
- Why PROM(s) is used (validation, outcome of intervention, prevalence, etc)
- Time points when PROM is administered (number, frequency)
- Method of administration (interview, paper, online)
- Psychometric properties of PROM assessed during the study or quoted from previous study (construct validity, content validity, internal consistency, reliability, responsiveness)
- Acceptability of PROMs to patients with cystic fibrosis as described by study authors (face validity or description of how PROMs are perceived by participants)

Study Quality and Assessment of Risk of Bias

The COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) risk of bias checklist will be used to evaluate the methodological quality of included studies [20]. This tool has been chosen, as it specifically assesses studies that use PROMs. The tool assesses 10 measurement properties of PROMs (PROM development, content validity, structural validity, internal consistency, measurement invariance, reliability, measurement error, criterion validity, construct validity, and responsiveness). Each property is evaluated against a number of items [20].

Two reviewers will independently appraise studies using the tool. As not all studies describe all properties, only relevant areas of the COSMIN checklist will be applied to each study [20]. Reviewers will rate each item on a 4-point scale denoted as very good, adequate, doubtful, or inadequate. Results will be summarized in a table presenting the lowest score for each property [20]. Any disagreements between reviewers will be resolved through discussion.

Analysis

A descriptive synthesis of the results will be undertaken in line with the outcomes of this study. Summary tables of characteristics of the included studies and PROMs will be presented. A description of included instruments will be given, along with the contexts in which they were used, how they were administered, and their acceptability to patients. This information will then be used to compare instruments. PROM(s) that may be suitable for inclusion into the ACFDR will be identified by considering the applicability and acceptability of instruments to a population of Australian adult and pediatric patients and caregivers. Quantitative synthesis will not be performed, as the included studies assess different outcomes.

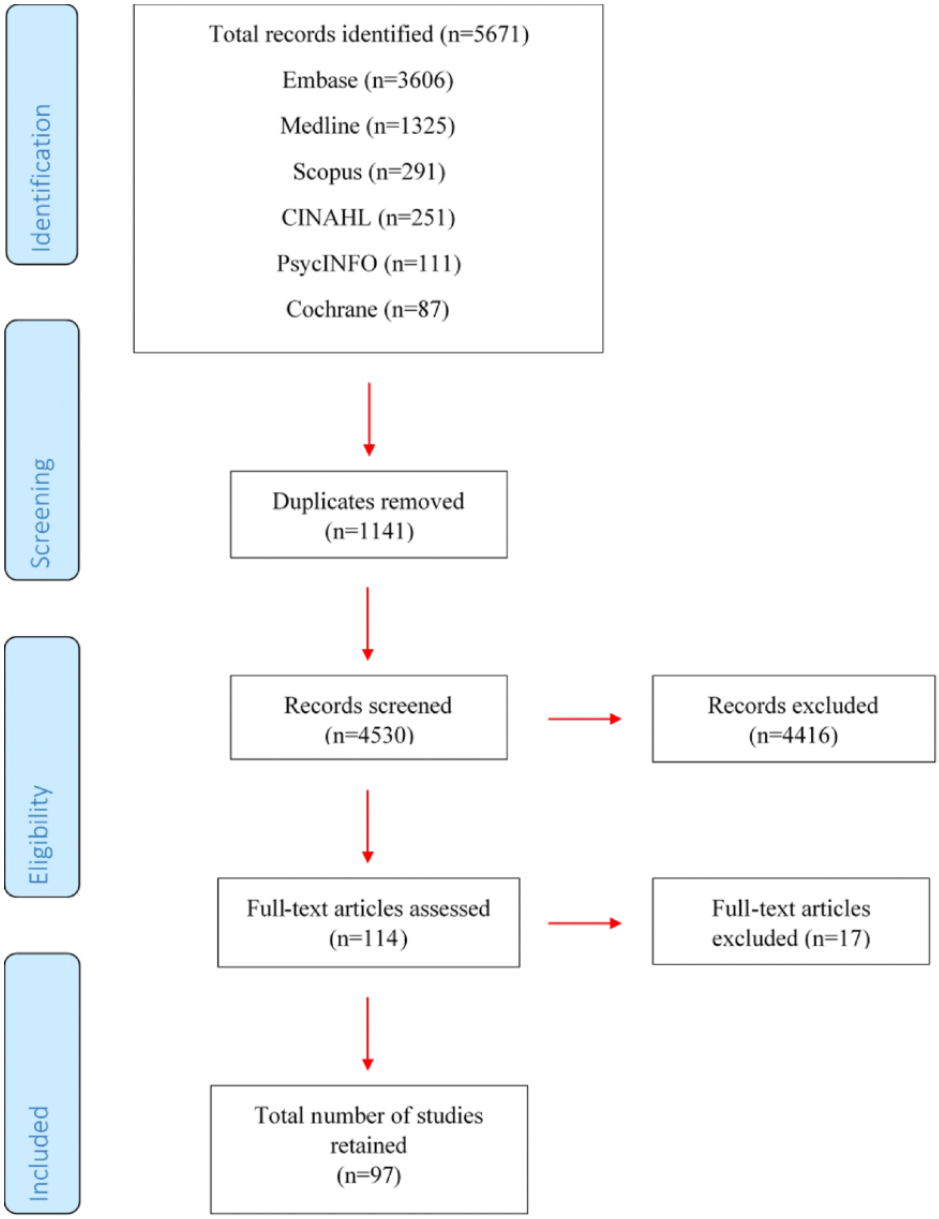
Ethics and Dissemination

Ethical approval is not required, as primary data was not collected. This project does not require patient or public involvement. Review results will be published in a thesis and peer-reviewed journal and will be presented at conferences. The study has been registered with the International Prospective Register of Systematic Reviews (PROSPERO); registration number CRD42019126931).

Results

Reviewers conducted the search in February 2019. The final search strategy in each database is presented in Multimedia Appendix 1. The search originally yielded 5671 studies and after deleting duplicates, 4530 articles remained. The initial screen of titles and abstracts identified 114 articles that fit the inclusion criteria. Two reviewers (IR and RR) conducted a further screen of full texts and eliminated 17 articles that met the exclusion criteria. A review of bibliographies identified no further studies. The number of studies at each stage is summarized in Figure 1. Reviewers then extracted data from the remaining 97 studies. As of February 2020, reviewers have commenced data analysis.

Figure 1. Flowchart of study selection and identification according to PRISMA-P (Preferred Reporting Items for Systematic Review and Meta-Analyses Protocol).



Discussion

To our knowledge, there is no recent systematic review describing the use of PROMs evaluating HRQOL in patients with CF. As interest in PROMs for CF grows, there is a need for a summary of all available information to understand which PROM(s) would be best suited for particular settings in CF. The proposed review aims to collate recent PROMs data used to evaluate HRQOL in patients with CF. It will identify how and in what patient populations they are administered, their effectiveness at assessing HRQOL, and their acceptability for the patient population. It will enable the identification of PROMs suitable for use in the modern Australian population with CF and in a national clinical registry setting.

This systematic review excluded randomized controlled trials (RCTs), which may limit the results regarding the extent of PROM use in CF research. However, a priori searches demonstrated that only one PROM was used in RCTs and that RCTs did not commonly provide information on the secondary outcomes of this review (administration methods, psychometric properties, or patient perspectives). Excluding RCTs may also enable a focus on observational studies, which have data collection methods more closely resembling clinical registries. Another limitation is that a search of the gray literature was not conducted, which may limit the scope of the systematic review. As preliminary gray literature searches identified no relevant sources, a formal search was not conducted.

In summary, this review will aim to identify PROM(s) that could be used to measure HRQOL in the ACFDR, a national registry collecting data from adult and pediatric patients with CF. Following identification of a suitable PROM, we plan to collect qualitative data on patient, caregiver, and clinician perceptions of the selected instrument.

Acknowledgments

IR, RR, and SA have contributed to developing the idea and methodology for a systematic review. IR registered the protocol with PROSPERO and drafted the first manuscript, which was reviewed by all authors. Constructive feedback was given from RR and SA and incorporated in the final version. All authors read and approved the final manuscript. The guarantor of this protocol is Dr Rasa Ruseckaite.

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Search strategy.
[PDF File (Adobe PDF File), 450 KB - resprot_v9i5e15467_app1.pdf]

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Abbreviations

ACFDR: Australian Cystic Fibrosis Data Registry
CF: Cystic Fibrosis
CFTR: Cystic fibrosis transmembrane conductance regulator
HRQOL: Health-related quality of life
PROM: Patient reported outcome measure

Edited by G Eysenbach; submitted 12.07.19; peer-reviewed by L Ranandeh, AR Safarpour, C Duncan; comments to author 21.10.19; revised version received 24.11.19; accepted 26.02.20; published 06.05.20.

Please cite as:
Ratnayake I, Ahern S, Ruseckaite R
Patient-Reported Outcome Measures in Cystic Fibrosis: Protocol for a Systematic Review
JMIR Res Protoc 2020;9(5):e15467
URL: https://www.researchprotocols.org/2020/5/e15467
doi:10.2196/15467
PMID:32374269

Protocol

Use of Simulation Modeling to Inform Decision Making for Health Care Systems and Policy in Colorectal Cancer Screening: Protocol for a Systematic Review

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Abstract

Background: Simulation modeling has frequently been used to assess interventions in complex aspects of health care, such as colorectal cancer (CRC) screening, where clinical trials are not feasible. Simulation models provide estimates of outcomes, unintended consequences, and costs of an intervention; thus offering an invaluable decision aid for policy makers and health care leaders. However, the contribution that simulation models have made to policy and health system decisions is unknown.

Objective: This study aims to assess if simulation modeling has supported evidence-informed decision making in CRC screening.

Methods: A preliminary literature search and pilot screening of 100 references were conducted by three independent reviewers to define and refine the inclusion criteria of this systematic review. Using the developed inclusion criteria, a search of the academic and gray literature published between January 1, 2008, and March 1, 2019, will be conducted to identify studies that developed a simulation model focusing on the delivery of CRC screening of average-risk individuals. The three independent reviewers will assess the validation process and the extent to which the study contributed evidence toward informed decision making (both reported and potential). Validation will be assessed based on adherence to the best practice recommendations described by the International Society for Pharmacoeconomics and Outcomes Research-Society for Medical Decision Making (ISPOR-SMDM). Criteria for potential contribution to decision making will be defined as outlined in the internationally recognized Grading of Recommendations Assessment, Development and Evaluation Evidence to Decision (GRADE EtD) framework. These criteria outline information that the health system and policy decision makers should consider when making an evidence-informed decision including an intervention's resource utilization, cost-effectiveness, impact on health equity, and feasibility. Subgroup analysis of articles based on their GRADE EtD criteria will be conducted to identify methods associated with decision support capacity (ie, participatory, quantitative, or mixed methods).

Results: A database search of the literature yielded 484 references to screen for inclusion in the systematic review. We anticipate that this systematic review will provide an insight into the contribution of simulation modeling methods to informed decision making in CRC screening delivery and discuss methods that may be associated with a stronger impact on decision making. The project was funded in May 2019. Data collection took place from January 2008 to March 2019. Data analysis was completed in November 2019, and are expected to be published in spring 2020.

Conclusions: Our findings will help guide researchers and health care leaders to mobilize the potential for simulation modeling to inform evidence-informed decisions in CRC screening delivery. The methods of this study may also be replicated to assess the utility of simulation modeling in other areas of complex health care decision making.

International Registered Report Identifier (IRRID): DERR1-10.2196/16103

Trial Registration: PROSPERO no. 130823; https://www.crd.york.ac.uk/PROSPERO

(JMIR Res Protoc 2020;9(5):e16103) doi:10.2196/16103

KEYWORDS

colorectal cancer screening; simulation modeling; decision-making; model validation

Introduction

The benefits of colorectal cancer (CRC) screening have been well cited including a reduced incidence of CRC, earlier stage of presentation, improved outcomes for patients with detected malignancy, and reduced CRC-associated mortality [1-4]. Screening uses fecal tests, diagnostic imaging, and endoscopic examination to assess the possiblity of CRC occurring among asymptomatic individuals at increased risk of developing CRC. Participation of eligible individuals is voluntary and remains low in many regions across our country [5]. Determining the best screening modality, delivery method, resource allocation, and follow-up for screening is complex because health policy and system decision makers must weigh the cost and benefits of screening, taking into account the sensitivity, specificity, and accessibility of various screening modalities. Furthermore, such interventions often cannot be tested in clinical trials because of multiple environmental, sociocultural, and health system factors that negate the feasibility and safety of a trial [6]. Researchers and decision makers have increasingly relied on simulation models to evaluate interventions in CRC screening [7,8].

A simulation model is a computer-generated representation of a real-world system or process that can be used to analyze the evolving behavior of a system over time, or modified to predict results of a variety of "what-if" scenarios [9]. Simulation models have been applied to a broad range of areas in health care to predict outcomes, unintended consequences, and costs of proposed interventions, thereby offering an invaluable decision aid for policy makers and health care leaders [7,10-12]. The purpose of simulation models is well defined, that is, to provide decision makers with evidence to facilitate decision making; however, the extent to which simulation modeling has fulfilled this purpose in CRC screening is unknown [13]. Simulation modeling has the potential to provide strong evidence for multiple aspects of informed decision making at the policy and health system level, including a proposed intervention's resource utilization, cost-effectiveness, feasibility, sustainability, potential impact, and acceptance among stakeholders [14,15]. For instance, by simulating what-if scenarios informed by clinical trials and observational data, the model can help to identify the appropriate age to initiate screening, superiority of one screening modality over another, or the most cost-effective frequency of screening a particular population in the long term. However, the extent to which simulation modeling has realized this potential impact in CRC screening is unknown.

For simulation models to be useful for decision makers, models must be sufficiently accurate and valid for application [13]. There have been concerns with model credibility in health care and reporting of model conceptualization, parameterization, and validation is not consistent in the literature [16-18]. For this reason, in this systematic review, each study will be assessed for adherence to best practice recommendations in model validation as detailed in the Methods section of this proposal [16].

From our review of the literature, we identified two gaps that we plan to address with this systematic review: (1) no systematic review has examined the application of simulation in CRC screening within the last 10 years and (2) no systematic review has specifically addressed the impact of simulation modeling on decision making in health care. The most recent systematic review that had examined CRC screening only included articles until 2007 inclusively [19]. Since that time, systematic reviews have been conducted examining the quality and cost-effectiveness of simulation modeling in breast cancer screening, but not for CRC screening [20,21]. For instance, a systematic review by Sobolev and colleagues [22] looked at the reported "utility" of simulation models in surgical patient flow and reinforced the need for evaluating the impact of models on decision making, but did not formally evaluate this in their review. Therefore, this study aims to address these knowledge gaps by assessing the validity and impact of simulation modeling on health system and policy decision making in CRC screening delivery. Publication of this protocol will allow for critical peer review of the aims and methods outlined for the intended study. This will help strengthen the rigor by which it will be conducted and validate its utility.

Methods

Protocol and Registration

This systematic review will be conducted in accordance with the Cochrane Library systematic reviews guide and the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) [23,24]. This protocol is reported in accordance with the PRISMA-Protocol checklist (Multimedia Appendix 1). The protocol has been submitted for registration in PROSPERO, and any amendments will be filed with PROSPERO (no. 130823).

Search Strategy and Eligibility Criteria

Studies will be selected by searching the academic and gray literature published between January 1, 2008, and March 1, 2019, conducted to identify articles that include (1) simulation modeling methods and (2) a focus on CRC screening. Only full-text articles available in English will be included. Studies will be identified from academic databases (Medline, Embase, Cochrane Central, Scopus, Web of Science, IEEEXplore, ACM Digital Library, Econolit, National Health Service Economic Evaluation Database, Health Assessment Database, and Cost-Effective Analysis Registry) using controlled vocabulary (Medical Subject Heading) and text word search terms selected by the author HS and an experienced librarian Alexandra Davis (Textbox 1).

Terms were selected to capture the most commonly used types of simulation models in health care (discrete event simulation, Markov chain model, Monte-Carlo simulation, agent-based model, and system dynamics model) [11]. This will be supplemented by hand searching of the gray literature and conference proceedings as well as citation searches of selected articles.

Textbox 1. Preliminary search strategies.

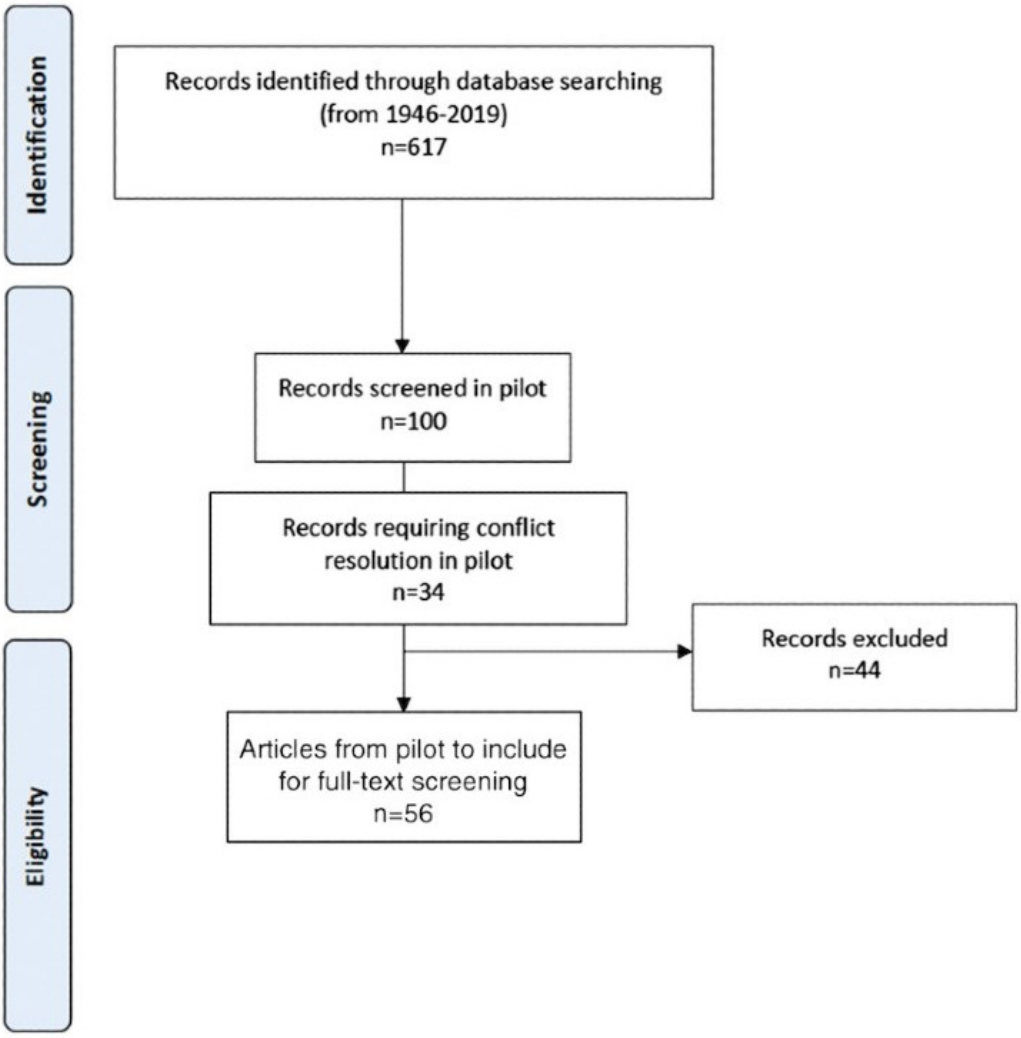
Database: Ovid MEDLINE(R) ALL <January 1, 2008 to March 1, 2019> Search Strategy:

1. Systems Analysis/
2. systems thinking.tw,kw.
3. systems science.tw,kw.
4. systems approach.tw,kw.
5. systems theory.tw,kw.
6. systems analysis.tw,kw.
7. system* model*.tw,kw.
8. simulation model*.tw,kw.
9. monte carlo method/ or Markov Chains/
10. (markov or monte carlo).tw,kw.
11. discrete event.tw,kw.
12. agent-based model*.tw,kw.
13. or/1-12
14. (system* dynamics or dynamic systems).tw,kw.
15. colonoscopy/ or sigmoidoscopy/
16. (colonoscop* or sigmoidoscop*).tw,kw.
17. FECES/ch or (f?ecal occult blood test or f?ecal immunochemical test or FOBT or stool DNA or stool test).tw,kw.
18. or/15-17
19. Mass Screening/ or “Early Detection of Cancer”/
20. (screening or “early detection”).tw,kw.
21. 19 or 20
22. exp Colorectal Neoplasms/
23. ((colorectal or colo-rectal or colon* or rectal) adj2 (cancer or neoplasm*)).tw.
24. 22 or 23
25. 21 and 24
26. CRC screen*.tw,kw.
27. 18 or 25 or 26
28. 13 and 27

Simulation modeling can be used in a broad scope of applications in cancer screening. To help refine the appropriate inclusion criteria and feasibility of this review, a preliminary search of the literature was conducted. A search of the literature published between January 1, 1946, and March 1, 2019, was conducted, and a pilot screening of 100 abstracts was performed by three independent reviewers (HS, PV, and CK) using the following inclusion criteria: (1) simulation model use and (2) CRC screening. This yielded 56 of 100 included abstracts after 24 conflicts were resolved through extensive discussion among all authors (Figure 1). To reduce conflicts, the inclusion and exclusion criteria were further refined to include only original articles describing a simulation model derived from clinical data focused on the delivery of CRC screening individuals with average CRC risk using one or all of the following modalities of screening recommended by the Canadian guidelines within the last 10 years: fecal occult blood test, fecal immunohistochemical testing, flexible sigmoidoscopy, and colonoscopy [25-27]. Excluded articles are those describing other screening modalities not recommended in the Canadian screening guidelines as identified above, commentary or review articles, simulation models that include screening of other cancers, or articles that have no mention of screening delivery. The time frame was also further restricted to only include articles published after 2008 because a systematic review on the use of simulation modeling in health care, including CRC

screening, was identified and had included articles published until the end of 2007 [19]. A second pilot screening was conducted using the revised criteria, which yielded fewer conflicts, and the revised inclusion and exclusion criteria were adopted for this systematic review.

Figure 1. Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) flow diagram of pilot search and reference screening.



Selection of Studies for the Review

All article titles and abstracts will be screened by three independent reviewers (HS, PV, and CK) using the abstract screening program Abstrakr (Brown University) followed by screening of selected full-text studies for compliance with the eligibility criteria as mentioned above using DistillerSR, version 2019 (Evidence Partners) [28,29]. Articles or reports of the same study will be linked together. Authors of the articles will be contacted to clarify study eligibility, where appropriate. Conflicts will be resolved through discussion between reviewers or consultation with author (RB), as needed.

Data Extraction

All included studies will be reviewed by three independent reviewers (HS, CK, and PV). Using DistillerSR version 2019, data will be extracted regarding the study and model description, and model validation as outlined in Table 1 [13]. Discrepancies will be identified and resolved through discussion, and missing data will be requested from the study authors as needed.

The validation of a simulation model is an important determinant of the risk of bias and applicability of a simulation model. All models will be assessed in accordance with the guidelines of the International Society for Pharmacoeconomics and Outcomes Research-Society for Medical Decision Making (ISPOR-SMDM) report [13]. From the literature review, several tools were identified to assist model developers and users with model validation [13,16,17,30-33]. The ISPOR-SMDM Taskforce has developed good practice guidelines for modeling in health care including recommendations on conceptualization, parameterization, and validation. Of the validation tools identified in the literature, the taskforce report had the broadest scope and most rigorous development process; therefore, it was selected to guide validation assessment in this review [16]. Authors (HS, CK, and PV) will individually assess whether authors report or conduct face validity (wherein experts evaluate model structure, data sources, assumptions, and results), verification or internal validity (check accuracy of coding), cross validity (comparison of results with other models analyzing the same problem), external validity (comparing model results with real-world results), and predictive validity

(comparing model results with prospectively observed events), as outlined in Table 1 [13].

Table 1. Model characteristics and validation.

Characteristics	Description
Country	Location of intended application.
Year	Year of publication.
Simulation model type	Type of approach (ie, system dynamics, Monte Carlo, Markov chain model, agent-based model, discrete event).
Intended application(s)	Area of application (ie, forecasting of cost, resource utilization).
Funding sources	Source of financial support of the project, if applicable.
Stakeholders	Identifies model users/decision makers and their role in the modeling.
Conceptualization	
Parameters defined	Defines the model parameters: values used to either define the characteristics of the model or calculate the performance indicators.
Structure	Demonstration of variables and their relationships (ie, in graphical formation).
Operationalization	
Model duration	Length of time simulated, number of runs, and if the model was terminating or steady state.
Inputs	List inputs of model.
Simulated outputs	List outputs of model.
Observed results	Observed outcomes, if available.
Data sources	Type of data sources (ie, primary or secondary).
Limitations	Assumptions and limitations of the model.
Software	Type of software used to develop the model.
Validation methods [13]	
Face validation	Model structure, data sources, problem formulation, and results are evaluated by people who have clinical expertise.
Verification/internal validation	Examination of the extent to which mathematical calculations are performed correctly and are consistent with the model's specifications.
Cross validation	Examination of the different models that address the same problem and comparison of their results.
External validation	Comparison of model's results with actual event data.
Predictive validation	Comparison of model's simulated outcomes to similar clinical trial or cohort study.

Studies will then be assessed for the extent to which the study has or could potentially have contributed evidence toward informed decision making. For reported contribution, each article will be searched in its entirety for statements referring to the simulation model results informing decision making. If not clearly stated in the publication, the information will be requested from study authors.

Recognizing that the impact of a simulation model on a specific decision may not be communicated at the time of publication, we plan to also assess the potential contribution a simulation model could have made to evidence-informed decision making based on whether the results align with important factors for making an informed decision [34]. We will assess articles to determine whether they include evidence considered to be important for decisions, as outlined in the internationally recognized Grading of Recommendations Assessment, Development and Evaluation Evidence to Decision (GRADE EtD) framework [14]. The GRADE EtD framework has been developed as part of the Developing and Evaluating Communication strategies to support Informed Decisions and practice based on Evidence (DECIDE) project in collaboration with researchers in the health system and public health internationally. It outlines a set of important factors that decision makers should consider and address with research evidence to guide their decisions in health policy or systems [35]. These criteria include information on an intervention's resource utilization, cost-effectiveness, impact on health equity, and feasibility (Table 2). We will assess whether the study results apply to the GRADE EtD criteria. Subgroup analysis of articles based on their GRADE EtD criteria will be conducted to identify methods associated with decision support capacity (ie, quantitative or mixed methods).

Table 2. GRADE EtD (Grading of Recommendations Assessment, Development and Evaluation Evidence to Decision) criteria of decision making for health system and public health decisions [14].

Criteria	Detailed questions
Is the problem a priority?	• Are the consequences of the problem serious (ie, severe or important in terms of the potential benefits or savings)? • Is the problem urgent? (Not relevant for coverage decisions.) • Is it a recognized priority (eg, based on a political or policy decision)? (Not relevant when an individual patient perspective is taken.)
How substantial are the desirable anticipated effects?	• Judgments for each outcome for which there is a desirable effect.
How substantial are the undesirable anticipated effects?	• Judgments for each outcome for which there is an undesirable effect.
What is the overall certainty of the evidence of effects?	• See GRADE guidance regarding detailed judgments about the quality of evidence or certainty in estimates of effects.
Is there important uncertainty about or variability in how much people value the main outcome?	• Is there important uncertainty about how much people value each of the main outcomes? • Is there important variability in how much people value each of the main outcomes? (Not relevant for coverage decisions.)

Do the desirable effects outweigh the undesirable effects?	• To what extent do the following considerations influence the balance between desirable and undesirable effects:
	  • How much less people value future outcomes compared to outcomes that occur now (their discount rates)?
	  • People's attitudes toward desirable effects (how risk seeking they are).
	  • People's attitudes toward undesirable effects (how risk averse they are).

How large are the resource requirements?	• How large is the difference in each item of resource use for which fewer resources are required? • How large is the difference in each item of resource use for which more resources are required?
What is the certainty of the evidence of resource requirements?	• Have all important items of resource use that may differ between the options being considered been identified? • How certain is the evidence of differences in resource use between the options being considered? (See GRADE guidance regarding detailed judgments about the quality of evidence or certainty in estimates.) • How certain is the cost of the items of resource use that differ between the options being considered? • Is there important variability in the cost of the items of resource use that differ between the options being considered?

Are the net benefits worth the incremental cost?	• Judgments regarding each of the six preceding criteria:
	  • Is the cost-effectiveness ratio sensitive to one-way sensitivity analyses?
	  • Is the cost-effectiveness ratio sensitive to multivariable sensitivity analyses?
	  • Is the economic evaluation on which the cost-effectiveness estimate is based reliable?
	  • Is the economic evaluation on which the cost-effectiveness estimate is based applicable to the setting(s) of interest?

What would be the impact on health equity?	• Are there groups or settings that might be disadvantaged in relation to the problem or options that are considered? • Are there plausible reasons for anticipating differences in the relative effectiveness of the option for disadvantaged groups or settings? • Are there different baseline conditions across groups or settings that affect the absolute effectiveness of the intervention or the importance of the problem for disadvantaged groups or settings? • Are there important considerations that should be made when implementing the intervention in order to ensure that inequities are reduced, if possible, and that they are not increased?
Is the intervention acceptable to key stakeholders?	• Are there key stakeholders that would not accept the distribution of the benefits, harms, and costs? • Are there key stakeholders that would not accept the costs or undesirable effects in the short term for desirable effects (benefits) in the future? • Are there key stakeholders that would not agree with the values attached to the desirable or undesirable effects (because of how they might be affected personally or because of their perceptions of the relative importance of the effects for others)? • Would the intervention adversely affect people's autonomy? • Are there key stakeholders that would disapprove of the intervention morally, for reasons other than its effects on people's autonomy (eg, in relation to ethical principles such as no maleficence, beneficence, and justice)?

Criteria	Detailed questions

Is the intervention feasible to implement?	• For decisions other than coverage decisions:
	  • Is the intervention or option sustainable?
	  • Are there important barriers that are likely to limit the feasibility of implementing the intervention (option) or require consideration when implementing it?
	• For coverage decisions:
	  • Is coverage of the intervention sustainable?
	  • Is it feasible to ensure appropriate use for approved indications?
	  • Is inappropriate use (indications that are not approved) an important concern?
	  • Is there capacity to meet increased demand if covered?
	  • Are there important legal, bureaucratic, or ethical constraints that make it difficult or impossible to cover the intervention?

Results

A preliminary search of the literature published between January 1, 1946, and March 1, 2019, was conducted, yielding 617 references and a pilot screening of 100 randomly selected abstracts was performed by three independent reviewers (HS, PV, and CK) using the following inclusion criteria: (1) simulation model use and (2) CRC screening (Figure 1). This resulted in inclusion of 56 of 100 (56%) abstracts after 24 conflicts were resolved through extensive discussion among all authors, leading to revision and clarification of the inclusion criteria as described in the section “Methods”. The revised search yielded 484 references to review. A repeated pilot screening resulted in the inclusion of 8 of 100 (8%) abstracts after 16 conflicts were resolved with minimal discussion. The publication of this article was funded by University of Ottawa Telfer School of Management Research Grant and a Discovery Grant from the Natural Sciences and Engineering Research Council of Canada.

The project was funded in May 2019. Data collection took place from January 2008 to March 2019. Data analysis was completed in November 2019, and are expected to be published in spring 2020.

Discussion

The purpose of simulation modeling in health care is generally to inform a decision [13,33,36]. The extent to which simulation modeling has fulfilled this purpose has not been assessed. We anticipate that this systematic review will help address this knowledge gap by assessing the contribution simulation modeling has made to informed decision making in an area of health care where it has been frequently used: CRC screening delivery. We will use the GRADE EtD framework to structure our analysis of potential decision impact of the models. This includes the model’s contribution to determining the feasibility of screening, acceptability of proposed screening strategies by stakeholders, and sustainability of screening over the long term. This analysis will help guide researchers by identifying methods in simulation modeling that have been associated with a greater success in decision support, such as mixed methods, participatory simulation model development, and group model building, which has been reported as beneficial in other applications of simulation modeling in health care [37,38]. It will assist decision makers and model users to identify areas where simulation modeling has proven to be useful, such as for identifying resource requirements or conducting cost-benefit analysis.

The dataset search yielded 484 references, which suggests that the body of literature on this topic is fairly robust. We anticipate there will be an adequate number of relevant models to conduct an informative systematic review on this topic.

We foresee several potential limitations to this study. The heterogeneity of articles may make it challenging to evaluate studies using a uniform framework from validation and decision-making criteria. Furthermore, the impact and decision support that a study provide are difficult to quantify and therefore will be subject to both authors’ and reviewers’ bias. We aim to mitigate this by using the GRADE EtD framework and by having reviewers with clinical (HS), health informatics (CK), and simulation (PV) expertise review each included study. Finally, our assessment of model validity will be limited by a lack of validation standards in the literature and reporting by authors on their validation process and outcomes [18].

In conclusion, the proposed systematic review will provide an insight into the contribution and validity of simulation modeling in CRC screening. The results have the potential to inform researchers, health care leaders, and policy makers to develop valid, informative simulation models that will support decision making. This analysis could be expanded to assess the use of simulation modeling in other areas of health care.

Acknowledgments

We thank Alexandra Davis from The Ottawa Hospital Library for her assistance in conducting the search.

Authors' Contributions

HS is the guarantor of this proposed review. HS, CK, and PV performed the pilot screening of abstracts outlined in this manuscript. All authors participated in the conceptualization and design of this review, and have read and approved the manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1
PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) checklist.
[PDF File (Adobe PDF File), 83 KB - resprot_v9i5e16103_app1.pdf]

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Abbreviations

CRC: colorectal cancer
GRADE EtD: Grading of Recommendations Assessment, Development and Evaluation Evidence to Decision

ISPOR-SMDM: International Society for Pharmacoeconomics and Outcomes Research-Society for Medical Decision Making

Edited by G Eysenbach; submitted 02.09.19; peer-reviewed by T V, A Young; comments to author 18.10.19; revised version received 09.11.19; accepted 26.11.19; published 13.05.20.

Please cite as:
Smith H, Varshoei P, Boushey R, Kuziemsky C
Use of Simulation Modeling to Inform Decision Making for Health Care Systems and Policy in Colorectal Cancer Screening: Protocol for a Systematic Review
JMIR Res Protoc 2020;9(5):e16103
URL: https://www.researchprotocols.org/2020/5/e16103
doi:10.2196/16103
PMID:32401223

Protocol

Reported Outcomes in Published Systematic Reviews of Interdisciplinary Pain Treatment: Protocol for a Systematic Overview

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Abstract

Background: Interdisciplinary pain treatment (IPT) is a complex intervention; its outcomes are very diverse, as are the methodologies for handling those outcomes. This diversity may hamper evidence-based decision making. Presently, there is no gold standard recommendation of how to select reported outcomes in published systematic reviews and meta-analyses to explicitly demonstrate the effectiveness of IPT.

Objective: In this systematic overview, we aim to evaluate the reported outcome domains and measurements across published systematic reviews and meta-analyses and to identify any methods, considerations, and discussion regarding the handling of the chosen outcome domains and measurements.

Methods: This article describes the protocol for a systematic overview of the outcomes reported in published systematic reviews and meta-analyses of randomized control trials for the effectiveness of IPT versus any control. To this end, we searched the PubMed, Cochrane Library, and Epistemonikos databases from inception to December 2019. Two independent investigators screened the titles, the abstracts of the identified records, and the full texts of the potentially eligible systematic reviews and meta-analyses, performed data extraction according to predefined forms, and rated the quality of the included systematic reviews and meta-analyses. The quality of the included systematic reviews and meta-analyses will be rated with AMSTAR (A MeaSurement Tool to Assess systematic Reviews) 2. Data will be analyzed descriptively and stratified by AMSTAR 2.

Results: We introduced the rationale and design of a systematic overview to summarize and map the chosen IPT outcome domains and the methods of handling these outcomes reported in published systematic reviews and meta-analyses. As of December 2019, we collected 5229 systematic reviews, of which 147 (2.81%) were examined in-depth for eligibility. Topline results are anticipated by September 2020.

Conclusions: The results of this study will be published as soon as they are available. Our results will fill a gap in the related literature and will be used to inform the development of a set of recommendations that can be applied in systematic reviews and hopefully serve as a gold standard.

International Registered Report Identifier (IRRID): PRR1-10.2196/17795

(JMIR Res Protoc 2020;9(5):e17795) doi:10.2196/17795

KEYWORDS

Interdisciplinary pain treatment; multidisciplinary rehabilitation; chronic pain; outcome domains

Introduction

Interdisciplinary pain treatment (IPT) is considered to be an optimal treatment option for chronic pain because it acknowledges the various pain complexities experienced by patients [1,2]. While many terms have been used to describe IPT in the literature (ie, multidisciplinary, multiprofessional, multimodal, and interprofessional), the International Association for the Study of Pain (IASP) has clarified the terminology for the different multicomponent treatments by defining IPT as "a multimodal treatment provided by a multidisciplinary team collaborating in assessment and treatment using a shared biopsychosocial model and goals" [3]. This definition makes a clear distinction between "multimodal treatment" and "multidisciplinary treatment" with respect to the biopsychosocial perspective.

As a result, IPT is based on a biopsychosocial framework provided by a team of professionals with distinct backgrounds; it contains one physical component and at least one educational, psychological, social, or occupational component [1-5]. Given this definition, the components of IPT can be activated independently or interdependently [6], leading to composite effects supported by known and unknown mechanisms. Each such effect is assumed to be an additive sum of the effects of its components [7]. As a result, IPT is a complex treatment [6,8]. Unlike pharmacological treatment, IPT targets the whole person rather than only targeting biochemical processes; therefore, complex patient conditions are paired with complex treatments [9,10].

Complex treatments such as IPT should incorporate multiple outcomes measured at multiple levels as well as strategies for handling those multiple outcomes [10,11]. For example, one systematic review including 46 randomized controlled trials (RCTs) reported a median of 9 outcomes per RCT [2]. However, outcomes in published systematic reviews are not usually divided into primary and secondary outcomes [4,5]. Additionally, the current practice for reporting RCTs is to analyze the outcomes as independent from one another [2,4,5]; meanwhile, a study from the Swedish Quality Registry for Pain Rehabilitation found significant intercorrelations between outcomes of RCTs [12]. Hence, the changes in these outcomes cannot be considered to be independent of each other because IPT is a complex treatment. This may mean that some outcomes are moderating and mediating variables; also, a change process occurs over time, with some changes occurring quickly while others occur more slowly.

Taken together, the great variation of the selected outcomes and procedures for handling multiple outcomes [2,13] may hamper direct and prompt comparison across RCTs in this field [14,15] and, thus, may hamper evidence interpretation [16]. Therefore, core outcome sets have been developed to standardize and improve the choice and reporting of outcome domains and to facilitate evidence-based decision making; examples include VAPAIN (Validation and Application of a core set of patient-relevant outcome domains to assess the effectiveness of multimodal PAIN therapy), IMMPACT (Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials), and PROMIS (Patient-Reported Outcomes Measurement Information System) [16-18]. Despite these efforts, methods of reporting and handling the selected outcome IPT domains and measurements across the published systematic reviews and meta-analyses remain mostly unstudied. For example, in 2008, Scascighini et al [1] proposed an approach based on predefined primary and secondary outcomes and what is necessary to classify an intervention as positive before reviewing RCTs. However, other definitions of positive outcomes of an IPT already exist (eg, the majority of outcomes must be significantly better than for the control intervention) [4,5]. On the other hand, the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach used for evidence ratings in systematic reviews may not adequately describe the evidence base of complex treatments [19].

Given this background, the aim of this systematic review is to provide an overview of the IPT outcomes reported in systematic reviews and meta-analyses. More specifically, the objectives of this study are to evaluate the reported outcomes according to VAPAIN statements and IMMPACT and PROMIS recommendations [16-18] and to describe the methods, considerations, and discussion for handling the chosen outcome domains and measurements.

Methods

This study protocol follows the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) recommendations [20].

Search Strategy

We searched the PubMed, Cochrane Library, and Epistemonikos databases from inception to December 31, 2019. A specific search strategy was developed for each database using the PubMed Systematic Reviews filter for systematic reviews and meta-analyses (see Textbox 1) combining MeSH keywords and other relevant terms, including multidisciplinary, interdisciplinary, patient care team, multidisciplinary biopsychosocial rehabilitation, chronic pain, and persistent pain, exploded when necessary.

Textbox 1. Database search strategy based on the PubMed Systematic Reviews filter.

("Chronic Pain"[Mesh] OR "Neuropathic Pain" [Mesh] OR chronic persistent pain [TIAB] AND "Pain/rehabilitation"[Mesh] OR ("Pain/therapy"[Mesh] OR multidisciplinary [TIAB] OR interdisciplinary[TIAB] OR multimodal[TIAB]) OR multidisciplinary biopsychosocial rehabilitation [TIAB] AND "Combined Modality Therapy" [Mesh] AND "Patient Care Team"[Mesh] NOT ("Neoplasms"[Mesh] OR surgery[TW]) AND (((systematic review[ti] OR systematic literature review[ti] OR systematic scoping review[ti] OR systematic narrative review[ti] OR systematic qualitative review[ti] OR systematic evidence review[ti] OR systematic quantitative review[ti] OR systematic meta-review[ti] OR systematic critical review[ti] OR systematic mixed studies review[ti] OR systematic mapping review[ti] OR systematic cochrane review[ti] OR systematic search and review[ti] OR systematic integrative review[ti]) NOT comment[pt] NOT (protocol[ti] OR protocols[ti])) NOT MEDLINE [subset]) OR (Cochrane Database Syst Rev[ta] AND review[pt]) OR systematic review[pt]

Study Selection and Eligibility Criteria

We will include only systematic reviews (with and without meta-analyses) of RCTs investigating the effectiveness of IPT for any chronic pain condition as strictly defined by the original authors in the systematic review inclusion criteria (ie, pain lasting at least 3 months).

Meta-analyses that examined IPTs versus any control (eg, treatment as usual, waiting list) or other treatment (eg, physiotherapy, surgery) will be eligible for inclusion. If a systematic review examines various forms of therapies, it will be considered eligible only if separate results or analyses of IPT are presented.

The following inclusion criteria will be applied:

- To identify adequate systematic reviews, an IPT definition must be described in the full text and the involved IPT professionals should be clearly reported by the original authors.
- Only systematic reviews of RCTs published in peer-reviewed journals in English or Swedish will be included.
- At least 75% of participants will be people ≥18 years of age.
- At least 75% of participants will have chronic/persistent nociceptive and/or nociplastic pain (ie, for at least 3 months or more), such as chronic low back pain, chronic neck pain including whiplash-associated disorders, chronic widespread pain, fibromyalgia, chronic migraine and other headaches, myofascial pain syndromes, Ehlers-Danlos syndrome, hypermobility syndrome, and chronic neuropathic pain, such as painful diabetic neuropathy, trigeminal neuralgia, postherpetic neuralgia or spinal cord injury, multiple sclerosis, or stroke-related neuropathy.

Two independent investigators will screen the titles, the abstracts of the identified records, and the full texts of the potentially eligible articles. In cases of discrepancy, a third investigator will be consulted until agreement is reached.

We will exclude systematic reviews if they (1) review other meta-analyses (eg, meta-reviews, umbrella reviews), (2) include study designs other than RCTs, (3) include fewer than 75% of participants diagnosed with chronic pain, or (4) include a diagnosis of chronic pain due to cancer, infection, inflammatory arthropathy, osteoporosis, fracture, pregnancy, rheumatoid arthritis, or other rheumatic pain (eg, lupus, ankylosing spondylitis, psoriatic arthritis, Sjogren syndrome, polymyalgia rheumatica).

Methodological Quality Assessment of Included Studies

Two independent investigators will rate the methodological quality of the selected systematic reviews using the AMSTAR 2 checklist [21]. The AMSTAR 2 is a 16-item instrument related to essential features of methodological rigor across systematic reviews. AMSTAR 2 does not generate an overall “score” but instead provides a rating scheme for the overall confidence in the results of the reviews as follows: high quality, moderate quality, low quality, or critically low quality [21].

Data Extraction

Two independent investigators will abstract the data using predefined forms. For each eligible systematic review, we will record the Cochrane or PubMed ID, first author, publication year, chronic pain conditions, control/comparison arms, number of RCTs of IPTs included in the systematic review, outcomes investigated (primary and secondary if such categorization exists), outcome measurements, and total number of participants. Furthermore, we will extract data regarding the duration of the treatment (weeks and hours), treatment components, setting, and follow-up length. We will also record any method, strategy, considerations, or discussion regarding how the authors chose which outcomes to study and which methods to use to evaluate the evidence (eg, the GRADE approach).

Data Synthesis

We will analyze data descriptively stratified by the methodological quality of the selected systematic reviews. We will provide the number of outcomes reported in each systematic review, the diversity of the reported outcomes, and the methodologies for outcome assessment. We will also evaluate the reported outcomes according to the VAPAIN statement on core pain outcome domains for IPTs [16], IMMPACT recommendations [17], and PROMIS recommendations [18]. According to VAPAIN, 8 core domains should be assessed in RCTs for IPT: pain intensity, pain frequency, physical activity, emotional well-being, satisfaction with social roles and activities, productivity (paid and unpaid, at home and at work, inclusive presentism and absenteeism), health-related quality of life, and the patient's perception of treatment goal achievement [16]. According to IMMPACT recommendations, the chronic pain trials should assess outcomes representing 6 core domains: pain, physical functioning, emotional functioning, participant ratings of improvement and satisfaction with treatment, symptoms and adverse events, and participant disposition (eg, adherence to the treatment regimen and reasons for premature withdrawal from the trial) [17]. Finally, according to PROMIS, the reported outcome domains should be classified in the following 3 core health areas: physical health (including the core health outcome domains of symptoms and function), mental health (including the core health outcome domains of affect, behavior, and cognition) and social health (including the core health outcome domains of relationships and function) [18]. We will also map and pinpoint any specific strategy by which the authors decided on the selected outcomes included in their systematic reviews and note whether there is any discussion on how to best evaluate the evidence of IPT, considering its treatment nature and complexity.

Results

We have introduced the rationale and design of a systematic overview to summarize and map the chosen IPT outcome domains and the methods of handling these outcomes reported in published systematic reviews with meta-analyses. As of December 2019, we collected 5229 systematic reviews, of which 147 (2.81%) were examined in-depth for eligibility. Topline results are anticipated by September 2020.

Discussion

The results of this systematic overview will fill a gap in the related literature and will be helpful to potential and practicing developers of IPT. By evaluating and mapping how the outcomes were selected and reported as well as which methods were used to evaluate the evidence in the published literature, we also hope to provide a proper way of framing the selection of research outcomes, which in turn may be a vital starting point to facilitate evidence synthesis and assessment of complex treatments for chronic pain in everyday clinical practice. The review results will be used to inform the development of a set of recommendations that can be applied in systematic reviews and hopefully serve as a gold standard.

Given the economic cost not only of pain itself but of its treatment, we expect that the results of this study will be of considerable interest to clinicians, academics, guideline developers, and policymakers; we will disseminate the findings widely through academic publications, conference presentations, and communication with health care providers.

Authors' Contributions

All the authors conceived the idea of the project and designed the study protocol. ED drafted the first version of the protocol, and all authors drafted the manuscript, provided critical comments on the paper for important intellectual content, and approved the final version. BG is the guarantor of the review.

Conflicts of Interest

None declared.

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Abbreviations

AMSTAR: A MeaSurement Tool to Assess systematic Reviews
GRADE: Grading of Recommendations Assessment, Development and Evaluation
IASP: International Association for the Study of Pain
IMMPACT: Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials
IPT: interdisciplinary pain treatment
PRISMA-P: Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols
PROMIS: Patient-Reported Outcomes Measurement Information System
RCT: randomized controlled trial
VAPAIN: Validation and Application of a core set of patient-relevant outcome domains to assess the effectiveness of multimodal PAIN therapy

Edited by C Hoving; submitted 15.01.20; peer-reviewed by B Thompson, M Linnett; comments to author 01.03.20; revised version received 16.03.20; accepted 17.03.20; published 22.05.20.

Please cite as:
Dragioti E, Dong HJ, Larsson B, Gerdle B
Reported Outcomes in Published Systematic Reviews of Interdisciplinary Pain Treatment: Protocol for a Systematic Overview
JMIR Res Protoc 2020;9(5):e17795
URL: http://www.researchprotocols.org/2020/5/e17795/
doi:10.2196/17795
PMID:32441660

Proposal

Triangle of Healthy Caregiving for Veterans With Spinal Cord Injury: Proposal for a Mixed Methods Study

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Abstract

Background: Spinal cord injury (SCI) is a debilitating injury that results in chronic paralysis, impaired functioning, and drastically altered quality of life (QOL). The Department of Veterans Affairs (VA) estimates that approximately 450 newly injured veterans and active-duty members receive rehabilitation at VA's Spinal Cord Injury/Disorders Centers annually. VA virtual health services use technology and health informatics to provide veterans with better access and more effective care management. The "Triangle of Healthy Caregiving for SCI Veterans" is a patient-centered intervention that incorporates SCI veterans' caregivers into the VA SCI health care team and extends into the homes of veterans with SCI by using real-time clinical video teleconferencing (CVT). CVT facilitates video-clinic visits, which can include different types of clinical evaluations, therapy (physical/occupational), or psychosocial services. The "Triangle of Healthy Caregiving for SCI Veterans" builds on interactive, interdisciplinary health care relationships that exist between the veterans with SCI, their caregivers, and the VA SCI health care team. SCI veterans' propensity to multiple secondary complications makes a healthy partnership crucial for the success of keeping better health and functional outcomes as well as quality of life while living in their homes.

Objective: The goal of the proposed mixed methods project will assess SCI veterans', their caregivers', and the VA health care team's perspectives and experiences in the "Triangle of Healthy Caregiving for SCI Veterans" to determine the benefits, challenges, and outcomes for everyone involved in the intervention.

Methods: Data collection methods will be implemented over three sequential phases. First, in-depth interviews will be conducted with the telehealth coordinators to systematically document the administrative procedures involved in enrollment of veterans with SCI into the CVT system. Next, structured observation of the CVT enrollment process and logistics of home installation of the CVT system will be conducted to validate the content of the in-depth interviews and highlight any discrepancies observed. Semistructured interviews will be conducted to assess specific elements of the "Triangle of Healthy Caregiving for SCI Veterans" program, their perceived utility, and effectiveness of the CVT system as well as the general impressions of the impact of the intervention on the SCI veterans' health and function outcomes, caregiver burden, and daily caregiver burden. Finally, the research team will conduct a focus group to evaluate the ways in which the "Triangle of Healthy Caregiving for SCI Veterans" is useful for health care delivery to veterans with SCI and support services to SCI caregivers.

Results: This proposal was funded in July 2017. It was reviewed and received institutional review board approval in March 2018, and the project was started immediately after, in the same month. As of September 2019, we have completed Phases I and III and have recruited 52 subjects for Phase II. We are beginning the data analysis. The study is projected to be completed in late summer of 2020, and the expected results are to be published in the fall of 2020.

Conclusions: The findings from this study will highlight the ways in which virtual health care technologies can be used to improve access to SCI specialized care for veterans and provide an estimation of the potential impact on clinical outcomes for veterans with SCI and their caregivers.

International Registered Report Identifier (IRRID): DERR1-10.2196/14051

(JMIR Res Protoc 2020;9(5):e14051) doi:10.2196/14051

KEYWORDS

veterans health; spinal cord injury; telemedicine; telehealth; delivery of health care; virtual health; health services accessibility; quality of life; patient care team; caregivers

Introduction

Background

Spinal cord injury (SCI) is a devastating and disabling medical condition with significant impact on quality of life (QOL) and finances on multiple levels for wounded members of the military, their families, and the health care system [1-3]. The Department of Veterans Affairs (VA) is the single largest comprehensive health care provider for SCI in the nation [4,5]. There are approximately 44,000 veterans with SCI receiving health care at VA facilities [4,5]. In addition to requiring specialized and costly clinical health care, SCI often results in physical limitations that make assistance from others critical to maintaining health and facilitating full societal integration [6,7]. As such, the role of caregivers is increasingly being recognized as instrumental to SCI health care management. Caregivers have been identified as critical members of the SCI medical rehabilitative team, who are responsible for providing assistance, supervision, and health care to persons living with an SCI, including veterans [8-13]. Despite the presence of a caregiver, accessing SCI specialty care may be further challenged with the development of complexities evident in chronic SCI, including the effects of aging, transportation costs, or the distance to the VA hospital or outpatient services [8-10,14-17]. Therefore, methods to facilitate improved access to rehabilitative medical care are crucial.

Virtual care is the practice of delivering health care to patients separated from the provider by a physical distance by using a variety of technologies [18]. It includes using land-based telephone communications as well as more advanced technologies as follows: (1) Telehealth, which uses technology that the patients use to enter health facts (eg, their blood pressure or fingerstick blood glucose level) that get transmitted to their provider, who can then make adjustments in the management of their condition based on this information. It also provides disease-specific education to the patients based on the patient's responses to specific questions. (2) Telemedicine videoconferencing (clinical videoconference technology) permits real-time, secured, face-to-face visits between providers and patients. The patients are able to meet with individual providers or multiple members of the team simultaneously. Physical examination of the patients can be performed via some of these technologies as well as education, counseling, and other assessments. (3) Secure messaging (eg, veterans communicating securely with their health care team by email, which interfaces with their electronic medical record) [18]. All of these modalities have specific features to help veterans and their providers access each other in a timely fashion.

Over the past 16 years, the VA New Jersey Health Care System's (VANJHCS's) Spinal Cord Injury & Disorders (SCI/D) SCI health care team (HCT) has successfully implemented veteran-centered care for the SCI/D population. This veteran-centered care views veterans and their caregivers as one system that works in partnership with the HCT. Through this partnership, described as "The Triangle of Healthy Caregiving," the HCT incorporates the use of virtual care technologies (real-time clinical video teleconferencing [CVT]) in their delivery of primary care and specialty services directly to the veteran and caregiver based on the clinical needs identified [19-21]. For the proposed project, the research team will use qualitative and quantitative data collection methods to assess the perspectives and experiences of key stakeholders involved in the intervention—veterans with SCI, their caregivers, and the VA health care team—to ascertain the benefits, challenges, and outcomes for these key stakeholders involved in the intervention.

Research Problem

Improved health care access helps prevent costly secondary conditions among people with SCI [1,22-24]. Patients with spinal cord injury require lifelong monitoring to effectively address and prevent secondary conditions while promoting stability in functionality as they age [25]. The lifetime cost of providing care to patients with SCI can range from US $40,589 to US $177,808 annually, depending on the level of injury and age of initial injury [24]. In fiscal year 2004, the Veterans Health Administration SCI program accounted for approximately US $716 million in direct medical costs for 18,539 enrolled veterans (Veterans Health Administration intranet) [1]. A cross-sectional study using the National Spinal Cord Injury Statistical Center database reported that a significant proportion of persons with SCI visited a doctor for at least one medical complication at the time of their annual checkup, which does not include other medical conditions they did not have treated [26]. Utilizing telehealth technologies to provide ongoing primary and specialty health care to veterans with SCI is essential, as we seek to improve the experience of our veterans and their caregivers while reducing the cost of travel and the need for emergency care [16,25,27].

VA virtual health services use technology and health informatics to provide veterans with better access and more effective care management [27,28]. VA is improving patient-facing and clinician-facing electronic health systems by expanding the development and use of health-related virtual modalities. These modalities include telehealth; electronic consult, where the consultant makes recommendations to the referring provider based on patient chart reviews; Secure Messaging in MyHealtheVet, which allows veterans to access their medical records, order medication refills, and communicate with their VA health care team, etc, through this secured patient portal; and mobile apps. VA is aligning virtual care technologies to

create a seamless, unified experience for all VA patient-facing technologies [27,28].

Despite advances in VA virtual care technologies and growing empirical evidence about the unique relationship between veterans with SCI and their caregivers, there is a growing need to fully understand how utilizing virtual care technologies impacts the health and QOL of both veterans with SCI and their caregivers [21]. Promising results from video/telecommunication technology studies with caregivers of veterans with SCI indicated improvements in the caregivers' problem-solving skills and QOL outcomes [10,16,29,30]. To address the health care needs of veterans with SCI, support their caregivers, and provide timely access to health care providers, the VANJHCS's SCI/D Department developed the "Triangle of Healthy Caregiving for SCI Veterans" [19-21]. The "Triangle of Healthy Caregiving for SCI Veterans" is a patient-centered program that incorporates SCI Veterans' Caregivers into the VA SCI HCT and extends into the homes of Veterans with SCI using real-time CVT. CVT facilitates video-clinic visits, which include clinical evaluations, therapy (physical/occupational), and supportive services (eg, social work). The "Triangle of Healthy Caregiving for SCI Veterans" builds on interactive, interdisciplinary health care relationships that exist between the SCI veteran, their caregivers, and the VA SCI HCT. SCI veterans' propensity to develop multiple secondary complications makes a healthy partnership crucial for the success of maintaining better health, functional outcomes, and overall QOL while the veterans live in their homes. Virtual medicine technologies can help improve accessibility by veterans with SCI and their caregivers to the VA SCI HCT in order to address issues in a timely fashion, reduce inconvenience or difficulties veterans with SCI may experience in reaching the health care facility to see their SCI specialists, and provide caregivers with timely educational and support services. The direct or indirect impact of the "Triangle of Healthy Caregiving for SCI Veterans" program has not yet been determined. The goal of this study is to assess the acceptability and utilization of the "Triangle of Healthy Caregiving for SCI Veterans" program by Veterans with SCI, Caregivers, and health care teams to modify, improve, and refine it accordingly.

Specific Aims

This study aims to conduct a mixed methods descriptive study to assess the implementation process and outcomes of using CVT in the model of health care delivery that the SCI Center uses, called "Triangle of Healthy Caregiving for SCI Veterans." Mixed methods research involves integrating quantitative and qualitative approaches to generating new knowledge. Combining methods activates their complementary strengths and helps overcome their discrete weaknesses [31]. Mixed methods have the advantage of allowing us to address these aims in a manner that is meaningful to those who are actively involved in the "Triangle of Healthy Caregiving for SCI Veterans": veterans with SCI, family caregivers, and SCI clinicians.

Aim 1

Our first aim is to evaluate the SCI veterans' experience in the "Triangle of Healthy Caregiving for SCI Veterans." Our research questions are as follows:

1. What are SCI veterans' perceptions about the provision and ways that the "Triangle of Healthy Caregiving for SCI Veterans" program impacts the delivery of health care?

2. What are the benefits and challenges the veterans with SCI experienced during implementation of the "Triangle of Healthy Caregiving for SCI Veterans" program in their homes?

Aim 2

Our second aim is to evaluate the SCI veteran caregivers' experience in the "Triangle of Healthy Caregiving for SCI Veterans." Our research questions are as follows:

1. What are SCI veteran caregivers' perceptions about the "Triangle of Healthy Caregiving for SCI Veterans" program in management of caregiver burden?

2. What are the benefits and challenges that SCI veteran caregivers experienced during the implementation of the "Triangle of Healthy Caregiving for SCI Veterans" program in the homes of SCI veterans?

Aim 3

Our third aim is to evaluate the VA HCT's experience in delivering health care and providing supportive services using the "Triangle of Healthy Caregiving for SCI Veterans." Our research questions are as follows:

1. How do the "Triangle of Healthy Caregiving for SCI Veterans" health care professionals use the program to deliver care to Veterans with SCI?

2. Which elements of the "Triangle of Healthy Caregiving for SCI Veterans" work better in facilitating health care delivery? What are the key components of the program? Which components need to be revised?

Methods

Study Design

Preliminary Studies

As a result of clinical observations and anecdotal reports, the VANJHCS's SCI Center's Outpatient Clinic identified the financial, psychosocial, and other intangible costs specific to veterans with SCI, which incurred when they come to VANJHCS for care: (1) exorbitant cost of travel to/from appointments ranges from US $600 to US $2000 per visit, depending on the mode of transport (ie, wheelchair coach, stretcher, and advanced cardiovascular life support transport) and distance of veteran's residence from medical center; (2) additional trauma to the wound during transport to and from the clinic appointment; (3) increased risk of developing more wounds during transport; and (4) inconvenience and discomfort for the veteran with SCI and caregiver.

Since the year 2000, the VANJHCS' SCI Center has successfully integrated virtual care technologies to address negative factors associated with the travel to the VANJHCS

SCI Center. The VANJHCS's SCI/D SCI HCT implemented veteran-centered care for the SCI/D population. The "Triangle of Healthy Caregiving for SCI Veterans" utilizes a three-pronged approach to evaluations and educational interventions:

1. *Caregiving balance*: This component of the program focuses on educating veterans on what caregiving is from a caregivers' perspective and the need for caregivers to care for themselves. Our veterans enlist in becoming caregiving partners with their caregivers, promoting a healthy relationship pattern.
2. *Caring for the caregivers:* This component educates and empowers Caregivers about ways to enhance the provision of care by learning to take care of themselves. Caregivers are also offered to participate in caregivers' conferences where they learn from groups of caregivers and health care professionals about creative techniques to care for themselves. For example, caregivers learn coping techniques (eg, memoir writing, dance, and meditation) and skills they can implement on their own.
3. *VA virtual care HCT*: Veterans with SCI and caregivers have timely access to the SCI HCT using virtual care technologies to help prevent complications of medical issues seen after SCI as well as emotional and psychological burdens that would impact them and their caregiver's capacity to provide the in home caregiving the veterans may need.

As a result of these key components, veterans with SCI report an increased understanding of what it means to be a caregiver to an SCI veteran. Our caregivers report a decreased sense of isolation and that they were implementing the coping skills they learned in their lives. Preliminary anecdotal feedback from the HCT indicate that veterans with SCI enrolled in the Home Telehealth Disease Management Protocols and the MyHealtheVet Secure Messaging platform have reported that the daily DMP sessions keep them focused on their health and wellbeing, and they learn new information through closer communications with their health care team. Veterans with SCI and caregivers reported that MyHealtheVet Secure Messaging is one of the best virtual care tools available because it is easy to use for renewing medications and messaging the SCI virtual HCT.

Key components and clinical procedures of the "Triangle of Healthy Caregiving for SCI Veterans" have been disseminated at professional conferences [19-36].

Participants

The veterans with SCI, SCI veteran caregivers, and virtual HCT will be recruited from the Spinal Cord Injury/Disorders (SCI/D) Department at the VANJHCS. The VANJHCS SCI/D Department serves an average of 480 SCI/D veterans on their patient registry with 147 veterans with SCI and 80 caregivers using the virtual care telehealth technologies.

Data Collection

Subject Recruitment

The proposed study will receive approval from the VANJHCS Institutional Review Board. The study will collect data from three key stakeholders involved in the "Triangle of Healthy Caregiving for SCI Veterans" model of care who use CVT as part of the delivery of health care: veterans with SCI, SCI Veterans' caregivers, and SCI virtual health care professionals (including telehealth coordinators). We will use purposive sampling to recruit a sample of veterans with SCI and caregivers who are newly referred and currently active or inactive users of CVT in the "Triangle of Healthy Caregiving for SCI Veterans" model of care. Purposeful sampling is a technique widely used in qualitative research that involves identifying participants that are especially knowledgeable about or experienced with a phenomenon [37].

Saturation is the point at which only minimal new information is gained from each new interview [38-40]. Data saturation has become the gold standard by which purposive sample sizes are determined in qualitative research [38-40]. The sample sizes proposed for each study phase described below are based on minimum sample size recommendations for common qualitative study designs [41]. Further, our sampling strategy will be flexible, evolving as the study progresses through the study phases until the point of redundancy in emerging themes is reached to meet the purposes of the study.

Veterans With Spinal Cord Injury

All veterans with SCI who receive clinical care at the VANJHCS are screened for enrollment on virtual care technologies as part of the "Triangle of Healthy Caregiving for SCI Veterans" program. However, based on the clinical experience of our research team, veterans with SCI at VANJHCS who are homebound, newly injured, affected by acute secondary complications (eg, pressure ulcer), and live in rural areas that are significant distance from the VANJHCS are more likely to enroll. There are currently 147 veterans with SCI actively using CVT in their homes. For the purposes of the study, we will recruit and enroll veterans with SCI based on the VANJHCS SCI/D clinical practice protocol. The inclusion criteria for the proposed study will include any veteran with SCI who is potentially or currently enrolled in the "Triangle of Healthy Caregiving for SCI Veterans" program. Veterans with SCI will be ineligible for entry into the study if any of the following exclusionary criteria are present: moderate to severe cognitive impairment or no ongoing landline or cell phone access.

Spinal Cord Injury Veterans' Caregivers

We will recruit caregivers of veterans with SCI at the VANJHCS who are potentially or currently enrolled in the "Triangle of Healthy Caregiving for SCI Veterans" program. There are currently 80 caregivers actively involved in the program. We will recruit a sample of 25-30 SCI veteran family caregivers who have provided care on a daily basis for at least 6 months to veterans with SCI and, preferably, these family members identify as the "primary" caregivers.

Telehealth Coordinators

We will conduct in-depth interviews with the two telehealth coordinators using an interview guide focused on existing structure and practices related to preparation and implementation of CVT in the homes of veterans with SCI who are enrolled in the "Triangle of Healthy Caregiving for SCI Veterans" program.

Spinal Cord Injury Virtual Care Clinical Team

Clinicians' perceptions are important because they may affect patient-provider relationships, the course, and the outcome of treatment. Clinicians have knowledge of the medical and functional consequences of SCI and experience providing training to veterans with SCI and their family caregivers to plan for adjusting to home life and community reintegration. The SCI virtual health care team includes the following professional staff: physicians, advanced nurse practitioners, nurses, therapists (ie, occupational, physical, and recreation), social workers, psychologists, nutritionists, and clergy. We will recruit 8-10 VANJHCS SCI clinicians who are currently treating veterans with SCI and supporting their caregivers enrolled in the "Triangle of Healthy Caregiving for SCI Veterans" program to participate in one focus group.

Data Collection Methods

Data collection methods will be implemented over three phases of sequential qualitative and quantitative data collection outlined in Table 1. Results from each phase will be analyzed separately and then merged to inform the content of the subsequent phases as well as a set of recommendations for the "Triangle of Healthy Caregiving for SCI Veterans" to the VA National Office of Telehealth and the National SCI/D Systems of Care office.

Table 1. Data collection methods, purpose, and products.

Phase	Data collection methods	Purpose	Products
I	• In-depth interviews	• Conduct 2 in-depth interviews with the telehealth coordinators for the SCI[a]	• Description of the enrollment and home installation process
	• Observations of SCI Veterans' enrollment and home installation	• Conduct 15-20 observations of the patient enrollment and home installation of equipment/devices	• Observation data of the enrollment and installation process
II	• Semistructured interviews	• Conduct 35-40 semistructured interviews with veterans with SCI enrolled in the "Triangle of Health Caregiving for SCI Veterans" program • Conduct 25-30 semistructured interviews with caregivers of veterans with SCI enrolled in the "Triangle of Healthy Caregiving for SCI Veterans" program	• Qualitative data (semistructured interview transcripts, field notes)
III	• Focus groups	• Conduct one focus group with virtual health care team professionals	• Focus group findings about the delivery of health care to veterans with SCI, education, and support to their caregivers

[a]SCI: spinal cord injury.

Phase I: Enrollment and Installation of Equipment/Devices

We will use two qualitative data sources to assess the processes and logistics of enrollment in the program and the installation of CVT capability (equipment/devices/software) in SCI veterans' homes: in-depth interviews and observations. In-depth interviews are one of the most common qualitative methods. In-depth interviews are open-ended interviews and enable respondents to discuss their point of view using their own language related to a topic with no predetermined list of responses. Structured observation of the CVT enrollment process and logistics of home installation of the CVT system will be conducted to validate the content of the in-depth interviews and highlight any discrepancies observed. Documentation data will consist of field notes that will be electronically recorded in Research Electronic Data Capture (REDCap) [42] (see Data Management System description below). The field notes will account for key events that took place during CVT enrollment and the home installation process and how the veteran with SCI or caregiver behaved or reacted in the interaction with the telehealth coordinator that services patients with SCI at VANJHCS.

In-Depth Interviews With Telehealth Coordinators

We will conduct two in-depth interviews with telehealth coordinators to systematically document the administrative procedures involved in the enrollment of veterans with SCI into the CVT system. For example, the research team will ask administrative technicians to describe the ways in which description of CVT and various modalities and explanation of CVT installation/equipment in the home are discussed with veterans with SCI, and logistics of the delivery of CVT material and equipment will be reviewed. Additionally, the research team will assess the types of real-time problems of delivering health care to the veterans with SCI from the administrative technicians' perspectives. They will summarize and review the information gathered from the interviews. The research team will use these data to develop observations forms to be used in the observations of the veterans' enrollment and CVT equipment/device installation in their homes.

Observations of Enrollments and Equipment/Device Installation

Direct observation will be performed of SCI veterans' enrollment in the CVT program during consultations with the telehealth coordinators. The goal of this observation is to validate the information gathered from the in-depth interviews

with the telehealth coordinators. Enrollment observations will record a face-to-face consultation with veterans with SCI (and caregiver) that was newly referred to the "Triangle of Healthy Caregiving for SCI Veterans" with the CVT administrative technician. The goal of the consultation is to provide veterans with SCI a description of CVT and various modalities, explanation of CVT installation/equipment in the home, and logistics of the delivery of CVT material and equipment and to obtain patient signatures (eg, commitment to ensure privacy during clinical visits, liability waiver, and protection of equipment the VA may give them).

Home observations of the installation process and utilization of the virtual care equipment in a sample of veterans with SCI households will provide the research team a context for the CVT installation process. The research team will take observation field notes to document the practicalities of CVT use in the home and any difficulties associated with home installation and usage. The observations will assess the length of installation time, the questions or concerns mentioned by the SCI veteran or caregiver during the installation, problems encountered by the CVT technicians during installation, and problems encountered during the testing of the CVT modalities (eg, accuracy of medical devices and display of educational modules).

Phase II: Semistructured Interviews

Semistructured interviews will be conducted to assess specific elements of the "Triangle of Healthy Caregiving for SCI Veterans" program, their perceived utility, and the effectiveness of the CVT system as well as general impressions of the impact of the intervention on the SCI veterans' health and functioning outcomes (caregiver burden and daily caregiver burden). The semistructured interviews will include open-ended questions, closed-ended questions, and outcome measures. One-on-one interviews (in-person or via virtual care technology) with veterans with SCI (n=35-40) and their caregivers (n=25-30) will be conducted to capture SCI veterans' and caregivers' perceptions (including benefits and challenges) and experiences of participating in the "Triangle of Healthy Caregiving for SCI Veterans" program by using CVT. After consent is obtained, the research assistant will contact participants to complete a demographic questionnaire and health, function, and community participation outcome measures (Table 2). Upon completion of the outcome measures and semistructured interviews, participants will be compensated for their time.

Table 2. Outcome measures of veterans with spinal cord injury and caregivers.

Measures/scale	Outcome	Administration time (minutes)
Veterans' outcome measures		
Spinal Cord Injury Functional Index Short Forms (Jette et al 2012 [43]; Heineman et al 2014 [44])	Will ask persons with SCI[a] to relate their perceived ability to complete function activities in four domains: wheel chair mobility, self-care, fine-motor function, and basic mobility	~5
Veterans RAND 12-Item Health Survey (Selim et al 2008 [45])	Will assess quality of life thorough eight domains including physical functioning, vitality, role limitations due to physical problems, role limitations due to emotional problems, bodily pain, general health, social functioning, and mental health	<5
Craig Handicap Assessment and Reporting Technique Short Form (Whiteneck 2011 [46])	Assess participation in society and subscales measuring physical independence, cognitive independence, mobility, occupation, social integration, and economic self-sufficiency	
Caregivers' outcome measures		
Caregiver Appraisal Scale (Lawton et al 1989 [47])	Measure caregiving satisfaction, perceived caregiving impact, caregiving mastery, caregiving ideology, and subjective caregiving burden	~15
Caregiver Burden Scale (Elmstahl et al 1996 [48])	Assess amount of burden caregivers feel using five categories including general strain, isolation, disappointment, emotional involvement, and environmental strain	~10

[a]SCI: spinal cord injury.

A semistructured interview guide will be developed based on previous literature and findings of Phase I of this project. The interview will ask participants to express their perceptions and experiences with the "Triangle of Healthy Caregiving for SCI Veterans" program by using CVT. These interviews will give the research team the opportunity to further explore the topics that were of greatest interest and concern based on the observations in Phase I of the study. To ensure data quality, interviews will be audiotaped and transcribed. After the interview is completed, the research coordinator and research assistant will summarize their notes and review the results with the research team. Spot checks of the transcripts comparing them with the audiotapes will be performed to ensure accuracy of the transcripts.

Phase III: Spinal Cord Injury Virtual Medicine Clinician Focus Group

We will conduct a focus group to evaluate the ways in which the "Triangle of Healthy Caregiving for SCI Veterans" is useful in health care delivery to veterans with SCI and support services to SCI caregivers. A sample of approximately 8-10 SCI virtual care clinicians will participate in 90-minute focus groups to derive a meaningful understanding of the ways in which CVT can provide health care to veterans with SCI and support to their

caregivers. Focus groups capitalize on group interaction to produce data and insights that might be less accessible without interaction among individuals with common experiences [49,50]. The SCI virtual health care team includes the following professional staff: physicians, nurses, therapists (ie, occupational, physical, and recreation), nurse practitioners, social workers, psychologists, nutritionists, and clergy. The focus group discussion will ask clinicians to describe some of the key positive outcomes/results that have occurred in terms of patient care as a result of the introduction of the "Triangle of Healthy Caregiving for SCI Veterans" program and use of CVT (eg, cost savings, clinical effectiveness, and quality of life).

Focus groups are an efficient way to collect data from several people simultaneously, and they explicitly use group interaction as part of the method [49,50]. Focus groups will allow us to elucidate clinicians' shared experiences and challenges of providing health care to veterans with SCI and support to veterans with SCI using the CVT technology in the "Triangle of Healthy Caregiving for SCI Veterans" program. The research coordinator or research assistant will take field notes on a structured data-recording sheet based on the focus group script/interview guide. The focus group will be recorded with a password-enabled digital recorder, and the recordings will be transferred to the secure VA network for transcription. The research team will debrief immediately after the focus group to share their impressions, critical points, and notable quotes.

Data Management System

We will utilize the VA Information Resource Center's REDCap electronic data capture tool hosted by the VA Information Resource Center to store and manage the qualitative and quantitative data from each phase of the study [42]. REDCap is a secure Web app for building and managing online surveys and databases and permits data collection via a Web browser either locally or from remote locations. The NVivo (version 12; QSR International Pty Ltd, Melbourne, Australia) software supports mixed methods research to help research teams organize, analyze, and identify insights in unstructured or qualitative data and integrate quantitative data. NVivo also facilitates the export of demographic and qualitative data into quantitative analysis tools like SPSS (IBM Corp, Armonk, New York), which will be used for the quantitative analyses. The research team will integrate the qualitative and quantitative data.

Data Analysis

Qualitative Analyses

Qualitative data analyses will be guided by the Consolidated Framework for Implementation Research [51,52] using intervention-specific codes that will be developed throughout Phases I, II, and III by using a constant comparison analytic approach [53]. The research team will construct a preliminary codebook both deductively and inductively from the qualitative data and previous literature. Potential codes may include impact on patient health and functional outcomes, impact on health care utilization, reimbursement issues, CVT utility, and communication with health care team members. These codes will be applied using NVivo to develop an initial set of themes. The codebook will be elaborated upon and adjusted as the results of each phase of the study are reviewed, until thematic saturation is achieved within and across each phase of the study. Additional sources of qualitative data (eg, field notes) will be included in the dataset. The research team will summarize the data coded to the themes that will be independently reviewed by each member of the research team, discussed to derive consensus, and synthesized for each research question.

Quantitative Analyses

In addition to identifying themes and patterns qualitatively, we will examine the health and functional outcomes observed among veterans with SCI and caregivers in terms of the outcome data (aim 1 and 2) and coded qualitative data. We will explore descriptive data from Phases I to III using descriptive statistics (eg, means, SDs, percentiles, and ranges) and graphical techniques (eg, histograms and scatter plots) to characterize participant groups on key aspects (eg, working status).

Standard outcome measure scores will be generated by normative data. Separate analyses will be conducted for SCI veterans' and caregivers' outcome scores using analysis of covariance, with age and education as covariates. Once the qualitative data have been coded, more complex statistical analyses can be employed through the transformation of coded data into theoretically meaningful units of measure, as previously outlined [31,54,55]. This will allow examination of the differences between strategy utilization and health, function, and community participation outcomes.

Integrating Findings: Practice Recommendations

To design a useful set of practice recommendations, we will analyze results from each study phase separately and compare and merge the results across the quantitative and qualitative data sources. Qualitative and quantitative data will be triangulated. Triangulation is a methodological approach that contributes to the validity and reliability of integration when both qualitative and quantitative data collection methods are employed [56,57]. Triangulation will allow us to compare, contrast, and integrate the results from observations, interviews, focus group, and outcome measures. Triangulation from these three sources will also allow us to ensure the results are confirmed across data sources and identify data that are uniquely provided by different data sources. This is a side-by-side comparative analysis of the qualitative data and outcome scores to validate the findings across both sources of data collection.

Using the themes generated from the triangulated data, the research team will identify the most frequently cited factors (ie, benefits and challenges) that are important to key stakeholders in the "Triangle of Healthy Caregiving for SCI Veterans," which are mentioned by more than one data source and across samples of participants—a process known as "group-to-group validation." [50]. We will apply similar review methods to the differential patterns in the outcome measures. The research team will hold bimonthly consensus meetings to evaluate aspects of the most frequently cited benefits and challenges generated from the data based on the importance across the samples and modifiability of factors. After identifying factors that are both important and modifiable, the research team will prepare a

summary of consumer-informed recommendations for the "Triangle of Healthy Caregiving for SCI Veterans" for the VA National Office of Telehealth and the national SCI/D Systems of Care office.

Results

This proposal was funded in July 2017. It was reviewed and received institutional review board approval in March 2018, and the project was started immediately after, in the same month. As of September 2019, we have completed Phases I and III and have recruited 52 subjects for Phase II. We are beginning the data analysis. The study is projected to be completed in late summer of 2020, and the expected results are to be published in the fall of 2020.

Discussion

SCI is a devastating, disabling medical condition with significant impact on quality of life and is very costly for patients, their families, and the health care system. Increasing access to specialized care can be paramount in preventing and managing the sequelae of SCI. Increasing the use and benefit of virtual care technologies in health care delivery have been noted, and the benefits of these technologies can also be seen when delivering care to people living with SCI. This study will help us understand the benefits, challenges, and outcomes of using virtual care technologies in health care delivery to veterans living with SCI by learning directly from veterans, their caregivers, and their health care team who have virtual health care integrated in the model of care. This information can also be expanded beyond the veteran population to potentially benefit all people living with SCI.

Acknowledgments

This project was funded by the Office of the Assistant Secretary of Defense for Health Affairs through the Spinal Cord Injury Research Program under Award No. W81XWH-17-1-0262. The contents of this paper, including opinions, interpretations, conclusions, and recommendations, are those of the author and are not necessarily endorsed by the Department of Defense. The authors would like to thank the research team who contributed to the conduction of the study: Yasheca Ebanks and Nicole Jones.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Peer-reviewer report.
[PDF File (Adobe PDF File), 115 KB - resprot_v9i5e14051_app1.pdf]

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Abbreviations

CVT: clinical video teleconferencing
HCT: health care team
REDCap: Research Electronic Data Capture
SCI: spinal cord injury
SCI/D: Spinal Cord Injury/Disorders
QOL: quality of life
VA: Veterans Affairs
VANJHCS: Veterans Affairs New Jersey Health Care System

Edited by G Eysenbach; submitted 18.03.19; peer-reviewed by M Guihan, B Dixon; comments to author 27.04.19; revised version received 30.06.19; accepted 07.07.19; published 12.05.20.

Please cite as:
Gibson-Gill CM, Williams J, Fyffe D
Triangle of Healthy Caregiving for Veterans With Spinal Cord Injury: Proposal for a Mixed Methods Study
JMIR Res Protoc 2020;9(5):e14051
URL: https://www.researchprotocols.org/2020/5/e14051
doi:10.2196/14051
PMID:32396130

Protocol

Evaluation and Dissemination of a Checklist to Improve Implementation of Work Environment Initiatives in the Eldercare Sector: Protocol for a Prospective Observational Study

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Abstract

Background: To measure sustainable improvements in the work environment, a flexible and highly responsive tool is needed that will give important focus to the implementation process. A digital checklist was developed in collaboration with key stakeholders to document the implementation of changes in eldercare sector workplaces.

Objective: This paper describes the study protocol of a dissemination study that aims to examine when, why, and how the digital checklist is spread to the Danish eldercare sector following a national campaign particularly targeting nursing homes and home care.

Methods: This prospective observational study will use quantitative data from Google Analytics describing use of the checklist as documented website engagement, a survey among members in the largest union in the sector, information from a central business register, and monitoring of campaign activities. The evaluation will be guided by the five elements of the RE-AIM framework: reach, effectiveness, adoption, implementation, and maintenance.

Results: The study was approved in June 2016 and began in October 2018. The campaign that is the foundation for the evaluation began in 2017 and ended in 2018. However, the webpage where we collect data is still running. Results are expected in 2020.

Conclusions: This protocol provides a working example of how to evaluate dissemination of a checklist to improve implementation of work environment initiatives in the eldercare sector in Denmark. To our knowledge, implementation in a nationwide Danish work environment has not been previously undertaken. Given that the checklist is sector-specific for work environment initiatives and developed through systematic collaboration between research and practice, it is likely to have high utility and impact; however, the proposed evaluation will determine this. This study will advance dissemination research and, in particular, the evaluation of the impact of these types of studies. Finally, this study advances the field through digital tools that can be used for evaluation of dissemination efforts (eg, Google Analytics associated with website) in the context of a rigorous research design activity.

International Registered Report Identifier (IRRID): DERR1-10.2196/16039

(JMIR Res Protoc 2020;9(5):e16039) doi:10.2196/16039

KEYWORDS

RE-AIM; implementation; workplace; digital

Introduction

Currently many countries are facing shortages of health care workers, and this is jeopardizing capacity to deliver residential care services [1]. The shortage of health care workers is associated with high rates of sickness absence, turnover, and early retirement among this professional group [2]. It is well known that high physical and psychosocial work demands are important risk factors for long-term sickness absence, turnover, and early retirement from the eldercare sector [3,4]. Thus, increasing and sustaining the eldercare workforce demands urgent attention. Several initiatives, including complex multilevel interventions, have been introduced to improve the work environment of eldercare workers during the past decades in Denmark and other countries [5-8]. However, despite availability of extensive research and policy efforts, employees in the eldercare sector have only experienced limited improvements in the work environment.

A reason for the lack of improvement in the work environment in this setting may be that the eldercare sector is continuously changing through care regimes, political reforms, and high turnover rates [9]. Such changes affect the stability of the organizations and may also challenge implementation of new knowledge and work environment policies or initiatives [9]. The work environment can be considered a moving target with continuously changing terms and starting points [10]. Therefore, interventions for such a moving target must be flexible and highly responsive to the changing needs in the work environment and facilitate the implementation process [10]. Therefore, we decided to collaborate with stakeholders from the target group to collect information about how to efficiently implement changes in the work environment in the eldercare sector [10]. The knowledge base was condensed to the Hitting the Moving Target framework, which summarized 11 components to consider in order to succeed with implementation [10]. The framework targets both managers and employees in the eldercare sector. From recommendations from the target group, the 11 components from the Hitting the Moving Target framework were used to develop an implementation tool in the form of a digital checklist containing the 11 concepts.

Another reason for the lack of improvement in the work environment in this sector may be the challenge of translation of policies and research knowledge into practice [11]. Many factors can influence whether the translation of research knowledge into practice is successful and whether policies or evidence-based practices are accepted and used by the target users [12]. Dissemination of research findings is an important step to bridge the gap between research and practice. Effective dissemination strategies include formative research to customize dissemination strategies to fit audience needs and preferences [13]. Distribution strategies should focus on ensuring that messages and materials from research reach intended audiences by use of multicomponent dissemination strategies (eg, mailings, websites, publications, webinar or in-person presentations, interpersonal connections, and mass media, among others) [13,14]. To be most effective, distribution should engage the channels that intended audiences already trust and access for information [13]. Previously, national campaigns have been used to reach a large proportion of the population for reducing musculoskeletal disorders [15,16]. But such campaigns are expensive and need to be well planned. In addition, the packaging and communication used to disseminate evidence-based knowledge determines the dissemination success [17]. Different approaches have been attempted to overcome this challenge. For example, in Sweden, guidelines aimed at improving the psychosocial work environment have been coproduced with practitioners [18]. Still, there is a shortage of knowledge on how to optimize dissemination, and the reach and effect of such initiatives is difficult to evaluate and rarely investigated.

This paper is the dissemination protocol that examines when, why, and how the checklist is spread to the Danish eldercare sector, in particular nursing homes and homecare. The protocol presents both the process of developing the digital checklist, planning the dissemination strategy (ie, the communication of the checklist through a national campaign), and the evaluation plan. Specifically, the protocol aims to investigate the adoption, reach, implementation, maintenance, and effectiveness of the checklist after a national campaign to improve implementation of work environment initiatives among eldercare workers in Denmark. The following four research questions will be investigated:

1. How many Danish eldercare workplaces use the checklist and what characterizes those who do from those who don't? (adoption)
2. Across Danish eldercare workplaces, what proportion of eldercare workers know about the campaign and what characterizes those who do from those who don't? (reach and representativeness)
3. Among the users, how is the checklist used and for what purposes? (implementation and maintenance)
4. Is the work environment practice improved among users of the checklist compared with nonusers? (effectiveness)

Methods

Study Design

This is a prospective observational study using a range of quantitative data collection approaches to accomplish the study aims. The study is described according to the Standards for Reporting Implementation Studies (StaRI) statement.

Study Setting and Population

The study setting is the eldercare sector in Denmark, and more specifically, selected nursing homes and homecare settings. In Denmark, there are approximately 5000 workplaces within the eldercare sector that employ about 100,000 eldercare workers.

Ethics Approval and Consent to Participate

According to Danish law as defined in Committee Act §2 and §1, the study described should not be further reported to the local ethics committee. The data use is approved by the Danish Data Protection Agency. According to Danish law, questionnaire- and register-based studies do not need approval by ethical and scientific committees or informed consent by participants.

Development of the Digital Checklist (Dissemination Object)

The translation from Hitting the Moving Target framework to a digital checklist was conducted in close collaboration with relevant partners. We involved two groups of stakeholders: (1) a practice-based research team (PBR) team and (2) a municipality team. They functioned as codevelopers with a central role in operationalizing the 11 implementation components from the Hitting the Moving Target framework into the checklist. The PBR team group consisted of 10 stakeholders with representatives from the largest union in the nursing home sector, Local Government Denmark, which is the central organization of all Danish municipalities, the Danish Work Environment Authority, the Knowledge Center for Work Environment, and the Sector-Specific Work Environment Community Organization for Public and Welfare workplaces. The municipality-based stakeholder group consisted of 5 work environment consultants employed in 4 different Danish municipalities, and this group helped us in the development, especially in making the checklist adaptable to existing practices and structures. As an example, the municipality-based stakeholder group helped us decide that the checklist should be directed at the Occupational Health and Safety (OHS) groups at the workplaces, which are groups consisting of both managers and employees with specific tasks related to OHS.

The feasibility of the checklist was assessed through cognitive interviews with a range of intended beneficiaries, both employees and managers in the eldercare sector (primarily those involved in OHS groups). The prototype of the Web-based checklist was then included in 40 tests conducted with employees, mainly OHS representatives at different nursing homes, to fit the digital solution to the user needs and make sure they could use the checklist as intended. The final 11 checkpoints can be seen in Figure 1.

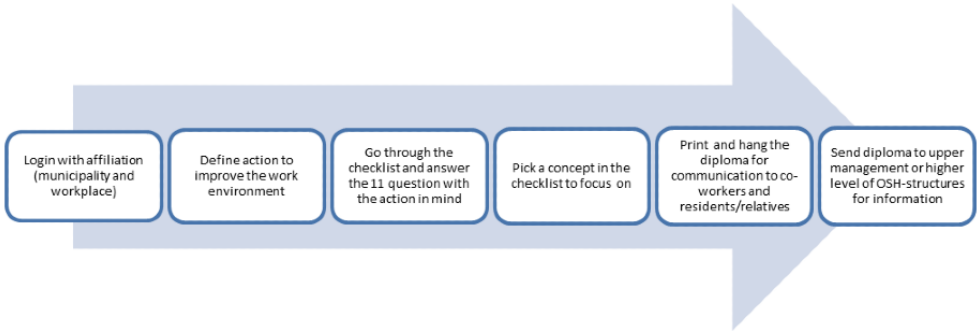
Figure 1. The wording of the checklist (translated from Danish). Before going through the checklist, the respondents had defined an action (free of choice, eg, “we wish to implement a new assistive device”) they wanted to focus on to improve the work environment.

- ❑ Does the action deal with an everyday problem?
- ❑ Does the action deal with what’s “top of mind” among the employees?
- ❑ Do you have the necessary support?
- ❑ Does your supervisor support the action?
- ❑ Have you involved all relevant employees?
- ❑ Have resources been allocated?
- ❑ Do you know who’s in charge of the action?
- ❑ Is it easy to see the output of the action, so it’s easy to get started?
- ❑ Is it easy to maintain, so the output remains?
- ❑ Do you tell people about the action in a good way?
- ❑ Does the action contribute to the sense of community?

Content and Use of the Web-Based Checklist

The checklist is an interactive digital platform that can be assessed through a website. Users (primarily the OHS groups) can use it in their work environment practice when implementing new routines, projects, or initiatives (termed *actions* in the checklist) to improve the work environment. The steps in the process of using the checklist are described in Figure 2. The user has to log in with their affiliation and then define the action (free of choice) they want to implement. The next step is to go through the checklist and pick one concept in the checklist that they want to focus on. Working with defined actions to support implementation is a task that the OHS groups already have in their portfolio to maintain a good work environment. After having gone through all the points of the checklist they get a result that indicates how many facilitators for implementation are in place, and they get information about the concept to focus on. It is possible to print a diploma that shows this and place it visibly at the workplace and automatically send an email to communicate the actions to others (ie, coworkers and upper management). In addition, it is possible to get tips for implementation on the website [19].

Figure 2. Overview of the steps on the Web-based checklist.



Dissemination Strategy

National Campaign

The aim with the campaign was to increase awareness of the existence of the checklist. The campaign was developed with our PBR and municipality teams. An initial workshop was held to identify central target users when disseminating the checklist to the eldercare sector. Through persona analysis, we characterized all potential users working with or within the eldercare sector and made a description of their role in the work environment, and thereby we were able to describe who would be the most relevant target group for the checklist. This workshop highlighted the importance of targeting the checklist directly to those who work within the work environment (eg, the OHS groups) at the workplaces. We planned the campaign to be nationwide and primarily driven through network on social media, websites, through newsletters, magazines, conferences, letters, and a campaign film by the researchers and stakeholders (especially the PBR team). The campaign was planned to run for 1 year (from September 2017 to September 2018).

Campaign Materials and Methods

The campaign materials included paper and digital elements. Paper elements included printed versions of the checklist such as postcards and letters, which were sent to the administrative departments of all municipalities and all identified home care units and nursing homes in Denmark informing about the new checklist. The digital elements included a short campaign movie, small instruction movies, and newsletters. We produced a campaign movie aimed at increasing awareness about the new checklist. The movie was distributed via social media (eg, Facebook, LinkedIn, and Twitter), and we aimed to create awareness of the newly developed checklist among the entire target population in the eldercare sector. Additionally, we produced small instruction movies showing how to use the checklist. Both were uploaded on the same webpage [20].

Presentations and Dissemination Partners

The researchers presented the checklist whenever possible at conferences and workshops where the target group was present. Furthermore, researchers presented the checklist for consultants working in this industry—for example, to consultants employed at a central position in the municipality or physiotherapists or occupational therapists working at one or more nursing homes. We focused on building a network with central work environment representatives in the municipalities of Denmark, emphasizing the close collaboration between researchers and practitioners. This enabled exchange of information from the municipalities about the work environment and for us to inform about the checklist and how to use it.

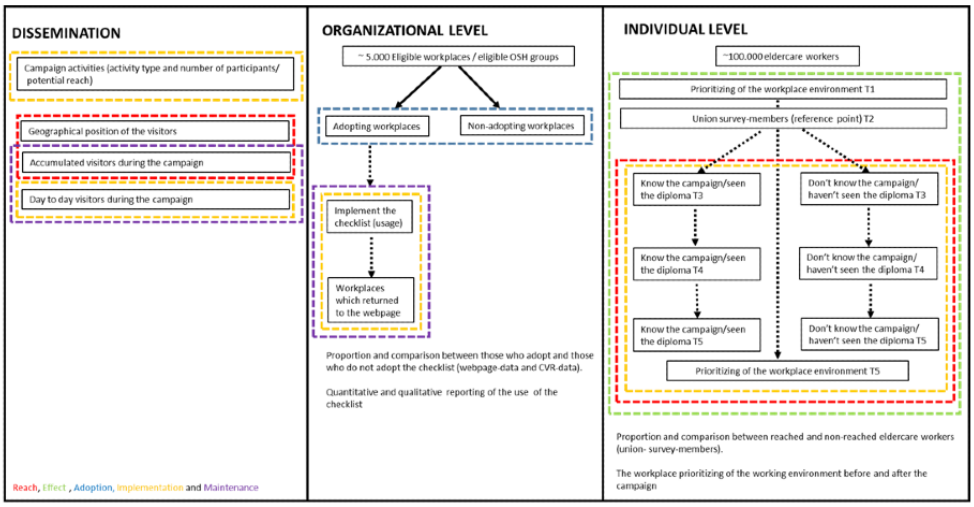
The stakeholders (especially our PBR team) functioned as dissemination partners. They referred to the checklist on their respective websites, Facebook pages, in magazines, in newsletters, etc. The PBR team also functioned as ambassadors for disseminating the checklist (eg, when visiting the nursing homes). Furthermore, the entire corps of inspectors from the Danish Work Environment Authority (N-90), who visit and inspect workplaces in Denmark regarding the work environment, were trained in the checklist and informed about the checklist before going out to the workplaces. Additionally, we established a partnership with work environment consultants connected to the eldercare sector. They were informed about the checklist when relevant—for example, when talking with the OHS groups about potential initiatives for improving the work environment and how to succeed with their initiatives.

Evaluation

This study aims to investigate the dissemination and effectiveness on work environment improvements of a checklist to improve implementation of work environment initiatives among eldercare workers in Denmark. A commonly used framework in the evaluation of implementation research is the RE-AIM (reach, efficacy/effectiveness, adoption, implementation, and maintenance) framework [21-24]. RE-AIM guides areas to consider when seeking to evaluate the potential public health impact of a program and consists of the 5 dimensions, reach, efficacy/effectiveness, adoption, implementation, and maintenance.

In this dissemination study, the indicators of reach, implementation, and maintenance are somewhat overlapping and may be used as indicators of more than one evaluation component. This is because the intervention can be considered as both the campaign, the checklist, and the action plan at the workplace and thus reach and implementation can occur at several levels (ie, societal, organizational, and individual level), and we aim to describe all levels in this study (see Figure 3).

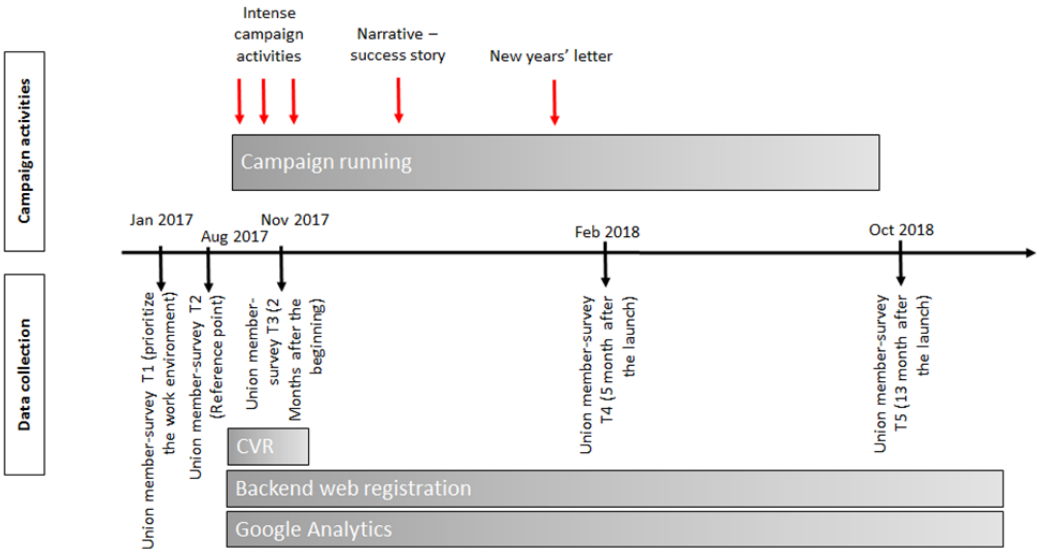
Figure 3. Overview of the evaluation. The different evaluation components are color-coded according to the RE-AIM framework.



Data Collection

We will use multiple data sources including data on campaign activities, data from the Central Business Register (CVR), data from Google Analytics, data regarding activity on the project website (use of the checklist), and data from a survey among members in the largest union in the industry. In Figure 4, the campaign (activities) and the data collection are illustrated.

Figure 4. Overview of campaign activities and data collection.



Central Business Register

The CVR contains information about all registered workplaces in Denmark. Factors available in the CVR are size (number of employees in intervals), type of workplace (nursing home, home care, hospital, etc), age (start-up date of company/workplace), and geographical position of the workplace (ie, municipality).

Google Analytics

The website [19] was associated with a Google Analytics account. Information on day-to-day visits and month-by-month geographical data on city level will be downloaded.

Online Checklist Website

From the backend of the website, we will collect user-specific information from visitors, defined actions to improve the work environment, and answers to the checklist.

Union Survey

The largest trade union for eldercare workers in Denmark organizes approximately 180,000 members primarily in the public sector. The union has more than 90,000 employed members engaged in social and health sector. Members belonging to the social and health sector can voluntarily sign up as a survey member to receive a questionnaire 4 to 6 times a year about work environments and other work-related topics. Union members can register and drop out as they want. The union survey is sent to approximately 7500 survey members each time.

The data sources above will be used to answer the research questions according to the RE-AIM framework. Multimedia Appendix 1 shows each of the components of the RE-AIM framework and their definition. In addition, the appendix shows

the specific research question(s) related to each component and their respective data source and operationalization.

Statistical Analysis

Using descriptive statistics, we will compare adopting (workplace that use the checklist) and nonadopting workplaces in terms of the number of employees, type of workplaces, and age and geographical position of the workplaces. To report reach, we will use descriptive statistics to compare gender, age, manager, position of trust, employer, and workplace of respondents with knowledge of the campaign and those not reached by the campaign. In addition, we will test for differences in adopters and nonadopters and in reached and nonreached, respectively, by *t* test or analysis of variance.

Effectiveness will be evaluated by comparing the change in the prioritization of the work environment efforts experienced by respondents from before the campaign until after the campaign. Analyses regarding the effectiveness will be performed after 12 months of campaign by means of analysis of covariance comparing employees with knowledge of the campaign and those without knowledge of the campaign. We will test whether it is relevant to control for confounders such as age and gender.

Results

The study started in September 2017 with the 1-year campaign. The main data collection was completed by September 2018, but data collection through the website is ongoing. Dissemination of results is expected in early 2020.

Discussion

Summary

This paper presents the protocol for the evaluation and dissemination of a checklist to improve implementation of work environment initiatives in the eldercare sector in Denmark. To our knowledge, this has not previously been undertaken in a Danish work environment context, and it is the first nationwide sector-specific checklist for implementing work environment initiatives. Also, evaluation of which checklist points have been most frequently (or rarely) ticked may give valuable information regarding which implementation challenges workplaces easily handle and which challenges they postpone.

The project will expand the understanding of the determinants of implementation and dissemination success and failure. New knowledge will be generated on industry-specific dissemination, which potentially can be used in industries other than nursing homes. It is hoped that the planned fine-grained evaluation outcomes will provide practical information that will give managers and government agencies well-tested tools and comprehensive process insights that with enable interventions to be more quickly and more effectively implemented to generate improved work environments and alleviate some of the shortages in the eldercare workforce.

Strengths and Limitations

A limitation in the evaluation of the impact of the checklist is that use is measured only through the website and not the potential use outside this setting. For example, the postcards with a print of the checklist given to workplaces can be used instead of logging in to the website checklist. Therefore, the evaluation will likely not cover the full dissemination and may actually underrepresent uptake of the checklist. Further, we have observed that some employees in eldercare may have limited access to computers during work hours. On the other hand, tablets and laptops are often present at the workplaces and Web-based work environment and safety systems are becoming a more regular practice. A limitation to the study is that we cannot generalize beyond eldercare. It is also a limitation that the data are self-reported and contained nonvalidated information. However, a strength is the use of multiple data sources and new digital data sources.

Conclusion

To have a wide and lasting impact, tools often need to be adapted to or reconstructed within practice settings. Consequently, to maximize the utility of our model and the resulting implementation checklist, extensive and systematic involvement of stakeholders was undertaken. Importantly, we also used this codesign process to develop the dissemination strategy. We intended that the ownership generated in key stakeholders would assist to ensure the development of a fit-for-purpose checklist and dissemination strategy and therefore generate strong positive outcomes. There is an ever-increasing demand for research to make a practical difference in policy and in society in general, but many products and programs fail deliver such outcomes. Given the methods used to develop our interventions and the approach to evaluation, we expect that the data generated from this study will generate novel insights into how to generate real-world impacts at scale. In conclusion, this study will advance dissemination research and, in particular, the evaluation of the impact of these types of studies. Finally, this study advances the field through digital tools that can be used for evaluation of dissemination efforts (eg, Google Analytics associated with website) in the context of a rigorous research design activity.

Acknowledgments

The study is funded by the Danish Working Environment Research Fund (33-2016-03 20165101121). The funders had no role in study design, data collection, and analysis; decision to publish; or preparation of the manuscript.

Authors' Contributions

CNR acquired funding for the project, designed the study, drafted the first version of the manuscript, and wrote the final version of the manuscript. HHJ designed the study, participated in discussions around the study, and critically revised the manuscript.

AKL, PKM, IJ, RO, LL, and LK participated in discussions around the study and critically revised the manuscript. MBJ acquired funding for the project, designed the study, participated in discussions around the study, and critically revised the manuscript. All authors have read and approved the manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Overview of evaluation and operationalization of the components in the RE-AIM framework: adoption, reach, implementation, effectiveness, and maintenance.
[DOCX File , 15 KB - resprot_v9i5e16039_app1.docx]

Multimedia Appendix 2
Funding documentation. Declaration of translation into English from Danish.
[DOCX File , 37 KB - resprot_v9i5e16039_app2.docx]

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Abbreviations

CVR: Central Business Register
PBR: practice-based research
OHS: Occupational Health and Safety
RE-AIM: reach, efficacy/effectiveness, adoption, implementation, and maintenance
StaRI: Standards for Reporting Implementation Studies

Edited by G Eysenbach; submitted 28.08.19; peer-reviewed by D Eerd, M Hong; comments to author 19.10.19; revised version received 13.01.20; accepted 04.02.20; published 13.05.20.

Please cite as:
Rasmussen CDN, Højberg H, Larsen AK, Munch PK, Osborne R, Kwak L, Jensen I, Linnan L, Jørgensen MB
Evaluation and Dissemination of a Checklist to Improve Implementation of Work Environment Initiatives in the Eldercare Sector: Protocol for a Prospective Observational Study
JMIR Res Protoc 2020;9(5):e16039
URL: https://www.researchprotocols.org/2020/5/e16039
doi:10.2196/16039
PMID:32401212

Proposal

Person and Family Centeredness in Ethiopian Cancer Care: Proposal for a Project for Improving Communication, Ethics, Decision Making, and Health

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Abstract

Background: Cancer is a major burden in Ethiopia. The Oncology Department of Tikur Anbessa (Black Lion) Specialized Hospital in Addis Ababa is the sole specialist unit for cancer care in the country. With only a handful of oncologists, a lack of resources, and a huge patient load, the work is challenging, especially in terms of achieving effective and ethical patient consultations. Patients, usually accompanied by family members, often wait for a long time to receive medical attention and frequently depart without treatment. Handling consultations effectively is essential to help patients as much as possible within such limitations.

Objective: The project has the following three main aims: (1) to enhance and expand the understanding of communicative and associated ethical challenges in Ethiopian cancer care; (2) to enhance and expand the understanding of the implications and use of person- and family-centered solutions to address such communicative challenges in practice; and (3) to plan and evaluate interventions in this area.

Methods: This project develops and consolidates a research collaboration to better understand and mitigate the communicative challenges in Ethiopian cancer care, with a focus on the handling and sharing of decision making and ethical tension among patients, staff, and family. Using theoretical models from linguistics, health communication, and health care ethics, multiple sources of data will be analyzed. Data sources currently include semistructured interviews with Ethiopian staff (n= 16), patients (n= 54), and family caregivers (n= 22); survey data on cancer awareness (n=150) and attitudes toward breaking bad news (n=450); and video recordings of medical consultations (n=45). In addition, we will develop clinical and methodological solutions to formulate educational interventions.

Results: The project was awarded funding by the Swedish Research Council in December 2017 for the period 2018 to 2021. The research ethics boards in Sweden and Ethiopia approved the project in May 2018. The results of the studies will be published in 2020 and 2021.

Conclusions: The project is the first step toward providing unique and seminal knowledge for the specific context of Ethiopia in the areas of physician-patient communication research and ethics. It contributes to the understanding of the complexity of the role of family and ethical challenges in relation to patient involvement and decision making in Ethiopia. Improved knowledge in

this area can provide a fundamental model for ways to improve cancer care in many other low-resource settings in Africa and the Middle East, which share central cultural prerequisites, such as a strong patriarchal family structure, along with strong and devout religiosity. The project will also serve to develop greater understanding about the current challenges in Western health systems associated with greater family and patient participation in decision making. In addition, the project will contribute to improving the education of Ethiopian health professionals working in cancer care by developing a training program to help them better understand and respond to identified challenges associated with communication.

International Registered Report Identifier (IRRID): DERR1-10.2196/16493

(JMIR Res Protoc 2020;9(5):e16493) doi:10.2196/16493

KEYWORDS

communication; culture; cancer; ethics; person-centered care; Ethiopia

Introduction

Background

The purpose of this project is to develop and consolidate a research collaboration between Sweden and Ethiopia to better understand and mitigate the communicative challenges in Ethiopian cancer care, with the aim of developing greater capacity and tools to address the identified problems. The project is a research collaboration between the School of Medicine and Tikur Anbessa (Black Lion) Specialized Hospital (TASH), Addis Ababa University in Ethiopia and the Department of Applied Information Technology, the Department of Philosophy, Linguistics and Theory of Science, and the Sahlgrenska Academy, University of Gothenburg, as well as the Sahlgrenska University Hospital in Sweden.

Through participating project investigators and researchers, as well as methodological and thematic connections and overlaps, the group will be associated with the International Network on Ethics of Families and the FORTE/VR research program “Addressing Ethical Obstacles to Person Centered Care” at Karolinska Institute, Stockholm, Sweden.

Cancer is killing more people in the developing world than HIV/AIDS, tuberculosis, and malaria combined [1-3], and it is a growing concern in Ethiopia [2,4]. Preventive actions, such as vaccination, or the prevention of cancer-inducing infections, such as human papillomavirus and HIV, and lifestyle adjustments to avoid cancer are generally rare [5]. The Oncology Department of TASH in Addis Ababa is the only facility that provides radiotherapy services to cancer patients in Ethiopia [6]. TASH currently treats about 10,000 patients per year; however, the estimated annual incidence of cancer is over 60,000 cases [7-9].

With few senior oncologists, only a couple of junior physicians, a lack of resources (at the hospital as well as among patients), and an enormous patient load from the entire country, the work environment is challenging, and it especially affects the prerequisites for effective and ethical consultations [10,11]. Patients wait for weeks to receive medical attention, and many depart without receiving any therapeutic or preventive assistance. Patients are usually accompanied by several family members, who are present when initial information is given and the results from diagnosis and treatment options are discussed. Handling consultations effectively is essential in order to help as many patients as possible within the mentioned limitations. It is also critical for many patients who cannot afford high-end treatments and who have to resort to simple self-care solutions at home in environments that are very different from the modern health care environments offered at TASH.

Field Survey

Little is known about physician-patient communication in Ethiopia in general and in cancer care in particular [12,13]. In 2015, a minor field study about physician-patient communication in cancer care in Ethiopia was carried out [14]. The findings showed that although health care staff, patients, and caregivers were satisfied with their communication, more patient involvement in decision making was desired. Linguistic and cultural diversity, as well as the socioeconomic status of patients complicate physician-patient communication. Further, professionals and students report scant training on communication and learning skills, and even less training on how to manage the resulting ethical challenges.

Person or patient centeredness and shared decision making are important benchmarks for the quality of health care, and communication is vital for achieving patient-centered care (PCC) [15-17]. In cancer care, these aspects are paramount for health professionals to design care interventions and home care and for patients and family caregivers to understand prognoses, treatment options, and possible side effects during the stages of treatment (ie, testing, treatment, and follow-up) [18]. At the same time, the implementation of PCC has been proven to raise complex challenges, where communication problems and ethical issues come together in ways previously unseen, as the notion of PCC also includes the idea of increased patient participation in and power over care decisions [18-20]. Specifically, complex problems arise when patients with a minority immigrant background are undertaking or involved in home care or self-care [21,22], where standard communication strategies may become counterproductive. A further complication arises when the care situation is characterized by the strong involvement of family members [17,23-25], which is common in the Ethiopian setting [26-28] and markedly different from the typical Western care situation. In addition, strong religious norms increase the potential for conflicts concerning what is ethically acceptable in communicative processes among patients, family members, and health care staff.

At the same time, enhanced communication is essential for a successful physician-patient relationship, and patient involvement and shared decision making may have positive

effects on health outcomes. If nothing else, these aspects are critical for the ability of the patient and family to approach the situation in a more informed way, thereby being better equipped to adapt and implement self-care [29].

The project's inception was associated with a need that was identified by the staff at the TASH cancer clinic, and as a collective research team, we will explore ways to analyze the communication of staff with cancer patients and family caregivers, the handling and sharing of linked decision making, and the ethical tensions among patients, staff, and family. We focus on the influences of family structures, culture, gender, and socioeconomic status, as well as the dire economic and institutional situation of Ethiopian health care. Although the project is unable to influence changes in these important structural background factors, its aim is to help health professionals reduce the effects of the burden of poverty on Ethiopian cancer patients and their families.

Ethiopia is a multicultural society with more than 80 different ethnic groups, 83 languages, and over 200 different dialects [30]. Although the majority of patients visiting TASH report coming from Addis Ababa, patients from a number of regions in Ethiopia, such as Oromio, Amhara, Tigray, and the Southern Nations, Nationalities, and Peoples' Region, are represented as well [1]. Language problems and cultural differences, reflected in views on health, illness, and treatment expectations [31,32], often complicate communication and necessitate the use of interpreters. When caregivers are interpreters, patients are less involved in consultations and decision making [14,33]. In addition, many patients come from rural areas, are poor, and either have low education or are noneducated, which further complicates their communication with physicians.

In this project, special attention will be paid to gender. About 73% of cancer patients in TASH are female [1]. Ethiopia has some of the lowest gender equality performance indicators in sub-Saharan Africa [34]. Women are often uneducated and do not participate in decision making because of gender relations [35]. As identified in our field study, in medical consultations, male caregivers often make decisions on behalf of female patients. In this project, we aim to raise awareness of diversity issues, develop approaches to encourage greater patient involvement (especially for women) in decision making, and create a more person- and family-centered approach.

Objectives

The project addresses the following three main aims: (1) to enhance and expand the understanding of communicative and associated ethical challenges in Ethiopian cancer care; (2) to enhance and expand the understanding of the implications and use of person- and family-centered solutions to address such communicative challenges in practice; and (3) to plan and evaluate interventions in this area.

The project's aims will also expand the base and context for understanding and addressing health communication- and ethics-related issues in person- and family-centered care in the contexts of Sweden and other developed countries, where health care for immigrants from Africa and other developing countries with a strong family culture is delivered.

Methods

Pilot Project (2015)

Description

The beginning of this project involved a pilot project conducted in Addis Ababa, Ethiopia, in spring 2015, as a part of the Master's in Communication thesis of Kebede [14]. The study consisted of the following two parts: a qualitative study about communication in cancer care and a quantitative study about cancer awareness among the general public.

Qualitative Study About Communication in Cancer Care

A qualitative study was conducted at the Chemotherapy and Radiotherapy Center of TASH in Addis Ababa in 2015 by GK and BL. The primary focus was on how physicians, cancer patients, and family caregivers experience communication during consultations. Patient and family involvement in decision making, breaking of bad news, and related communication problems experienced in consultations were particularly emphasized.

The participants in the pilot study (physicians, patients, and family caregivers) were purposively sampled [36]. We aimed to attain a heterogeneous sample in terms of gender, cancer type (patients), and work experience (physicians).

In the pilot study, we adopted an ethnographic explorative qualitative study design, using triangulation of data collection that combined semistructured interviews with direct observations and video recordings of authentic interactions among physicians, patients, and family caregivers during hospital rounds. We aimed to obtain as complete a picture as possible of the challenges associated with communication in cancer care [37].

Quantitative Study About Public Awareness of Cancer in Ethiopia

In the pilot study, we also aimed to explore the level of public awareness of cancer in Ethiopia by undertaking a survey on 150 randomly chosen adult Ethiopians. Participants from the general public (aged above 18 years) were chosen using convenience sampling. The information from both studies was only partially analyzed, and it serves as an initial starting point for work in this project.

Project Plan (2018-2021)

Description

The project is scheduled to occur over a 4-year period (2018-2021). The project's research team members are from the University of Gothenburg and the Sahlgrenska University Hospital in Sweden and from Addis Ababa University and TASH in Ethiopia. Each of the project investigators has allocated existing human resources in relevant disciplines to the project, including senior collaborators and junior assistants, as well as PhD and master's-level students.

The three main aims of the project will be addressed in parallel and undertaken through a series of joint workshops. In between the joint workshops, the respective research teams will work on data analysis, methodology development, and development

of interventions for improving physician-patient communication. The aim is to have 1 to 2 joint workshops per year across a 4-year period and to alternate these between Addis Ababa and Gothenburg. We prioritize the needs of Ethiopian professionals, which form the project's starting point, albeit also creating valuable input for the Swedish health care and research contexts. The project has been in progress for 2 years, with 2 years remaining for completion. Below, the project phases are presented.

Phase I: Project Commencement

Workshop 1 (Spring 2018)

The project commenced in Gothenburg. There were initial briefings on the Ethiopian situation and on current knowledge regarding health communication, person- and family-centered care, knowledge transfer in global health, and associated ethical challenges. The workshop involved initiation of the analysis of existing data, as well as planning of the work required and division of tasks. Additionally, it involved joint discussions of the methodology for future data collection and planning of research studies. The ethics application was submitted for the analysis of existing data.

The key project activities following Workshop 1 were as follows: (1) Deciding on the initiation of six research studies in the project (Table 1); (2) Conducting Study 1 involving analysis of the interviews and video recordings of hospital rounds from the pilot study. The audio-recorded interviews were transcribed verbatim and translated into English. Thematic content analysis [38] was used for data analysis. The video recordings were translated from Amharic into English and transcribed using a simplified version of the Gothenburg Transcription Standard [39]; and (3) Planning a communication training program for health care staff in Ethiopia in 2020.

Table 1. Overview of research studies.

Study #	Title	Data collection/analysis	Period
1	Explorative study of communication in cancer care (a general overview of the communicative challenges in cancer care in Ethiopia)	Analysis of the interviews and video recordings from the pilot project	2018-2019
2	Awareness of cancer in Ethiopia	Analysis of the survey data from the pilot project	2019-2020
3	Shared decision making in cancer consultations: A qualitative study	Conduction and analysis of video recordings of medical consultations	2019-2020
4	Attitudes toward shared decision making and breaking bad news: patients, family caregivers, and the general public	Survey to patients, family caregivers, and the general public	2019-2020
5	Attitudes toward shared decision making and breaking bad news: health care staff	Survey to health care staff	2020-2021
6	Development of a model of decision making in cancer care	Analytical model based on the results of the studies and discussions with research team members	2018-2021

The project was submitted for ethics approval to the Ethical Review Board of Western Sweden and the institutional review board (IRB) at the Department of Oncology, School of Medicine, College of Health Sciences, Addis Ababa University. Ethical challenges associated with data collection for the project included placing minimal burden on research participants and securing informed voluntary participation for patient consultations and interviews with staff, which were to be recorded. As the project includes ethical issues among its research questions, it will, of course, actualize these as part of the study and endeavor to contribute to a better understanding of ethical challenges in Ethiopian cancer care, as well as further inform about ethical theorizing for person-centered care in a Western immigrant context.

Workshop 2 (Spring 2019)

The workshop was conducted in Addis Ababa. There was a site visit to TASH and a discussion with the staff, as well as on-site researchers with an interest in health communication and related ethics. The workshop involved a presentation of the state of ongoing data analysis, discussion of how person- and family-centered care solutions could be applied in the Ethiopian context, and identification of possible hurdles. There was a continued discussion about data collection and intervention design. Additionally, it involved identification of possible adaptions of person-centered care solutions and development of methodological solutions in meetings with Ethiopian researchers, PhD students, and health care staff.

The key project activities following Workshop 2 were as follows: (1) Conducting Study 2 involving analysis of survey data on cancer awareness in Ethiopia. Simple descriptive statistics were used for the analysis; (2) Conducting Study 3 involving video recordings of medical consultations. Twenty-four physician-patient consultations were video recorded to study decision making and family involvement. It involved an initial analysis of data (transcriptions and quality check); (3) Conducting Study 4 involving the development of a survey about attitudes toward shared decision making and breaking bad news (patients, family caregivers, and the general public). It involved piloting and conducting the survey. The study used a comparative cross-sectional design to analyze the similarities and differences in attitudes toward the disclosure of clinical information to cancer patients and the inclusion of relatives in that process, among the following three groups: cancer patients, relatives, and the general public (150 participants per cohort, 450 in total). The data were coded, cleaned, edited, and entered into EpiData version 3.1 (EpiData Association, Odense, Denmark) to minimize logical errors. Thereafter, the data were exported to SPSS Windows Version 25 (IBM Corp, Armonk,

New York, USA) for analysis. The analysis was undertaken by computing proportions and summary statistics for the three groups (cancer patients, relatives, and the general public). The attitudes of each group toward the disclosure of cancer status and family involvement were compared using the chi-square test; and (4) Initiating Study 6 involving the development of a model for shared decision making.

Phase II: Data Analysis and Securing Mutual Benefits

Workshop 3 (Spring 2020)

The workshop will be conducted in Gothenburg. Consultants and suitable specialists from relevant programs and networks in Scandinavian countries will be invited to attend this workshop to expand the Ethiopian partners' professional networks. This workshop will concentrate entirely on the issues faced by the Ethiopian partners and will involve further discussion of the outcomes of data analysis from Phase I, methodological developments for data collection and analysis, and initial planning for the proposed publications.

The key project activities following Workshop 3 are as follows: (1) Submitting the manuscript of Study 1 to *PLOS ONE*; (2) Drafting the manuscript of Study 4 for submission; (3) Finalizing the analyses for Studies 2 and 3; (4) Conducting Study 5 involving the development of a survey for health care staff about attitudes toward shared decision making and breaking bad news, piloting and conducting the survey, and drafting a manuscript for submission to *Patient Education and Counselling*; (5) Continuing discussion of the model of decision making in cancer care (Study 6); and (6) Identifying possible adaptions of person-centered care solutions, developing methodological solutions for data collection and analysis, and planning communication training in Ethiopia.

Workshop 4 (Autumn 2020)

This workshop will be conducted in Addis Ababa. It will involve topical focus on how the Ethiopian experience can benefit health communication in the contexts of Sweden and other developed countries. Additionally, it will involve continued discussion of the data analysis and publication drafts. Communication training based on results from the conducted studies will be provided to medical students and health care staff in TASH. The developed model of decision making will be tested in the training course.

The key project activities following Workshop 4 are as follows: (1) Drafting manuscripts for papers related to Studies 2 and 3; (2) Preparing publication drafts related to Studies 5 and 6; and (3) Further developing the communication training course.

Phase III: Project Completion

Workshop 5 (Spring 2021)

This workshop will be conducted in Addis Ababa. It will involve finalizing publications from the current project, as well as discussion of a new project plan for future data collection and interventions. Additionally, it will involve briefing and discussion with local health care staff and networks about the current project's results, as well as development of a new project plan for future data collection and interventions.

The key project activities following Workshop 5 are as follows: (1) Submitting publications to journals in the areas of health care communication, public health, and oncology and (2) Revising a new project plan for future expanded data collection and intervention studies.

Workshop 6 (Autumn 2021)

The concluding workshop will be conducted in Gothenburg. It will involve continued briefing and discussion with local health care staff and networks about the current project's results, as well as submission of a new project application.

The key project activity following Workshop 6 is as follows: Finalizing and submitting a new project application for expanded data collection and intervention studies.

Results

This study was awarded funding by the Swedish Research Council in December 2017 for the period 2018 to 2021. Ethics approval was obtained from the Ethical Review Board of TASH for the pilot project (April 14, 2015). The research ethics boards in Sweden and Ethiopia approved the project in May 2018 (DNR 520-18 and ONC IRB 27, respectively). The results of the studies will be published in 2020 and 2021.

Discussion

This study contributes to the understanding of the complexity of the role of family, along with patients' dependency on family members for communication, support, and access to care, which creates particular ethical dilemmas for medical staff. Better understanding of communication and the factors that influence cancer patients' health-seeking behaviors and adherence to treatment can lead to improved health care services and better handling of health care ethical challenges in this context.

This project is the first step toward providing unique and seminal knowledge for the specific context of Ethiopia in the areas of physician-patient communication research and ethics. The project also contributes to the quality of cancer care in developing country settings and does so by deepening the understanding of key practical and theoretical challenges in physician-patient communication through sharing of expertise from Sweden to Ethiopia in ways that are designed to leave a lasting impact. The Ethiopian case can be a foundational model for improving communication in cancer care in other low-resource settings, which share central cultural prerequisites, such as a strong patriarchal family structure, along with strong and devout religiosity.

The project also aims to improve the education of health professionals and medical students in Ethiopia by developing a communication training course, with a focus on ethical aspects and shared decision making. We believe that this work will have important contributions to mainstream research in health communication, health care ethics, and global health.

Finally, communication and interaction among health professionals, patients, and family caregivers actualize a broad spectrum of welfare considerations particularly regarding how to prioritize between different needs within health care and

within families and how to handle the ensuing ethical dilemmas that each of these groups face. The project will also serve to develop further understanding about current challenges in Western health systems associated with greater family and patient participation in decision making.

Acknowledgments

This work is supported by the Swedish Research Council (Vetenskapsrådet; grant number: 2017-05410, https://www.vr.se/).

Authors' Contributions

NBL is the principal investigator; CM, AAW, RA, and BGK drafted the manuscript; and AB, BL, and WT read the manuscript and contributed to the studies.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Previous peer-review reports: Final statement from the review panel of the Swedish Research Council (Review panel: UF-5).
[PDF File (Adobe PDF File), 112 KB - resprot_v9i5e16493_app1.pdf]

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Abbreviations

IRB: institutional review board
PCC: patient-centered care
TASH: Tikur Anbessa (Black Lion) Specialized Hospital

Edited by G Eysenbach; submitted 04.10.19; peer-reviewed by J Rousseau, T Cruvinel; comments to author 23.12.19; revised version received 04.03.20; accepted 10.03.20; published 19.05.20.

Please cite as:
Berbyuk Lindström N, Woldemariam AA, Bekele A, Munthe C, Andersson R, Girma Kebede B, Linderholm B, Tigeneh W
Person and Family Centeredness in Ethiopian Cancer Care: Proposal for a Project for Improving Communication, Ethics, Decision Making, and Health
JMIR Res Protoc 2020;9(5):e16493
URL: https://www.researchprotocols.org/2020/5/e16493
doi:10.2196/16493
PMID:32427112

Protocol

Development of Cognitive and Physical Exercise Systems, Clinical Recordings, Large-Scale Data Analytics, and Virtual Coaching for Heart Failure Patients: Protocol for the BioTechCOACH-ForALL Project

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Abstract

Background: Heart failure is a chronic disease affecting patient morbidity and mortality. Current guidelines for heart failure patient treatment are focused on improving their clinical status, functional capacity, and quality of life. However, these guidelines implement numerous instructions including medical treatment adherence, physical activity, and self-care management. The complexity of the therapeutic instructions makes them difficult to follow especially by older adults.

Objective: The challenge of this project is to (1) measure real-life adherence to a regular physical exercise program and (2) attempt to influence older adult patients with heart failure toward embracing a more physically active self-care lifestyle.

Methods: This research consists of two studies, including a lab experiment and a pragmatic evaluation of technology at patients' homes. The lab experiment aims at exploring in an objective way (measuring neurophysiological responses to stimuli) patient engagement with different characteristics of virtual agents, while the home study is a 3-phase prospective study where the developed technology platform is tested by heart failure patients in their own home environments. Patients undergo evaluation of their physical activity and cognitive status using standard evaluation methods (6-minute walk test, questionnaires) and receive wearable devices to accurately measure everyday life activity levels (home study phases 1-3). During home study phases 2 and 3, exergames (serious games for physical exercise) to provide a physical exercise plan as a joyful activity are delivered to patients' private households and e-coaching techniques are implemented in the final phase (home study phase 3) of the protocol, to influence patient attitudes toward a more healthy and recommended lifestyle.

Results: The trial is still ongoing. Recruitment is ongoing, and the project has progressed for some participants through phase 2 of the home study. The sample size for both studies is 28 participants; 10 have already been included in the study, and both baseline clinical and patient-reported outcome data are retrieved. Phases 2 and 3 of the home pilot study are expected to be completed within 6 months.

Conclusions: The main challenge of the project is the change of attitude of older age heart failure patients through an e-coaching system. Given the adoption of a cocreation and living lab approach and the main objective for real-life evaluation, the project is ready to react to any collected feedback, even during the implementation of the research plan. Clinical assessment and objective evaluation are expected to provide all required information for reliable findings.

Trial Registration: ClinicalTrials.gov NCT03877328; https://clinicaltrials.gov/ct2/show/NCT03877328

International Registered Report Identifier (IRRID): DERR1-10.2196/17714

(JMIR Res Protoc 2020;9(5):e17714) doi:10.2196/17714

KEYWORDS

chronic heart failure; treatment adherence; exergames; e-coaching; adherence; electroencephalogram; wearable monitoring

Introduction

Background

Heart failure (HF) is a clinical syndrome affecting more than 15 million people in Europe and more than 30 million patients worldwide [1]. Despite advances in its management, prevalence of the disease is expected to increase mainly due to the aging of population, making the disease a constantly worsening global problem. Studies have proven the effectiveness of rehabilitation programs consisting of systematic physical exercise and self-care in HF patients [2-6]. Among them, regular aerobic exercise is recommended in HF patients in order to improve their functional capacity and symptoms [7]. However, changing lifestyle and engaging self-care, especially in older adults, is a difficult task and a barrier to engaging older adults with HF in regular physical exercise. Although therapeutic interventions seem to reduce admission rates for patients with HF, effective management of the disease remains a contemporary challenge. Current guidelines for HF patients emphasize improvement of clinical status, functional capacity, and quality of life, implementing complex regimens of multiple self-care behaviors (systematic exercise, fluid and sodium restriction, adherence to medical therapy, and close monitoring of the development of disease symptoms, etc) to medical treatment [7]. The complexity of the instructions and necessity of lifestyle modifications in combination with possible comorbidities and cognitive decline make the guidelines difficult to follow, especially in older adults [3].

The challenge of this project is to measure real-life adherence to a regular physical exercise program and attempt to influence older age patients with HF toward being more active. To do so, BioTechCOACH-ForALL uses wearable devices to measure activity levels, exergames (serious games for physical exercise) to deliver a physical exercise plan as a joyful activity, and e-coaching techniques to influence patient attitudes toward HF self-care and more healthy lifestyles.

Protocol Concept and Rationale

Cardiovascular disease is common among older adults. In developed countries, prevalence of HF in adult population is 1% to 2%, rising up to more than 10% in people over 70 years old [1]. Late complications of the disease and comorbidities such as coronary artery disease, systemic arterial hypertension, diabetes mellitus, history of stroke, anemia, dementia, kidney dysfunction, lung disease, and obesity contribute to the burden of hospitalizations and mortality [7] and are targets of treatment.

According to current guidelines, the goals of treatment in patients with HF are to improve clinical status, functional capacity, and quality of life. Although these are surrogate markers of treatment success, the need for reduction of hospitalizations and mortality is also clearly indicated [7]. Furthermore, lifestyle modifications like implementing healthy nutrition and systematic exercise and smoking cessation as well as self-care including but not limited to monitoring body weight and avoiding excessive fluid and salt intake are deemed necessary [2]. Although the disease may sometimes be life-limiting, exercise is encouraged in all clinically stable patients with HF, and regular aerobic exercise is recommended in HF patients (class IA according to current guidelines [7]) in order to improve their functional capacity and symptoms [8]. Various exercise rehabilitation programs have been used in HF, consisting of bicycle ergometer training, dumbbell training using low weight (<1 kilogram), respiratory training, and walking about 5 times per week. Fatigue severity, 6-minute walking distance, respiratory function, and quality of life are improved via increased physical activity of HF patients [7,8]. To this extent, close monitoring of daily mobility and sedentary patterns with wearables and tailor-made e-coaching systems based on activity profiles and routines of HF patients, implemented in everyday life, may promote exercise integration by making it challenging for the patient, who may set their own realistic activity goals.

Patients with HF should also follow their medical pharmacotherapy, a task that might be difficult because of cognitive disorders and coexisting comorbidities leading to polypharmacy, often obligating a caregiver to help them with this daily task. Despite clear evidence of the benefits of adherence to medical therapy to the rates of morbidity and mortality and number of cardiovascular-related emergency department visits in HF, rates of patient adherence to medical and supportive therapy (the extent to which a patient's behavior with regard to medication intake or lifestyle changes is consistent with therapeutic recommendations) vary significantly, fluctuating between 10% and 98% [7,9,10]. On the other hand, there is more clear evidence on the nonadherence (noncompliance to treatment) of patients, which was found to be almost 25% in the general population, with men and women showing the same rates of noncompliance to treatment. It has been shown that adherence to HF medication is related to patient institutionalization (including hospitalizations and nursing home visits) [11], while patient self-care (eg, self-care management; self-care maintenance; sodium, fluid, and alcohol intake restriction; physical activity; smoking cessation; monitoring signs and symptom; and keeping up follow-up appointments) is positively related to the length of time since the patient was diagnosed with the disease [12].

Given the constantly increasing number of patients with HF, patients' demands on health care services are expected to increase greatly in the coming years. The need for more innovative and cost-effective treatment strategies led to studies of electronic health (eHealth) programs showing promising results in patients with HF [13-15]. These studies increased political and clinical attention to eHealth strategies as a mean of improving outcomes in patients with HF. However, the role of eHealth systems in the management of patients with HF and in particular in the practical implementation of adherence (eg, by promoting packages of measures concerning medical treatment and active living, patient education and active participation in the context of shared decision making to develop

realistic expectations of their own disease course, and being active and adopting individual responsibility) is an emerging field of high scientific interest.

Designing an eHealth System Using Virtual Coaches

Designing an eHealth system to promote self-care of patients remains challenging. User engagement constitutes a key component for considering technologies successful. O'Brien and Toms [16] defined user engagement as follows: "Engagement is a category of user experience characterized by attributes of challenge, positive affect, endurability, aesthetic and sensory appeal, attention, feedback, variety/novelty, interactivity, and perceived user control." At the same time, the presence of human social models has been shown to affect attitudes, beliefs, and behaviors of users [17,18]. Moreover, anthropomorphic agents could have impact on cognitive functioning and exert social influence comparable to that of humans [16] while also promoting motivational characteristics such as self-efficacy and attitude change [19]. Furthermore, the use of pedagogical or virtual agents could facilitate learning [20]. Therefore, using a virtual coach with specific characteristics could possibly increase both technology acceptance and user engagement.

The influence of virtual agents on users could vary depending on different characteristics such as availability, communication skills, believability, functionality, and customizability in appearance [20]. In that sense, social models were found to be more effective as they resemble the observer or a projected ideal virtual self of the observer [19]. Existing evidence on learning showed that agents who had similar characteristics to trainees, with respect to appearance-related traits such as age and race/ethnicity, could be more influential [19]. However, prior expectations and stereotypes could influence the desired outcomes [20]. Additionally, perception of self in a virtual environment affects task-related, verbal, and nonverbal behaviors [21]. In line with that, researchers introduced the Proteus effect, which describes the condition where people conform to their avatar representation regardless of how other people perceive them [22]. Another study showed that a physically similar avatar to the observer could affect the emotional valence and arousal more than a neutral one. Additionally, the induced emotional states were more intense than those from neutral avatars [23]. Therefore, appearance is considered to be an important attribute while designing a virtual agent. Another important design element was shown to be that the agent stays within the field of vision of the participants [24,25].

The way that a virtual agent uses to communicate is another component for customization. Social presence consists of verbal and nonverbal cues. However, agent communication through voice has been found to be more beneficial than text. More precisely, the use of a human-like voice could enhance social presence and interaction with technology [16]. Moreover, facial expressions and deictic gestures are considered to be crucial for promoting learning-related outcomes. However, the large-scale study of Baylor and Kim [19] stressed that facial expressions—but not gestures—seem to enhance focus on the motivational message delivered by the virtual agent.

The evaluation of technology acceptance and user engagement in an explicit way remains a challenge. Fairclough et al [26] defined user engagement in a task in terms of cognitive activity (mental effort), motivation (approach or avoidance), and affective state (positive, negative), and they associated the user engagement's components with psychophysiological measurements. Revisiting the literature, they found that increased theta activity in frontocentral sites along with decreased alpha activity in occipital sites was associated with higher mental effort due to working mental load. Pupil dilation was observed to be greater when complex cognitive processing is performed.

On the other hand, motivation and emotional experience (affect) were correlated to frontal asymmetry. More precisely, greater levels of left frontal activity were associated with positive emotions and motivational approach, whereas higher right frontal activity was linked to negative emotions and motivational avoidance. Other biomarkers of motivation were considered to be sympathetic nervous system indices, such as systolic blood pressure. In another study, user approval of an online avatar was explored by means of skin conductance, heart rate, and respiration. Results indicated that higher respirations were positively correlated with the degree of agent approval [27].

Peters et al [24] proposed user attention as another metric of human-agent interaction. They modeled user attention using three components: gaze detection; neurophysiological analysis; and an attention representation module for storage, integration, and interpretation of attention information.

Study Objectives

High rates of noncompliance to treatment plan indicate the need for developing sustainable solutions to support and enhance the self-care of HF patients. BioTechCOACH-ForALL, implemented within the framework of the operational program Human Resource Development, Education, and Lifelong Learning and cofunded by the European Social Fund and national resources, investigates and researches a potential response to this challenge.

The main goals of the project are as follows:

- Extension of previous experience in developing and applying innovative systems for physical training of elderly (webFitForAll [13]), in living labs or even at their home [28], encouraging physical exercise and promoting independent living. In addition, the e-coach platform will be enriched by a decision support system (smart algorithms that will personalize the interaction of the e-coach with patients) based on analysis and collection of interaction data. Commercial nonintrusive sensors will collect activity data in order to capture daily activity patterns [29] and activity volume. Daily activity patterns will be used to track their daily activity level regarding the doctor's recommendation and readjust e-coaching system parameters (home study phases 1 and 2)
- Development of an e-coaching system (home study phase 3) based on neuroscience evidence (lab study), incorporating exergaming [30] and remote health monitoring [29] techniques

- Patient engagement with different user interface interaction means, such as virtual projected coaches with different characteristics (presence/absence of medical uniform, gender, age) will be explored by means of electroencephalogram (EEG) and analyzing various biosignals such as heart rate, electrodermal activity, external body temperature, and eye gaze tracking

Methods

Overview

Two studies will be performed. The first study aims to optimize patient acceptance of the delivered technology solution and in particular the e-coaching virtual agent by evaluating different design characteristics introducing a novel lab experiment and objective measurement of patient engagement with the use of EEG and biosignal markers, while the second (at home) study aims to introduce the technologies and interventions (exergaming and e-coaching) to the HF patients' daily routine. Results and findings of the first study will drive the design of the e-coaching intervention that will be applied in the third phase of the second study.

Laboratory Study

The rationale of EEG study is to explicitly capture the way patients perceive images of virtual agents by recording different biosignals. In that sense, analysis of multichannel event-related EEG data could reveal differences in spatial distribution and temporal sequencing of neural activity between different conditions such as presence versus absence of medical uniform, old versus young, and female versus male [21,31,32]. Moreover, other biosignals such as electrodermal activity, external body temperature, heart rate, and eye gaze tracking have already been applied to evaluate affective and cognitive impact of projected stimuli [24,33]. As such, HF patients will undergo a 2-part experimental procedure in which various biosignals will be recorded via EEG, E4 smartwatch (Empatica Inc), and GP3 eye tracker device (Gazepoint). In both parts of the experimental procedure, participants were instructed to freely observe the images. In the first part, participants will passively observe images of virtual agents, presented on screen as stimuli having different appearance characteristics such as age, gender, and presence/absence of medical uniform. In the second part, stimuli presented to participants will be pairs of virtual agents followed by a fixation cross on black background. The pair of agents differs regarding the presence/absence of medical uniform but preserves all other characteristics (age, gender).

At-Home Study Design

General Design

BioTechCOACH-ForALL home study is a prospective, multiple baseline across subjects, nonrandomized, single-arm, single-center study following a within-subject design to assess the feasibility and efficacy of the Virtual Coach Program in older age patients with HF. The study will be delivered in three phases, each of them fulfilling a different scope. All participants will go through all study phases. Each phase will allow participants to familiarize themselves with the delivered technology of that phase. A multiple baseline approach will be followed so that the effects of each phase are as isolated to the previous phases as possible, allowing for effect comparison among them. Clinical and quality of life assessment and exercise behavior and attitude will be measured repeatedly in both the baseline phase and the two intervention phases. This way any cause-effect relationships among the intervention and patient outcome measures will be demonstrated.

The study conforms to the ethical guidelines of the 1975 Declaration of Helsinki, all participants will sign informed consent, and the study protocol has been approved by the bioethics committee of the School of Medicine of the Aristotle University of Thessaloniki (Protocol No. 1.45/21.11.2018) and registered at ClinicalTrials.gov [NCT03877328]. The study protocol is structured in a manner that incorporates three different phases, coming one after the other. Each patient will enter the study in the phase 1 and complete their participation in phase 3.

Phase 1

Phase 1 introduces the objective measurement technology, the wearable monitoring device. This technology will be running throughout the project's lifetime and will provide objective information on patient activity. This information, along with the doctor's baseline and intermediate assessment, will be used as an indicator of the effectiveness of phases 2 and 3.

Phase 2

Phase 2 introduces a joyful way of exercising, allowing patients to exercise in the comfort of their homes. Patients will be assigned a structured recommended schedule with a goal of 3 sessions per week for a total of 36 sessions in 3 months. Frequency and intensity of the training program are indicated by patient functional capacity. All patients will undergo a 6-minute walk test, and their performance will be used for determination of the exercise program. By protocol, patients performing more than 500 meters in the 6-minute walk test at baseline will be prescribed a more intense exercise program in terms of the number of exercise repetitions. The exercise protocol offers 50 minutes of exercise implementing aerobic and resistance endurance exercises including upper and lower extremities. Regular blood pressure and heart rate monitoring will be performed manually by the patient with the use of dedicated devices in time intervals specified in the protocol. Exercises will be implemented as fun, full-body interactions, processed and recognized through a depth-camera–based sensor and computer vision and translated into computer game actions and scenarios integrated within a Web application [14].

Phase 3

Phase 3 introduces the coaching aspects, where exergames are introduced and delivered through home surface projection, apart from the personalized recommendations and suggestions (designed by the doctor).

Patient Population

Both studies can fulfill their objectives only if appropriate subjects are enrolled. The following eligibility criteria are designed to select subjects. These criteria must be met before a subject is assigned to the study. Subject eligibility should be

reviewed and documented by a qualified member of the investigators' study team before subjects are included in the study. All patients included in the study protocol will undergo all three home study phases, in addition to the EEG experiment in the lab. For the latter phase, a percentage of patients, without the need to proceed with the whole study protocol, will be recruited.

Selection Criteria

Subjects must meet all of the inclusion criteria to be eligible for the enrollment:

- Male and female patients aged over 55 years with HF of any etiology, with either reduced or preserved ejection fraction, diagnosed according to international guidelines [7]
- Must be in New York Heart Association (NYHA) functional class II-IV
- Must be in stable clinical condition and on stable medical treatment for the underlying disease for at least 3 months prior to inclusion to the study
- Must be willing and able to comply with scheduled visits, treatment plan, and trial procedures
- Must provide personally signed and dated informed consent document indicating that the subject has been informed of all pertinent aspects of the study

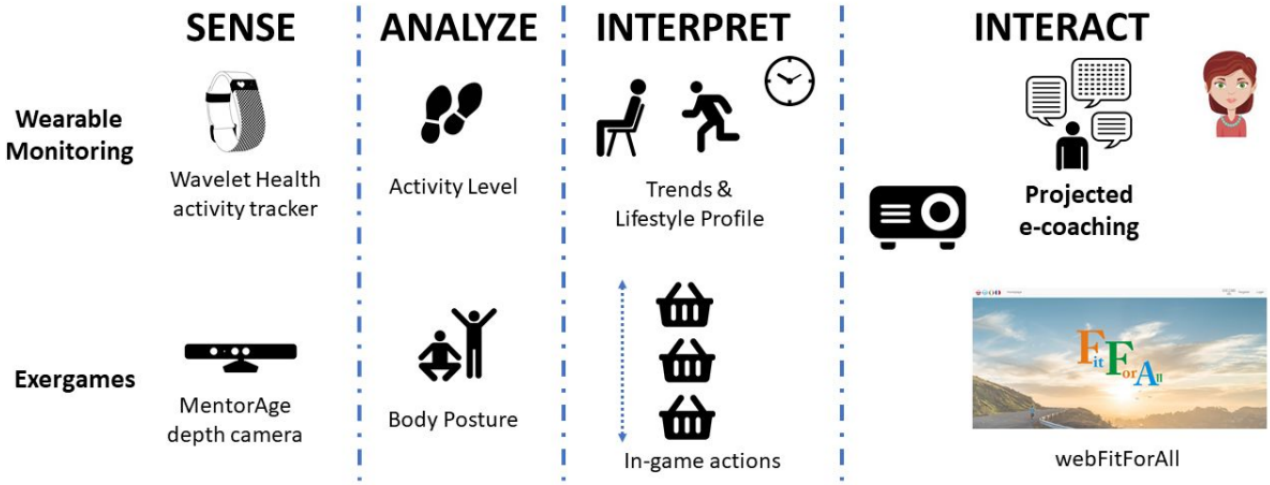
Subjects presenting with any of the following will be excluded from the study:

- Unstable disease with evidence of decompensation, recent hospitalization, or undergoing investigation for clinical deterioration
- Recent history of chest pain, palpitations, light-headedness, dizziness, or syncope on exertion
- Contraindications to physical activity or with physical obstruction to perform the prescribed training program (eg, patient uses wheelchair)
- Any severe acute or chronic medical or psychiatric condition that may increase the risk associated with trial participation or interfere with interpretation of trial results
- Investigational site staff members directly involved in the conduct of the trial and their family members; site staff members otherwise supervised by the investigator
- Participating in any other experimental studies
- Not willing to provide signed informed consent

Materials and Technologies

The technologies to be used for BioTechCOACH-ForALL along with their scope are presented in Figure 1 and include wearable continuous monitoring and lifestyle patterns discovery, exergames, and projected, smart e-coaching.

Figure 1. Protocol phases and technology introduced in each phase.



Wearable Monitoring

The wristband monitoring device (Wavelet Health) [34] includes a clinical-grade (red plus infrared) photoplethysmogram sensor along with accelerometer and gyroscope and can collect continuous physiological and activity data processed using robust algorithms. Actigraphy capture rates spanning from 1 Hz to 20 Hz, while light sensor capture rate can be either 43 Hz or 86 Hz. To balance energy consumption, light sensor capturing is enabled in cycles. This means it does not measure all the time, but it remains idle for some time and collects a single averaged measurement over the remaining time of the cycle.

Computed features include steps, calories, beats per minute, heart rate variability, SpO_2, breathing rate, sleep staging (awake, light, deep), and total sleep time. These fitness and lifestyle analytics will be calculated both as intraday and interday time series so as to form different patterns within a day (allowing the system to understand daily habits) and trends in specific time periods (to quantify health and lifestyle changes). Different detailed levels of information will be explored like per minute or hour. Active time periods against sedentary moments will also be used as a way to explore patients' activity habits during the day.

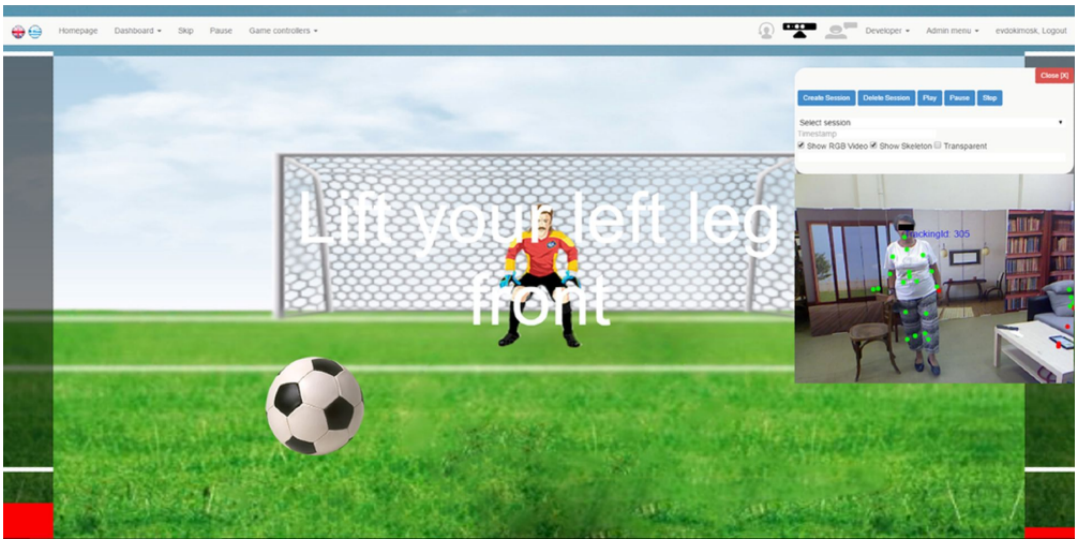
Collected information will be used as objective, real-life measurements for evaluation of different interventions compared with the baseline (activity levels as proxy indicator for active lifestyle habits) and as a way to personalize different parameters of the intervention (eg, time of the day or weekdays to suggest that patients perform exercise regimes).

Exergames Promoting Physical Exercise

In order to deliver a structured protocol of physical exercise to HF patients, a computerized intervention will be developed in the form of exergames as part of home study phases 2 and 3.

An existing exergame platform, webFitForAll [14], incorporates physical exercises recommended by the American College of Sports Medicine and American Heart Association [29] focusing on upper and lower strength, stretching and flexibility, and aerobic exercise, will be used for delivery of the tailor-made physical exercise program. An example of the webFitForAll interface is presented in Figure 2.

Figure 2. webFitForAll interface.



Adherence to the right execution of exercise is feasible by comparing several predefined parameters concerning the movements of patients. Joint angles are continuously monitored based on the tracking of body skeleton joints having as inputs the MentorAge device (Nively SAS) embedded RGB and infrared cameras, thus providing smart feedback to patients with respect to successful execution of the exercises. This mechanism ensures correct administration of the protocol and adherence of the patient to the instructions. webFitForAll allows patients to track their progress by evaluating their in-game performance with a single score. Motivational messages are delivered at the end of a game and the end of a training session to keep patients engaged with the intervention.

e-Coaching

This is the most important part of the solution (introduced at the last phase of the home study) since it integrates all previous components and their respective information while being the main patient-system interaction point. Daily recommendations about activity and patient self-management together with a virtual coach that will be selected based on findings of the neurophysiological study will be projected on a predefined surface in the patient's home. The type of messages and time of delivery will be chosen/scheduled based on the personal profile of the patient (eg, nocturnal patterns of activity). Leaving the home environment intact is considered key to increase the acceptance of the e-coaching system by the patient. Therefore, any information visualization will happen only at predefined moments and will disappear instantly, by simply turning the projector off.

An added value of the study is personalization of the e-coaching system by means of evaluating the virtual agent characteristics using EEG, eye gaze tracking, and other physiological measurements.

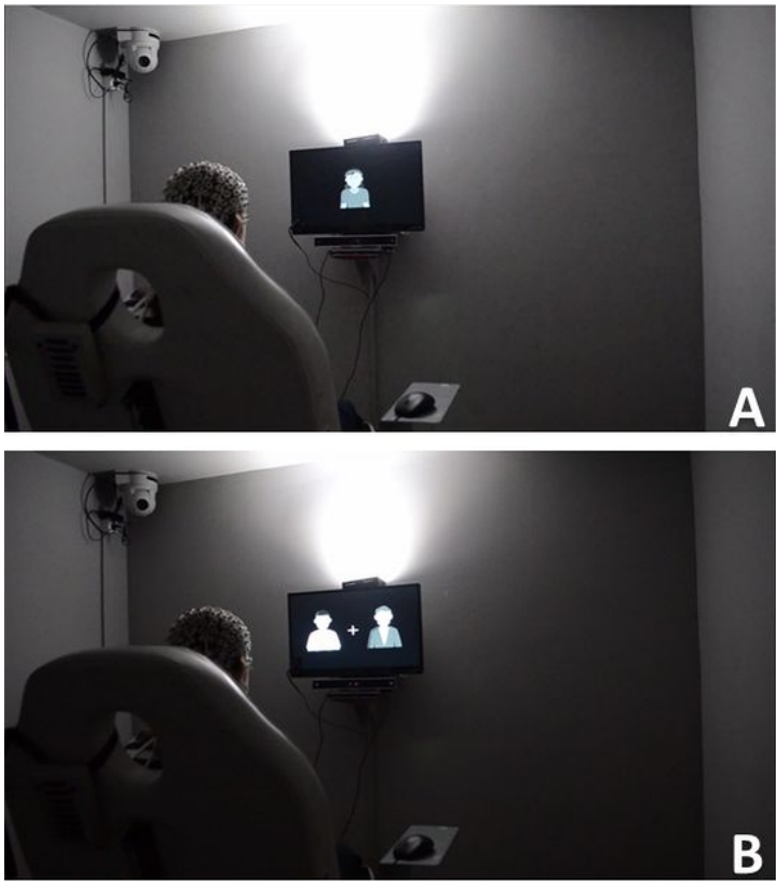
Procedures

Apart from the home study, a study in laboratory settings will be conducted to explore the design elements of the virtual agent that will be part of the e-coaching technology. Participants will undergo a 2-part experimental procedure in order to investigate the impact of different appearance-related characteristics of virtual coaches on user engagement, set up as follows: the study takes place in a magnetically shielded, sound attenuated, and dimly illuminated room hosted in the Laboratory of Medical Physics. EEG recordings are performed by means of a 128-channel EEG recording system (Nihon Kohden Corp) and a sponge-based passive electrode system (R-Net cap, Brain Products GmbH) applying the international 10-20 positioning system. Participants are comfortably seated in an armchair in front of a 23.5-inch computer monitor at a distance of 75 cm.

In the first part, the HF patients initially undergo EEG recordings during resting state with eyes closed (5 minutes). Participants then passively view 32 agents presented on screen as stimuli in a random order, grouped with respect to their appearance characteristics such as age, gender, and presence/absence of medical uniform (Figure 3A). During each trial, the stimulus (image of a virtual agent, height 6.22 cm, width 4.57 cm) is presented for 2000 ms in the center of the screen followed by a 2000 ms interstimuli period during which a black screen with a fixation cross is displayed. Each participant completes 256 trials (128 trials displaying images of virtual agents, 128 trials displaying black screen with fixation cross). In the second part, the stimuli presented to the participants during each trial consist of pairs of virtual agents and a fixation cross between them. The pair of agents differ regarding the presence/absence of

medical uniform but are similar with regard to all other characteristics (age, gender; Figure 3B). Each stimulus appears for a duration of 2000 ms followed by an interstimuli period of 2000 ms, during which a black screen with a fixation cross is displayed in the center of the screen. The overall number of trials in this second part is 512 (256 trials displaying pairs of virtual agents, 256 trials displaying black screen with fixation cross) [35]. In both parts, participants are instructed to freely observe the images of virtual agents. During the EEG study, electrodermal activity, blood volume pulse, external body temperature, and eye gaze tracking are recorded for each participant. Biosignals will be collected by means of an E4 smartwatch (Empatica Inc), while eye gaze tracking will be performed using a GP3 eye tracker (Gazepoint).

Figure 3. Electroencephalogram (EEG) study protocol. (A) Patient undergoes EEG while passively viewing single virtual agents. (B) Patient undergoes EEG while passively viewing combinations of virtual agents.



Intervention Setting

The first phase of the protocol will start in the 1st Department of Cardiology, AHEPA University Hospital of Thessaloniki, where all clinical assessments (6-minute walk test, questionnaires, clinical assessment, etc) will be completed, and it will continue in a dedicated area in the Laboratory of Medical Physics in the Faculty of Health Sciences of the Aristotle University of Thessaloniki, where patients will undergo the lab study/protocol. After the lab study, some of the patients will be included in the second study situated in their own homes, where they will keep performing their everyday activities. The physical training and e-coaching interventions (phases 2 and 3) will take place at patients' homes as well.

Patient Recruitment

According to the protocol, signed informed consent will be obtained by each participant at the baseline visit. It is the investigator's responsibility to ensure that each study subject is fully informed about the nature and objectives of the study and possible risks associated with participation. The investigator will obtain written informed consent from each subject before any study-specific activity is performed. The investigator will retain the original of each subject's signed consent document.

Baseline, Intermediate, and Follow-Up Measurements

Brain Electrical Source Analysis software version 6.0 (BESA GmbH) will be used for data preprocessing. Visual inspection of the recordings will be performed to detect bad channels that will be interpolated using an interpolation algorithm of BESA software. The signal will be band-filtered at 1-30 Hz and a notch filter will be also applied.

Dimensionality of the data will be diminished by using principal component analysis, and an extended independent component analysis [36] will be performed. The reconstructed dataset will then be visually inspected. Subsequently, epochs will be averaged for different stimuli conditions (eg, female, male, old, young, doctors, peers). The randomization graphical user interface (Ragu toolbox [37]) will be used for statistically analyzing the multichannel event-related EEG data. More precisely, the total strength of scalp field differences will be estimated by means of global field power [38], and total count of significant time intervals [39] will be identified by running

topographic analysis of variance. Afterward, cortical current density reconstruction will be calculated by low-resolution electromagnetic tomography [40] using BESA software in time intervals that will be derived by the aforementioned analysis.

Statistical parametric mapping will be applied for reslicing and statistical comparison of the current density reconstruction images exported by the BESA software between conditions using the SwE toolbox that applies the sandwich estimator method described by Guillaume et al [41], allowing analysis of longitudinal and repeated measures data. Other biosignals will be compared between conditions (young vs old, female vs male, doctors vs peers) after extracting the grand average values for each condition.

Clinical Assessment

Patients will be clinically evaluated before entering each of the two studies and on the initiation of each protocol phase (meaning before entering phase 1, phase 2, and phase 3, and at the end of phase 3, which will mark the end of study), completing 4 on-site clinical visits for the impact of each intervention to be assessed.

On the baseline, intermediate, and follow-up assessments, patient clinical condition, quality of life, and health-related costs will be considered. More specifically, blood pressure, heart rate, blood oxygen saturation, and body weight will be measured for the clinical assessment. To assess physical status, the 6-minute walk test and NYHA functional class will be used for exercise intolerance. Patient-related outcomes to be used include the Beck Depression Inventory [42] and the Dukes questionnaire [43]. As for the evaluation of quality of life, the Short Form Health Survey questionnaire [44,45] will be employed. Self-efficacy for exercise behavior scale will be used for evaluation of changes in patient perspectives on exercise [46]. Finally, for health-related costs, the effect on number of hospital admissions along with the effect on health care use (number of primary and secondary care contacts, social care contacts, relevant medication use) will be calculated during all three phases.

Real-world data will be collected continuously (across all phases of the home study) to assess several aspects of the interventions planned. Continuously measured activity levels expressed in daily steps taken by the patient will be compared across the different study phases. Real-life adherence of the HF patients to the proposed intervention will be measured in terms of attendance at the webFitForAll platform using wearable heart rate monitoring data as well as online activity logs and telephone and clinic follow-up. Real-world adherence will be compared within-subjects for the second and third phases of the study. Use analytics (virtual coach used, content and delivery time of messages/recommendations) of the e-coaching system and juxtaposed relevant outcomes (such as activity levels collected by the activity tracker and adherence to the webFitForAll training program given any system logs) will be routinely collected. Patients adherence will be evaluated by measuring attendance at the webFitForAll and heart rate monitoring data as well as by activity logs and telephone and clinic follow-up.

Statistical Analysis

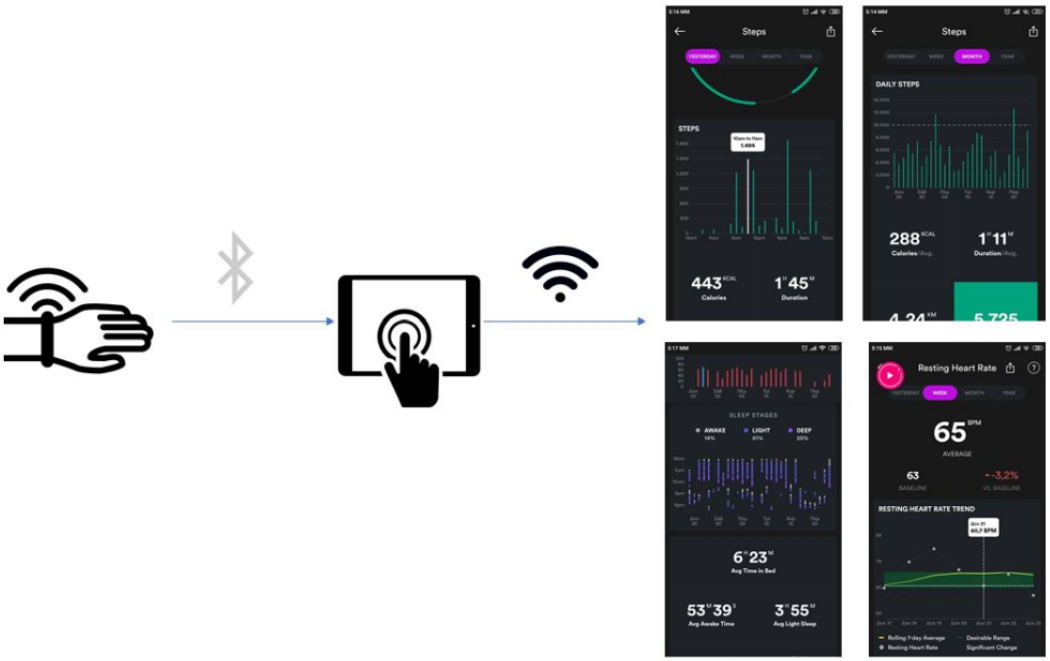
Continuous variables with normal distribution will be reported as mean and standard deviation, while those with nonnormal distribution as median and interquartile range. Categorical variables will be expressed as frequencies and percentages. Continuously data collected will be explored for normality assumption by means of a Shapiro-Wilk test to calculate the appropriate descriptive statistics [47].

Repeated measured analysis of variance or Friedman test will be used to assess changes on continuous data with normal and nonnormal distribution, respectively, between baseline, follow-up, and end-of-study visits. Possible associations between variables will be investigated using Pearson or Spearman correlation coefficients. We estimated sample size conducting power analysis using G*Power software (version 3.1). We performed repeated measures analysis of variance (3 time conditions) using 80% power, a medium effect size of 0.25, and significance level of 5%. The sample size was estimated to be 28 participants. One-third of this patient population that will agree to proceed to home study (phases 1 through 3) will enter the next steps of study protocol [48]. All statistical analyses will be performed using SPSS Statistics version 23.0 (IBM Corp) or R for Windows version 3.1.3 (R Foundation for Statistical Computing).

Technical Solution Deployment and Release

Given that the project relies on deploying the releasing of technology and devices, special attention has been paid on the planning of the releases. To be more specific, the off-the-shelf activity trackers (Wavelet Health wristbands) are delivered first (home study phase 1). The activity tracker will be set up to synchronize its raw data to the server through an app installed on the smartphones of patients. Patients not owning a smart device compatible with the provided software and hardware will be provided one. Synchronization will be done periodically through the day without any need for the patients to interact with the app installed in their phones. The app will synchronize in the background all gathered raw data, which will then be analyzed on the server to derive all meaningful features. Figure 4 presents a schematic approach of the wearable monitoring attached in the protocol.

Figure 4. Wearable devices used to evaluate patient protocol adherence.



Next, the webFitForAll platform along with the MentorAge device, which embeds a depth and RGB image sensor, will be introduced to patients in lab settings in order to train them on how to interact with it. MentorAge will be installed to monitor body movements by extracting and analyzing the body's skeleton and silhouette. MentorAge operates on Android OS and can support any graphics, thus being able to act as an end-user terminal. To do so, a mini projector will be plugged in and set up by team members in MentorAge to display the e-coaching output to any home predefined surface, taking into account unobtrusiveness and patient acceptability. After an introductory session, patients will have the exergaming platform installed at their homes (home study phases 2 and 3). Safety precautions and instructions on how to perform exercises will be given by a nurse.

Results

Patient recruitment is completed, and the project has progressed through phase 2. In total, 10 patients have been included in the study, and baseline clinical and patient-reported outcome data are retrieved. All participants included were male with a mean age of 63.60 (SD 8.78) years suffering from HF due to coronary heart disease (8/10, 80%) or arterial hypertension (1/10, 10%) while 1 (10%) patient suffers from dilative HF. The majority of participants (7/10, 70%) reported active employment status. The most common comorbidity of participants was diabetes mellitus whereas other conditions mentioned were arterial hypertension, chronic kidney disease, and chronic obstructive pulmonary disease. In terms of their social status, 9 of 10 participants live with their family, and 80% (8/10) of participants were married. The majority of patients had preserved functional capacity, classified as NYHA class II (6/10, 60%). The mean distance walked on the 6-minute walk test was 443.00 (SD 99.78) meters. Phases 2 and 3 of the pilot study are expected to be completed within 6 months.

Discussion

Expected Outputs and Potential Impact

The main challenge of the BioTechCOACH-ForALL project is changing attitudes of older age HF patients toward a more active lifestyle through an e-coaching system. To achieve this scope, the project implements two studies, a lab experimental study and an at-home staggered 3-phase pilot study, the former being a preparatory step for the realization of the latter. Thorough clinical evaluation preceding each study and phase will ensure patients safety. Lab study will explore the design elements (visual appearance) of the virtual agent that make it more engaging to the patient and will allow the choice of the most suitable ones for implementation of the e-coaching intervention during home study. Home study phase 1 will provide valuable information on patient clinical capacity and daily activity levels that will be used to build an individualized exercise program to be used in home study phases 2 and 3. The third and most challenging phase (home study) of the described protocol will implement an e-coaching system to provide personalized recommendations received by the patient in the comfort of their home. Main innovation points of the envisioned e-coaching technology implementation and evaluation include (1) radical new human-computer interaction paradigms through projected content on home surfaces, (2) neuroscience-backed design of virtual agents as coaches for the patients, and (3) large-scale analytics of continuous, real-life outcome metrics passively generated by patients.

Strengths and Limitations

An important strength of this study is the fact that is the first to examine the potential of neuroscience-backed e-coaching toward

patient activation and adoption of active lifestyle by HF patients. There is currently a significant gap with respect to the adoption and use adherence by chronic patients of eHealth interventions delivered at home.

This study also has some limitations. As heart failure with reduced ejection fraction is more common in men than in women (who in turn are more susceptible to heart failure with preserved ejection fraction), the percentage of male participants is expected to outrange that of females. So far, only male participants have accepted and started the study. In addition, as the inclusion criteria indicate, only patients with adequate level of technology proficiency can participate in the study. This fact complicates the generalizability of the results for older HF patients and women in particular.

The second limitation is that the nature of this study (single-case series) does not allow for a distinct control group. Each case will serve as both control and intervention participant, and analysis will be performed on an individual basis. However, one of the main strengths of this evaluation design is its real-life nature and that any validity threats will be mitigated by detailing the context and participants when results are reported.

Acknowledgments

This project has been financed by the operational program Human Resources Development, Education, and Lifelong Learning and is cofinanced by the European Union (European Social Fund) and Greek national funds.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Peer-reviewer report from the funding agency.
[PDF File (Adobe PDF File), 266 KB - resprot_v9i5e17714_app1.pdf]

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Abbreviations

EEG: electroencephalogram
HF: heart failure
NYHA: New York Heart Association

Edited by G Eysenbach; submitted 07.01.20; peer-reviewed by R Almeida, A Astell, A Vallée, S Schüssler; comments to author 19.02.20; revised version received 04.03.20; accepted 12.03.20; published 04.05.20.

Please cite as:
Billis A, Pandria N, Mouratoglou SA, Konstantinidis E, Bamidis P
Development of Cognitive and Physical Exercise Systems, Clinical Recordings, Large-Scale Data Analytics, and Virtual Coaching for Heart Failure Patients: Protocol for the BioTechCOACH-ForALL Project
JMIR Res Protoc 2020;9(5):e17714
URL: https://www.researchprotocols.org/2020/5/e17714
doi:10.2196/17714
PMID:32364512

Protocol

Supporting Workers to Sit Less and Move More Through the Web-Based BeUpstanding Program: Protocol for a Single-Arm, Repeated Measures Implementation Study

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Abstract

Background: The web-based BeUpstanding Champion Toolkit was developed to support work teams in addressing the emergent work health and safety issue of excessive sitting. It provides a step-by-step guide and associated resources that equip a workplace representative—the champion—to adopt and deliver the 8-week intervention program (BeUpstanding) to their work team. The evidence-informed program is designed to raise awareness of the benefits of sitting less and moving more, build a supportive culture for change, and encourage staff to take action to achieve this change. Work teams collectively choose the strategies they want to implement and promote to stand up, sit less, and move more, with this bespoke and participative approach ensuring the strategies are aligned with the team's needs and existing culture. BeUpstanding has been iteratively developed and optimized through a multiphase process to ensure that it is fit for purpose for wide-scale implementation.

Objective: The study aimed to describe the current version of BeUpstanding, and the methods and protocol for a national implementation trial.

Methods: The trial will be conducted in collaboration with five Australian workplace health and safety policy and practice partners. Desk-based work teams from a variety of industries will be recruited from across Australia via partner-led referral pathways. Recruitment will target sectors (small business, rural or regional, call center, blue collar, and government) that are of

priority to the policy and practice partners. A minimum of 50 work teams will be recruited per priority sector with a minimum of 10,000 employees exposed to the program. A single-arm, repeated-measures design will assess the short-term (end of program) and long-term (9 months postprogram) impacts. Data will be collected on the web via surveys and toolkit analytics and by the research team via telephone calls with champions. The Reach, Effectiveness, Adoption, Implementation, and Maintenance Framework will guide the evaluation, with assessment of the adoption/reach of the program (the number and characteristics of work teams and participating staff), program implementation (completion by the champion of core program components), effectiveness (on workplace sitting, standing, and moving), and maintenance (sustainability of changes). There will be an economic evaluation of the costs and outcomes of scaling up to national implementation, including intervention affordability and sustainability.

Results: The study received funding in June 2018 and the original protocol was approved by institutional review board on January 9, 2017, with national implementation trial consent and protocol amendment approved March 12, 2019. The trial started on June 12, 2019, with 48 teams recruited as of December 2019.

Conclusions: The implementation and multimethod evaluation of BeUpstanding will provide the practice-based evidence needed for informing the potential broader dissemination of the program.

Trial Registration: Australian New Zealand Clinical Trials Registry ACTRN12617000682347; https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=372843&isReview=true.

International Registered Report Identifier (IRRID): DERR1-10.2196/15756

(JMIR Res Protoc 2020;9(5):e15756) doi:10.2196/15756

KEYWORDS

implementation trial; workplace; sitting; health promotion; activity; health and safety; public health; occupational; evaluation; web-based

Introduction

Background

A growing body of recent evidence links high volumes of sitting time to risk of major chronic diseases and premature mortality [1]. Only very high volumes of moderate- to vigorous-intensity physical activity (≥60 min per day), which are achieved by less than 5% of the population, have been seen to attenuate the risk of death associated with high sitting time, according to a recent meta-analysis using data from over 1 million adults [2]. Correspondingly, the national physical activity and health guidelines have a dual message of move more *and* sit less [3].

Sitting time can be strongly contextually driven, dictated by the environmental and social settings in which it occurs [4]. For many working adults, the majority of daily sitting time is accrued in the occupational environment [5], with desk workers spending on average 70% to 80% of their working day sitting [6]. Much of this sitting time is accrued in prolonged, unbroken bouts of 30 min or longer [6]: a pattern that potentially places them at increased risk for poor cardiometabolic [7,8] and musculoskeletal [9] health. As the proportion of industry sectors that involve desk-based work has increased substantially in recent decades, with further increases being forecast [10], the desk-based workplace has been identified as a key setting in which to target reductions in prolonged sitting time [11]. The relevance for occupational health and safety, as well as for public health, of addressing this behavior is reflected in Safe Work Australia's acknowledgment of prolonged workplace sitting as an emergent work health and safety issue [12].

Within this context, the Stand Up Australia collaborative research program was developed [13]. Its aim was to understand how to reduce prolonged sitting time in the workplace and the benefits that may ensue, with the explicit intention of informing translation into practice. A series of pragmatic, researcher-led intervention trials, with participant numbers ranging from 32 to 231, assessed the effectiveness of different strategies (organizational, and environmental, individual; alone or in combination) to support workers to stand up, sit less, and move more in the workplace, with a particular focus on the desk-based workplace [6,14-18]. This Stand Up Australia program of research demonstrated that it is feasible and acceptable to introduce strategies within desk-based workplaces to create a dynamic work environment (which encourages more movement, more often) and to do so without detrimentally impacting on productivity [19]. Such strategies can lead to reductions in workplace sitting time that are substantial (eg, >1.5 hours per 8 hours at the workplace [14]) and sustained (≥12 months [6]). These findings have further been corroborated by other research groups [20,21] and supported by several systematic reviews [22-26]. With a body of evidence on the feasibility and benefits of reducing workplace sitting time, there is now a strong demand for advice, assistance, and support in implementing evidence-based strategies into policy and practice. However, tools and resources to support such implementation at scale do not exist. To meet this appetite, the BeUpstanding Champion Toolkit was developed collaboratively based on evidence from Stand Up Australia and the broader sedentary behavior and health research field.

The no-cost, web-based BeUpstanding Champion Toolkit [27] provides a step-by-step implementation guide and associated multimedia resources to enable a workplace champion to deliver the intervention program (BeUpstanding) within their own work team, independent of input from external expert stakeholders (ie, researchers) [13]. In line with better practice [28] and existing frameworks for program delivery [29], the program is underpinned by a participative and collaborative approach, tailoring of strategies to the organization, visible organizational

support for the program, a strong evaluation framework, and communication of program outcomes, including through automated reports. The program allows for repeated delivery, with champions encouraged to continue to make sustainable changes and build on previous success within their work teams. However, in a key distinction from the researcher-led Stand Up Australia interventions, BeUpstanding was designed specifically for delivery by workplace champions (ie, dedicated staff members). A *train-the-champion* approach was used as workplace champions have been shown to be critical to the success of workplace interventions, acting as role models and drivers for staff participation and work team change [30-32]. This approach also facilitates wide-scale delivery as the workplace (rather than the research team) is responsible for program delivery.

The translation of what has been learned from the Stand Up Australia intervention trials to the BeUpstanding program has involved multiple, iterative phases [13]. These phases have been underpinned by the key principles guiding dissemination of broad-reach health behavior programs [33], including partnerships with key stakeholders, ensuring fit of the program with the organizational goals, integration of outcomes important to informing funders and advancing science, systematic tracking of the resources needed for implementation and intervention, and the maintenance of program fidelity while being flexible and responsive. Central to this has been the development of the technology platform underpinning the toolkit. This platform has not only enabled the evaluation of the effectiveness of the program but has also facilitated insights into the levels of engagement with the program components.

Phase 1, described in detail elsewhere [13], involved initially creating BeUpstanding from the Stand Up Australia interventions. This development occurred in close collaboration with government occupational health, safety, and well-being partners to ensure strong alignment with existing workplace health, safety, and wellness frameworks. It was also developed with consideration of the partner requirements (optimization criteria [34]) that the program have the following attributes: low cost or no cost to workplaces, feasible for workplaces to deliver, scalable, and compatible with existing programs, including the frameworks and language used. These considerations, and the learnings from the preceding trials, collectively led to the "train-the-champion" approach, the use of a web-based toolkit, and the framing of the intervention around the three stages commonly used in government workplace health, safety, and well-being programs (ie, *Plan*, *Do*, and *Review*). The low cost/no cost requirement also meant that sit-stand workstations, which have been shown to effectively reduce workplace sitting (particularly when part of a multicomponent approach) [35], are not a core component or requirement for participation in the program.

Phase 2 involved a quantitative and qualitative evaluation of a small-scale pilot of the beta (test) version of the toolkit [36]. Seven teams of workers in mostly desk-based occupations were included, collectively covering diverse sectors: blue and white collar sectors; government and nongovernment; metropolitan and regional; and small, medium, and large organizations. Overall, the pilot phase demonstrated that the BeUpstanding Champion Toolkit (beta version) was feasible and acceptable for use by workplace champions and that the program delivered through the toolkit was effective at raising awareness, building a supportive work team culture, and reducing workplace sitting time [36,37]. The piloting of the toolkit showed an average reduction in self-reported workplace sitting time of 34 min per 8-hour workday (95% CI −51 min to −14 min) following approximately 3 months of intervention. This level of effect on sitting time has previously demonstrated significant improvements in some indicators of cardiometabolic health [38]. Champions typically spent 30 min to 1 hour per week on the program during this pilot phase [36]. Notably, interviews with the workplace champions 12 months after initial implementation found that teams continued to support the strategies, including through policy development (eg, centralized printers) and dedicated resource funding (eg, purchase of sit-stand desks) [37].

The learnings from phase 2 then informed the optimization of the toolkit (phase 3) to ensure it was fit for purpose for an implementation trial. Phase 3 included the development of a web-based, user-friendly onboarding system (to both promote the toolkit and enable champions to sign up for the toolkit) using human-centered design principles [39], enhanced backend capacity of the toolkit (to facilitate multiple simultaneous users), development of an embedded survey management and data collection system, and enhanced graphic design.

This updated version was tested via a *soft launch* of the program, with over 100 champions enrolling in the program during this period (September 2017 to May 2019). Several key learnings were gained from these early adopters. Firstly, despite the minimal promotion during the soft launch, there was strong uptake of the program, with champions enrolled from throughout Australia and across multiple sectors. This provides strong indication that there is an industry need for a program such as BeUpstanding. Secondly, workplaces were at different stages of readiness, with some champions wanting only to use select program materials (eg, posters) to help raise awareness of the importance of sitting less and moving more, whereas others were ready to run the full program. Thirdly, there was wide variation in how champions engaged with the toolkit, measured by the number of log-ons, with some champions repeatedly logging on throughout the program and others logging on rarely and/or infrequently. Finally, we found that although the toolkit was designed well for delivery by a single champion to their team of workers, it was not sufficiently flexible for larger organizations with large workplaces. It was identified that in a number of instances, there was a combined team formed of several teams led by champions who each adopted more nuanced roles (such as oversight without necessarily directly intervening on staff). Adaptations to the toolkit were made accordingly to suit a range of toolkit user roles.

These key learnings, which were complemented by discovery interviews and in-depth case studies with select participants (chosen to capture insights across sectors, locations, organizational size, and toolkit engagement), were used to inform further optimization of the program and toolkit and the protocol development for the national implementation trial of the BeUpstanding program (phase 4). Adaptions were done

taking into account considerations from multiple perspectives, including the end users, the partners, the researchers, and the financial constraints [34,40]. The aims of this paper are to describe the current version of the BeUpstanding program and the methods and protocol for evaluating the BeUpstanding program in the context of a national implementation trial.

BeUpstanding Program

The BeUpstanding program is designed to be implemented within a workplace (broadly, defined as from one organization, with the same workplace policies) by a champion to their work team (colocated members of the workplace) of which the champion is also a member. Larger workplaces may run BeUpstanding by having several champions deliver the intervention to their teams concurrently. For the purposes of accrual targets and statistical analyses, these multiple teams are counted as one combined *team*. There are three phases to the program (plan, do, and review) and five steps as part of the BeUpstanding program (Table 1). Each step has associated tasks for the champion to complete, noting that not all tasks may be relevant for all champions because of their workplace and/or work team requirements. The toolkit provides information (*training*) on the purpose of each step and task and resources to support the implementation of each task. As part of the implementation trial, champions will receive further training via coaching calls. The most critical step of the program is the staff workshop (Step 3.3). This step is designed to get everyone in the work team on board in terms of why and how the team can BeUpstanding together. In line with participatory design principles [41], work teams are encouraged to collectively choose three strategies to stand up, sit less, and move more to implement, based on which best suit their team's needs and existing culture. Some strategy suggestions, according to the hierarchy of control [42], are provided within the toolkit (Table 2 shows a modified version of this resource). Staff members may choose to implement more than the three team strategies. Alternate suggestions for raising awareness and enabling this collective decision making are provided when running the workshop with all staff at the same time is infeasible (eg, because of shift work). Champions are encouraged to run the BeUpstanding program for 8 weeks from the launch, sending emails and rotating posters on a weekly basis for the first 4 weeks and fortnightly for the second 4 weeks, with the posters and emails organized according to the recommended schedule. Collectively, the workshop, posters, and emails are designed to raise awareness of the benefits of sitting less and moving more, build a supportive culture for change, and encourage participants to take action to achieve this change. Owing to the participative nature of choosing the strategies, and the ability of the champion to tailor the emails, the actual intervention program is bespoke for each work team. The champion is responsible for running and evaluating the program, which includes sending all staff in their work team links to the web-based evaluation surveys (Task 2.2; Task 5.1). Champions are also encouraged to hold staff events (eg, a lunchtime walk and wear your sneakers to work day) and to celebrate and promote individual and whole-of-team success. All staff in the work team will potentially be exposed to the intervention messages (posters and emails), and all staff can choose their level of involvement with both the strategies and the evaluation components. The toolkit encourages champions to run BeUpstanding (or components of thereof) with their team on an annual basis.

Table 1. Phases, steps, champion tasks, supporting resources and rationale for the steps of the BeUpstanding Champion Toolkit.

Phase and steps	Champion tasks	Supporting resources	Rationale of step
Plan, approximately 1-2 months (variable)			
Step 1: Getting support from management	1. Make a case for BeUpstanding 2. Formalize management's commitment in writing	• Business case template • Sample policy • Journey map	• To build the business case for running the program and formalize management commitment (if required)
Step 2: Needs assessment	1. Conduct a workplace audit[a] 2. Conduct a staff survey[a]	• Staff email templates and posters • Links to workplace audit and staff survey • Audit report and links to staff survey results	• To help the champion: assess their current workplace environment and existing policies and identify available resources and facilities and opportunities to support staff to stand up, sit less and move more. • To assess the need for BeUpstanding and provide a baseline to be able to measure any changes arising from the program in terms of staff behaviors, attitudes, beliefs, and health, productivity, and well-being indicators.
Step 3: Preparing for the program	1. Create and maintain a support network 2. Hold a well-being committee workshop 3. Hold a staff consultation workshop[a] 4. Promote BeUpstanding strategies[a]	• Well-being committee member invitation template/video/staff consultation planning tool • BeUpstanding PowerPoint presentation for staff workshop • BeUpstanding staff information video • Strategy survey and associated poster generation	• The well-being committee (recommended 3-6 members, mix of management and general staff, and fortnightly meetings) is intended to provide support to the champion in implementing the BeUpstanding program. • The staff consultation workshop (or equivalent) is designed to create ownership of the program and strategies by the workteam and ensure everyone has the same base level of knowledge regarding the benefits of sitting less and moving more. • The web-based strategy survey enables data collection of the team strategies chosen and promotional support for these strategies via the generation of a customized poster.
Do, approximately 8 weeks			
Step 4: Putting it into practice	1. Set an action plan and launch 2. Promote with posters and health information[a] 3. Promote with email reminders to staff[a] 4. Encourage change champions, and celebrate success	• Action plan example and template • BeUpstanding posters • No/low-cost tips and tools • Recommended emails and additional email guide/templates • Change champion guide	• To support champions to put their BeUpstanding strategies into practice through highlighting key activities and people involved, resource requirements, and the program timeline including evaluation tasks and tools. • To raise awareness, build culture, and encourage action around standing up, sitting less, and moving more.
Review, approximately 1 month			
Step 5: Evaluation	1. Do follow-up staff survey[a] 2. Do program completion survey[a] 3. Where to from here	• Links to follow-up surveys and staff survey results • Team performance report and completion certificate	• To support the champion and the work team to evaluate and reflect on their progress and plan for sustainability.

[a]Steps marked as critical within the toolkit (core components).

Table 2. Suggested team-level strategies to BeUpstanding according to the Hierarchy of Control (adapted from Resource 3.2).

Hierarchy of control	Strategies
Elimination	• Use technology (eg, voice recognition software) to eliminate prolonged sedentary tasks
Substitution (redesign)	• Enable internal stair access and workplace re-design to facilitate more movement where possible • Move water, bins, and printers away from desks • Install height-adjustable workstations • Provide designated standing areas (eg, in tea rooms and meetings rooms) • Provide facilities such as showers and lockers to encourage active transport and physical activity • Use phone support accessories (eg, headphones and speaker phones) to facilitate standing during phone-based tasks
Administration	• Create a walking track around workplace • Encourage workers to leave desks during breaks • Provide organizational support for flexible hours for lunch breaks to encourage physical activity (eg, gym visits) • Encourage face-to-face interaction with colleagues • Stand up and move around when taking a phone call (where possible) • Undertake walking meetings • Conduct standing meetings • Encourage staff to regularly walk to top up water glass/bottle • Use signage (eg, posters) to support BeUpstanding messages • Use computer software to prompt breaks from sitting • Provide physical prompts at desk to stand regularly (eg, stickers) • Leave desk in standing position when leaving workspace (if using height-adjustable workstations) • Conduct daily group activity sessions • Undertake a team challenge (eg, 10,000 steps challenge)

BeUpstanding Intervention Messages and Behavioral Targets

The program's behavioral targets are to achieve an even 50:50 split between sitting and nonsitting (ie, upright) activities at work and to alternate posture at least every 30 min between sitting and upright (or vice versa)—consistent with public, occupational, and clinical guidelines [43-45]. To support these targets, the BeUpstanding intervention messages are to *Stand Up, Sit Less, Move More*. *Stand Up* is a prompt to break up long periods of sitting, *Sit Less* is a prompt to reduce overall sitting time throughout the day by swapping some sitting with either standing or moving, and *Move More* is a prompt to increase physical activity (primarily opportunistic, incidental activity) throughout the day. Increased activity and decreased sitting are primarily targeted through organizational, environmental, and social approaches. Messaging throughout the resources encourages regular postural shifts and reminders to *listen to your body* in recognition that there are also adverse outcomes associated with prolonged unbroken standing [46-48]. No specific individual-level support for staff is provided through the toolkit.

BeUpstanding Website

The BeUpstanding program is delivered via the BeUpstanding Champion Toolkit hosted on the BeUpstanding website [27]. The website is hosted, maintained, and updated by project staff, with all data stored in a secure, cloud-based system (Microsoft Azure) that is backed up weekly to the University of Queensland servers (lead investigator's team: GH, AG, JB, JJ, LU, EW). The toolkit itself is powered through a bespoke platform that includes in-built systems that facilitate survey design, project management, and user tracking, enabling the research team to readily track a champion's progress and engagement through the program and collect survey-based data. In addition to the toolkit, the BeUpstanding website (freely available) also includes pages on the business case and associated promotional materials for running the BeUpstanding program, the evidence base supporting the BeUpstanding program, a checklist to ensure program readiness, a link to the BeUpstanding blog and social media, a frequently asked questions section, and details on the investigators and partners. Champions are encouraged to visit the blog via monthly electronic newsletters for the latest research evidence and tips for running the program.

Methods

Aims and Research Questions

The aim of this study is to evaluate the BeUpstanding program in the context of a national implementation trial. The research questions to be answered are those important to informing the dissemination (phase 5) [13]: in particular, who takes part in the program, how the program was delivered, did the program work (and for whom did it not work), and how much did it cost. The RE-AIM (Reach, Effectiveness, Adoption, Implementation, and Maintenance) Framework [49] will be used to guide the evaluation, with assessment of the *adoption/reach* of the program (the number and characteristics of work teams and participating staff), program *implementation* (completion by the champion of core program components), *effectiveness* (on workplace sitting, standing, and moving), and *maintenance* (sustainability of changes). The implementation trial is funded by a National Health and Medical Research Council (NHMRC) of Australia Partnership Project Grant (number 1149936), which includes cash and/or in kind support from the five partners (see below). Ethical approval was gained by The University of

Queensland Human Research Ethics Committee (approval number 2016001743). The trial was prospectively registered on May 12, 2017 (ACTRN12617000682347), before the soft launch of the program and last updated on the June 11, 2019. All participants will provide informed consent to participate.

Study Design

A single-arm design will be used to evaluate the BeUpstanding program, with repeated cross-sectional evaluations at preprogram (0 weeks), end of program (approximately 8 weeks; primary endpoint), and at 9 months postprogram (approximately 12 months post sign up). Repeated cross-sectional evaluations provide a flexible evaluation protocol [50] that can assess change within retained members of the baseline survey cohort over time and more general time trends (owing to both changes over time within participants and some fluidity in work team membership, such as because of workforce turnover).

Study Eligibility and Accrual Targets

On the basis of data reported by the champion as part of the web-based registration process, eligible Australian-based work teams will be those who had not run the BeUpstanding program previously with a minimum of five staff members, job roles or tasks that predominantly involve desk-based work, and a staff member willing to perform the duties of a workplace champion. Champions must also be planning to run the program within the recruitment window. For large organizations, including those located across numerous sites, multiple work teams from the one organization will be eligible to participate. These will be treated as a single combined *team* when the intervention is concurrent and within a workplace as per the criteria; otherwise, separate teams will be permitted to participate. Each champion will invite all employees within their work team to participate in the program and its evaluation. All workers invited will be considered eligible unless they indicate within the staff survey that they are unable to currently walk or stand for at least 10 min without an assistive device or requiring assistance from another person. Accrual targets have been set at 50 or more work teams per priority sector and 10,000 or more staff exposed to the program in total (see sample size). Performance against these accrual targets will be reviewed at the quarterly steering committee meetings, with the promotion and marketing plan adapted as required to ensure targets are met.

Study Partners and Promotion

The implementation trial will be conducted in partnership with five Australian workplace health and safety policy and practice organizations: Safe Work Australia, Comcare, Queensland Office of Industrial Relations, The Victorian Health Promotion Foundation (VicHealth), and Healthier Workplace Western Australia. These organizations are responsible for developing, implementing, and/or promoting Australian workplace health and safety policy. Each partner has committed to endorse and promote the toolkit across their relative jurisdictions. Desk-based employees from a wide cross-section of industries will be targeted, inclusive of sectors collectively identified as priorities by the partners (small business, regional, call center, blue collar, and government). To ensure efforts are coordinated, a detailed action-mobilization plan will be developed with the partners. The plan, which will include an annual promotional *push* via an awareness raising event, will build on and coordinate with existing communication channels and resources from the partners and participating institutes, including social media, web links, email listservers, newsletters, workplace health promotion and occupational health networks, conferences, and workshops.

Study Protocol for the Implementation Trial

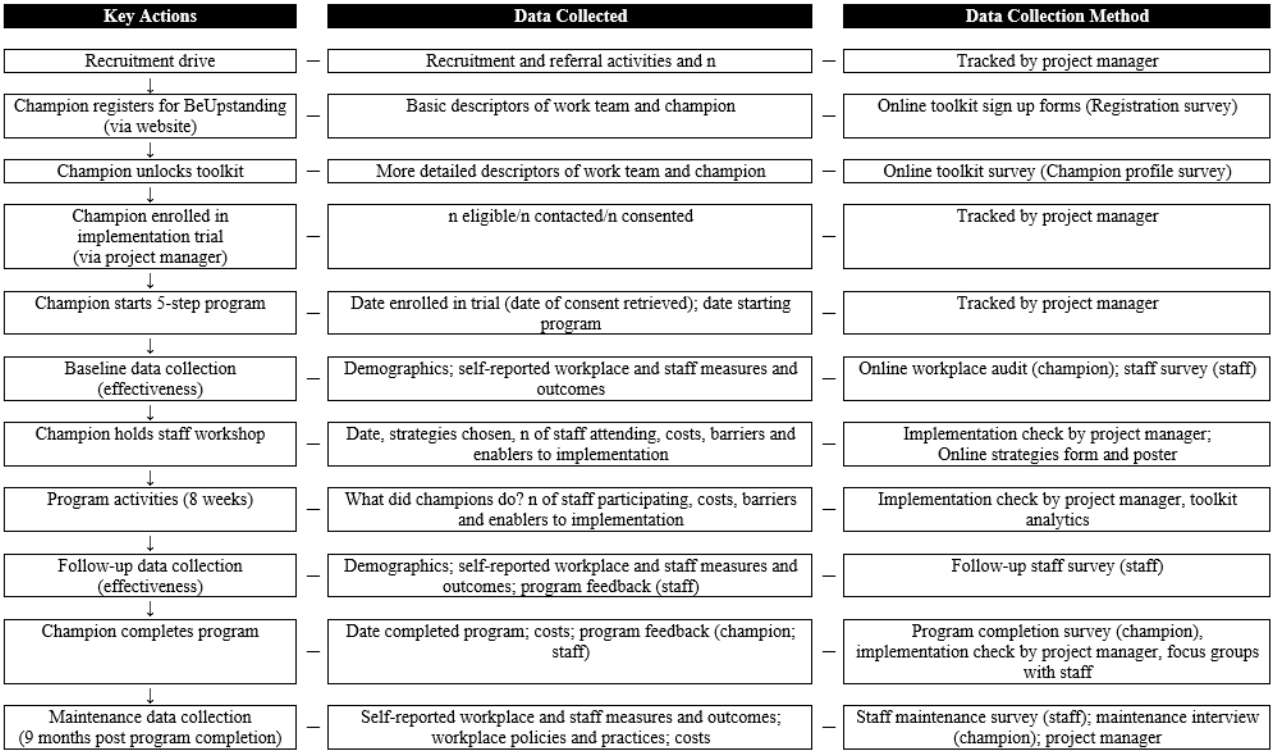
The BeUpstanding website [27] is designed for workplace champions; however, anyone can freely sign up to use the BeUpstanding Champion Toolkit via the registration survey (sign up form) on the BeUpstanding website. At signup, a user identifier is generated and a welcome email is automatically sent that includes details regarding the implementation trial. To unlock the toolkit contents, the user is required to complete the champion profile survey and is asked to nominate their intended role as a toolkit user (which might be a workplace champion or another nondelivery role, such as senior decision maker, interested staff member.). Following completion of this survey, champions with work teams that appear eligible for the implementation trial will be invited via a phone call from the research team to participate in the implementation trial, with recruitment continuing until accrual targets are met. This phone call with the champion will be used to confirm the eligibility of the work team for involvement in the implementation trial, ascertain from the champion the likely readiness of the work team to participate in the program, and confirm the contact details of the workplace champion (and an alternate contact). Those eligible and indicating interest in trial participation will be sent additional information on trial participation requirements, namely, confirmation of organizational support to run the five-step BeUpstanding program and commitment to the implementation trial evaluation components. The champion's electronic consent to the trial will be required before implementation trial enrolment.

Data Collection

Outcome and process data and the characteristics of the workplaces, champions, and staff taking part in the implementation trial will be collected via the dedicated, stand-alone BeUpstanding website (Registration Survey; Champion Profile Survey; Workplace Audit; Staff Surveys—baseline, end program, and maintenance; Strategy Survey; Program Completion Survey; and toolkit analytics) and by the project manager (implementation checks and qualitative interviews), as outlined in Figure 1. Champions will be required to provide informed web-based consent for their data to be used by the research team before completing the Champion profile survey, with further consent required to participate in the implementation trial. Staff will be required to provide informed consent for their data to be used by the research team before completing each of the staff surveys. Data for staff are anonymous; however, to enable participants to be tracked across data collection points, each staff survey includes three questions designed to generate a unique (but anonymous) identifier for the staff participant when used in combination with the champion ID: day of the month they were born on, first letter

of mothers first name, and last three digits of their mobile number.

Figure 1. Key actions, data collected, and data collection method of the BeUpstanding implementation trial. Staff focus groups will be conducted in a sub-sample of teams only; separate consent will be sought from staff members for participation in this component.



The promotional activities undertaken by partners will be recorded at the 6-weekly partner meetings, with their impact on registrations tracked through the analytics in the toolkit website. The promotional pathways will be tracked through URL identifiers, through Google Analytics, and via champion self-reporting through the champion profile survey. Factors potentially influencing uptake and engagement with the program (eg, number of teams within a workplace participating in the program) will also be tracked via the registration survey and implementation checks. To ensure minimum data accrual targets are met, the project manager will follow up with champions (via email/phone) where necessary to encourage and support data collection.

The project manager will have a minimum of five telephone contacts with the champion across the implementation trial evaluation: (1) recruitment, (2) confirmation of consent and explanation of next steps, (3) as soon as possible following the staff workshop, (4) at the end of the program, and (5) 9 months after the end of the program. Focus groups will be undertaken with a subsample of consenting staff from participating teams (n was approximately 15) at the end of the program to assess their perspectives on the processes and outcomes of the program. A mix of teams who made small/no, midrange, and large improvements and from different sectors will be purposively sampled, with focus groups conducted either in person or on the web via a virtual meeting room.

Outcomes and Measures

Outcomes and measures are shown in Table 3, along with the relevant RE-AIM indicators and measurement tools. As adoption logistically occurs before reach, RE-AIM is reported as ARIEM.

Table 3. Outcomes, measures, and assessment tools of the BeUpstanding implementation trial according to the Reach, Effectiveness, Adoption, Implementation, and Maintenance framework.

Reach, Effectiveness, Adoption, Implementation, and Maintenance dimensions	Collection method/assessment tools
Adoption by teams	
Champions registering for BeUpstanding (n)	Registration (sign up) survey
Champions unlocking the toolkit (n)	Champion profile survey
Characteristics of champions and their organizations and their work teams (including size of organization and number of staff)	Champion sign on, Champion profile survey; workplace audit
Reasons for taking up the program	Champion profile survey
Champions eligible and enrolling in implementation trial, n (%) of eligible	Champion profile survey
Champion withdrawals from implementation trial (n) and reasons for withdrawal	Implementation check
Reach of Staff in Teams	
Staff in work team (n as reported by champion)	Champion profile survey; implementation check
Percentage of staff in work team that participate in choosing BeUpstanding strategies	Strategy survey; implementation check
Participation in staff surveys, n (%)	Staff surveys (champion-reported n for %)
Characteristics of staff taking part in the evaluation	Staff surveys
Implementation	
Completion rates	Toolkit analytics; implementation check
Engagement with the program	Toolkit analytics, implementation check; program completion survey
Strategies chosen by work team	Strategy survey; implementation check
Sit less, move more strategies (staff)	Staff surveys
Barriers and enablers to implementation	Implementation check
Effectiveness	
Workplace sitting and activity	Staff surveys
Activity preference alignment	Staff surveys
Organizational social norms	Staff surveys
Enablers to sitting less and moving more	Staff surveys; staff focus groups[a]
Perceived barriers to sitting less and moving more	Staff surveys; staff focus groups[a]
Work performance and engagement	Staff surveys
General health	Staff surveys
Adverse/unintended consequences (end program only) for champions and staff	Implementation check; staff follow-up survey; program completion survey
Costs to deliver the BeUpstanding program	Program completion survey; implementation check
Program satisfaction and perceived impact (end program only) for champions and staff	Follow-up staff survey, program completion survey, implementation check, staff focus groups[a]
Maintenance	
Self-reported workplace sitting time collected 9-months after end-of program	Staff maintenance survey
Use of activity policies and practices	Staff maintenance survey, champion interviews

[a]In a subsample only.

Adoption

Work team characteristics to be measured include organizational size, workplace location (postcode), industry, and team size. Team size is asked initially on the registration survey and confirmed by the project management team. Team size is visibly displayed on the feedback reports (staff surveys reports, performance completion reports) for champions, and champions have the opportunity to modify their team size within their individual profile page. To assess eligibility and inform accrual

targets, information on sector, job roles, and proportion of the team undertaking desk-based work will also be assessed. To understand the health and well-being culture of the work team, champions will be asked if their team is currently participating in any other workplace wellness/health promotion programs, the everyday interest of the team in health and well-being (1=nonexistent, no one interested, to 5=very high, all/nearly all interested), the team's motivation to sit less and move more at work (1=nonexistent, no one motivated, to 5=very high, all/nearly all motivated), and their team's level of stress (1=minimal/no stress to 5=severe stress). Workplace readiness for change will be assessed via the context, change efficacy, and change-related effort subscales of the Workplace Readiness Questionnaire [51]. The workplace audit, which was adapted from the Checklist of Health Promotion Environments at Worksites [52], will be used to capture information on office layout, availability of height-adjustable desks, the physical environment (eg, access to public transport and centrally located bins), and the cultural/policy environment (eg, flexible work options).

Champion characteristics to be measured include sex; age (years), job classification (employee, team leader/middle management, and senior management/executive), and job title (open ended). Champions will also be asked if they have a Health and Safety role in their workplace, whether they have done any training in workplace health programs before, and whether they have delivered and/or evaluated a workplace health program before, with responses of yes, no, and unsure for each item. Champions will be asked what they hope to achieve with the program, an also to describe their current workplace culture in terms of sitting, standing, and moving (including any potential barriers and enablers to change).

Reach

The extent of participation of staff in the various BeUpstanding activities will be determined from the champion-reported team size, and champion-reported numbers or percentages participating in BeUpstanding events (eg, well-being committees, staff information workshop, launch party). Staff characteristics to be collected via the staff survey include age, sex, education, job classification, work hours, and the number of days in the last week where they had done a total of 30 min or more of physical activity, which was enough to raise their breathing rate [53]. Staff will also have the option to enter data about their postschooling education qualifications, whether they speak a language other than English at home, home postcode, height (cm), weight (kg), smoking status, and the number of times per week they usually did vigorous activity, walking, and other moderate-intensity activity [54]. The size and characteristics of teams taking part compared with the broader organization will be compared using champion-reported data collected via sign on and the Champion Profile Survey.

Implementation

The primary implementation outcome is program completion. At a minimum, successful completion is considered as completing all the core elements of the program (Table 1). Secondary implementation outcomes are engagement with the program (assessed through, eg, the number of log-ons to the toolkit, duration of using the toolkit, duration of running the program, and use of program materials), barriers and enablers to implementation, and costs of implementation (including time taken by the champion to plan, deliver, and evaluate the program, including gaining management support; see economic evaluation). Strategies chosen by the work team to BeUpstanding will be considered at a basic descriptive level (number of strategies chosen, frequency of certain strategies chosen) and according to the hierarchy of control (Table 2). Other factors tracked will include adaptions made (and desired) to the program materials by the work teams and participation by champions in activities to support engagement/implementation (eg, workshops for champions, champion forums).

Effectiveness

Workplace Sitting and Activity

The primary effectiveness outcome is self-reported workplace sitting time. This will be measured by the Occupational Sitting and Physical Activity Questionnaire (OSPAQ) [55], which asks about the percentage of time on a typical workday in the last 7 days spent sitting, standing, walking, and/or in heavy labor or physically demanding tasks. As such, it will also capture key secondary activity outcomes concerning time spent in other active behaviors at work: standing, walking, heavy labor, and moving (ie, walking + heavy labor). Measures from the OSPAQ have acceptable reliability and validity against posture-based activity monitors [56] and are responsive to change [56]. Participants will also be asked to estimate how many breaks from sitting they typically took in each hour while at work (six response options from 0 to 5 or more [57]) and the percentage of their sitting time at work they think is accrued in prolonged, unbroken, continuous bouts of 30 min or more (whole percentage from 0 to 100). This latter question was developed for the BeUpstanding study to capture change in prolonged sitting time. Unpublished testing within one of the early adopting workplaces (a call center; n=28 participants) showed acceptable test-retest reliability (r=0.74, 95% CI 0.51 to 0.87) and criterion validity (r=0.54, 95% CI 0.20 to 0.76) against workplace sitting in bouts of 30 min or more as recorded by the activPAL3 [58].

Activity Preference Alignment

Participants will be asked "if you were given a choice at work, what percentage of the time would you want to spend: sitting, standing, moving." Activity preference alignment at work will be calculated as the absolute value of the difference between their preferred behavior and their self-reported behavior. The alignment scores for sitting, standing, and moving each theoretically range from 0 (desired and performed are exactly the same) to 100 (desiring 100% and doing 0% or vice versa) [36].

Organizational Social Norms

In line with the measure used in the pilot study [36], staff will be asked on a 5-point Likert scale (1=strongly disagree to 5=strongly agree) the extent to which they agree or disagree with five statements regarding control of how much they sit and stand at work; how much their organization is committed to supporting staff choices to sit, stand and move at work; whether

management is supportive if they want to stand and move more at work; whether management *walks the talk* when it comes to modeling standing and moving more at work; and whether their work team has a culture that supports standing and moving. These five items will be used to create an *organizational social norms* score.

Enablers to Sitting Less and Moving More

Staff will be asked (yes/no) whether they believe that too much sitting is detrimental to their health and well-being, whether a dynamic work environment is beneficial to their productivity, whether they want to sit less at work, and whether they have access to a height-adjustable desk. These four items will be used to create an *enablers score*.

Perceived Barriers to Sitting Less and Moving More

Participants will be asked on a 5-point Likert scale (1=strongly disagree to 5=strongly agree) the extent to which they agree or disagree with seven statements regarding perceived barriers to sitting less and moving more at work: I am too busy to sit less at work, I worry that I would be perceived as being unproductive if I sat less at work, I need new equipment (eg, desk or headphones) to support me to sit less at work, the tasks I have to do in my job prevent me from being able to sit less at work, I worry that I would be perceived as *weird* if I sat less at work, my health prevents me from standing and moving more at work, and I need prompting to remember to sit less at work. Scores from these items will be used to create a *barriers score*. Participants will also be asked an open-ended question on any other factors that are preventing them from being able to sit, stand, or move at their desired levels at work.

Use of Activity-Promoting Strategies

Participants will be provided with a menu of common strategies that have been used to promote standing up, sitting less, and moving more in the desk-based environment inclusive of those promoted in the BeUpstanding resources [15,18,59] and will be asked on a 5-point Likert scale to indicate the extent to which they used these strategies (never, rarely, sometimes, often, very often/always, and not applicable). Scores from these items will be used to create a *strategy use score*.

Work Performance Indicators

Self-rated job performance [60] and job satisfaction [61] will be measured using single-item 7-point Likert scales. Participants will also be asked to rate on a 5-point scale (1=not at all to 5=extremely) the extent in the last week at work that they felt productive, creative, and part of a team. They will also be asked the number of days in the last 4 weeks (0-28 days) that they have stayed away from work for more than half the day because of health problems [62].

Perceived Health Status

Musculoskeletal symptoms in the last week will be measured using 3-items adapted from the Nordic Musculoskeletal Questionnaire [63,64] to assess the level of discomfort in (1) upper back, neck, shoulders, elbows, wrists, or hands; (2) lower back; and (3) hips, thighs, buttocks, knees, ankles, or feet. Each item will be assessed on an 11-point scale, from 0 (no discomfort at all) to 10 (severe discomfort). Current physical and mental health will each be rated on a single 5-point scale (1=poor to 5=excellent) [65,66]. To provide an indication of current stress and energy levels, participants will also be asked to rate on a 5-point scale (1=not at all to 5=extremely) the extent in the last week at work that they felt stressed, alert, energetic, and creative.

Adverse Events

The experience of any adverse events associated with program participation will be asked of both champions and staff.

Program Satisfaction and Feedback

Feedback on the BeUpstanding program will be sought from both champions and staff using fixed-option questions and qualitatively via open ended questions and qualitative interviews (in a subsample). Questions will cover program awareness, enjoyment, satisfaction, and potential for improvement. At the end of program, the staff survey will gather staff perceptions of the impact of the BeUpstanding program (negative impact, no/minimal impact, or positive impact) on five success dimensions: the culture in their work team around sitting, standing, and moving; their knowledge of the benefits of sitting less; their attitudes toward sitting, standing, and moving; their awareness of their sitting behavior; and their activity outside of work. Champions will be asked to report, using a 5-point Likert scale (1=not at all to 5=complete success), their perception of the extent to which the program raised awareness of the benefits of sitting less in the team, built a culture in their work team that supports sitting less and moving more, and reduced the amount their team engaged in prolonged unbroken sitting time. Adaptions and modifications to the program or program resources by the champions will be collected and recorded through the scheduled implementation checks.

Maintenance—Understanding Sustainability

At postprogram assessment (approximately 9 months after the 8-week program completion), champions will be interviewed to understand current workplace policies and practices related to sitting less and moving more and ongoing or new BeUpstanding strategy use. All staff will be sent the maintenance survey (a repeat of the baseline staff survey) to understand the sustainability of any changes.

Economic Evaluation

The economic evaluation will address the costs and outcomes of scaling up to national implementation, including intervention affordability and sustainability. The economic analysis will be undertaken from a societal perspective, but with the major focus on a workplace perspective (covering both costs and benefits to employers and employees). The study design lends itself to a cost-outcome description as a full economic evaluation such as cost-effectiveness analysis would require a control arm. The primary economic analysis will comprise the analyses of costs, outcomes, and the relationship between costs and outcomes. Detailed pathway analysis will be used to identify all resource use associated with the intervention delivery. The intervention will be assumed to be operating in steady state (ie, up and running at its full effectiveness potential), all costs associated with preplanning and development will be excluded. The included costs will relate to workplace recruitment (promotion

events, social media, newsletters, etc) and intervention delivery (such as the staff workshop, posters, conduct of toolkit components, champion time, meetings of staff well-being committees, maintenance of website, etc). Data on the strategies adopted by individual work teams (including estimated costs) will be collected via the implementation checks. All resources will be valued in Australian dollars for the 2019 reference year. The economic outcomes for the implementation study will be presented as total costs, average costs per work team, and per work team of different size. Analysis of who incurs the associated costs (government, employers, individual employees, and research team) will be undertaken to assess intervention affordability and sustainability.

Data Analyses

Adoption, reach, and implementation outcomes will be described overall and within each priority sector. Effectiveness outcomes will also be evaluated overall and within each priority sector, with all work teams that are located in multiple sectors (eg, regional and small businesses) examined as part of every sector to which they belong. Effectiveness outcomes collected at the end of program only from champions and/or staff (eg, satisfaction) will be described. Effectiveness of the intervention on the primary outcome and secondary outcomes (continuous) collected repeatedly in the staff surveys will be assessed using mixed models that account for nonindependence in the form of individuals with repeated observations (baseline, end of program, and postprogram) and *team* clustering. The primary endpoint is the end of program (approximately 8 weeks). The pragmatic aspects of the champion-led collection of anonymous data from staff within a workplace means the staff surveys will be sent out to all staff who are team members at the time in a repeated cross-sectional fashion. Most are likely a core cohort sent all surveys (not known to the research team) who may respond to none or any number of the three surveys. In addition, some team members will be added or lost with workforce turnover. Accordingly, the evaluation will consist of assessing both changes within baseline responders who are followed up over time, and as this may be a select motivated subset, also assessing time trends in all evaluable cases (responders to any survey). Time trends will be considered both unadjusted and adjusting for potential compositional differences between responders at each assessment (because of variations in team membership with workforce turnover and who responds to each survey). To evaluate sensitivity of conclusions to missing data handling, multiple imputation analyses will also be performed. Team-level variation in effectiveness will be considered. If applicable, then program engagement, characteristics of the work teams and workplace champions, and the timing (month/year) of the intervention will be explored as reasons for the differential effectiveness.

Qualitative data from the focus groups with staff (effectiveness—barriers, enablers, and satisfaction) and semistructured interviews with champions (maintenance—use of policies and practices) will be audio-recorded and transcribed verbatim. Data from focus groups and champion interviews will be analyzed separately. Consistent with the recognized guidelines for qualitative data analyses [67], two members of the research team will independently code each transcript, where deductive codes will be identified based on the a priori constructs of interest (barriers, enablers, and satisfaction). Furthermore, all transcripts will be read to look for emergent themes (inductive coding). Initial codes will be grouped together into subthemes and overarching themes and relevant data to each theme collated. The coding frameworks developed by the research team members will then be compared for similarities or differences. Any discrepancies will be discussed with at least one other team member for consensus of the coding framework.

Sample Size for Primary Effectiveness Outcome

For the primary effectiveness outcome (work sitting), the minimum difference of interest will be 20 min per 8 hours at work, which is equivalent to two-thirds of the effect in the pilot (30 min/8 hours) [36] and what we might expect to see maintained in the long term [6]. Calculations using the GLIMMPSE software (version 2.2.8) indicate the study requires 47 to 62 teams to detect a change of this magnitude with 80% to 90% power and 5% two-tailed significance. Calculations assume, based on the pilot and early BeUpstanding data, an average of five workers per team will provide data (after attrition): SD 90, r=0.5, and intracluster correlation=0.1. Thus, to provide an adequate sample size to test effectiveness within every priority sector and overall, at least 50 work teams per priority sector will be recruited, with no fixed upper limit to recruitment within these priority sectors or other sectors.

Results

Funding for the trial was obtained from June 1, 2018, to May 31, 2021. The protocol for the data collection was originally approved by the institutional review board on January 9, 2017, with the national implementation trial consent and protocol amendment approved on March 12, 2019. The start date for the trial was June 12, 2019. As of December 2019, 48 teams have been recruited into the trial.

Discussion

Desk-based workers spend on average an estimated 70% to 80% of their workday sitting [6], putting their present and future health and productivity at risk. This novel implementation trial in work teams of desk-based workers across Australia will determine whether the BeUpstanding Champion Toolkit is a feasible, effective, safe, and economical resource for sustainably reducing workplace sitting. The multilevel and mixed method evaluation will also enable examination of the predictors of success across a wide range of employment sectors, including sectors that have been underserved and underresearched. Through explicit consideration of a wide range of potential benefits and possible adverse events, it should be possible in the future to provide many of the answers to questions and concerns that could arise during more widespread adoption. Findings will provide the fundamental practice-based evidence needed to inform workplace health, policy, and practice on effective and sustainable ways to promote more movement and less sitting without compromising productivity or worker health. These practice-based findings will also inform the potential for broader dissemination of the toolkit, providing an opportunity to advance the translational evidence base. Importantly, as the

program is freely available with no upper limit to enrolment, there is the opportunity to compare outcomes and engagement of those recruited into the implementation trial compared with those participating in the BeUpstanding program but not taking part in the trial.

Limitations and Strengths

As an implementation study, there are some inherent limitations. The use of a single-group, pre- to poststudy design is primary among these. A randomized controlled trial (RCT) design was considered, as this design would provide more robust effectiveness outcomes. However, an RCT would not provide better data for the reach, adoption, and implementation outcomes. It was also unclear how to conduct an RCT while preserving the key intervention model being tested of a workplace champion delivering and evaluating the intervention, particularly given the BeUpstanding toolkit is already live and freely available. Experience from the pilot and early adopters phases (phases 2 and 3) led us to expect that we would not be able to recruit champions willing to act as controls and complete all the evaluation but receive none of the intervention (even if they received a delayed intervention). Even the evaluation requires a reasonable amount of effort on the part of the workplace champion: researchers have no contact with the staff. Anyone can sign up to the toolkit (including potential control organizations) meaning contamination would be very difficult to control in those who sign up and are allocated to the control arm. We would also need to expend significant resources tailoring the toolkit to perform the evaluation but not the delivery intervention functions for those champions whose teams were allocated to a control condition. Therefore, on balance, it was considered that the pre-post design was the most appropriate to evaluate the implementation trial.

Providing a menu of options and supporting work teams to collectively choose which intervention strategies will work best for them is a key strength of the program, with findings likely to provide key insights into possible higher order strategies to effectively support workers to sit less and move more [68], but this approach does mean that findings across work teams will not necessarily be directly comparable. It also means that strategies known to successfully achieve shifts in workplace sitting time, such as the use of sit-stand workstations as part of a multicomponent approach [35], will not necessarily be implemented by work teams. Furthermore, for some individuals, the strategies chosen by the team to BeUpstanding may not be appropriate for them personally. However, the primary questions to be answered are about the uptake, implementation, and costs of wide-scale implementation and the outcomes that can be achieved in this context; questions that are being answered through RE-AIM—a widely used framework for understanding dissemination [49]. Further strengths of the study include its pragmatic design. The toolkit readily facilitates uptake and delivery with minimal follow-up required from stakeholders. The program is also designed to be easily integrated into existing wellness, health, and safety initiatives. This presents an innovative model that has a high likelihood of being able to be generalized more broadly. Importantly, all five industry partners are ideally suited to use trial findings to directly shape and deliver national and international workplace policy and practice.

Acknowledgments

The authors acknowledge and thank Steve Goodwin, Sarah Hyne, Richard Dawson, Rayoni Nelson, Natalie Quinn, Kevin St Mart, Karen Pegrum, Melanie Chisholm, Hayley O'Connell, Trevor Shilton, Leanne Sweeny, and the Work Health Design Branch, Workplace Health and Safety Queensland for their contribution to the BeUpstanding program. They would also like to thank all the workplaces, champions, and staff involved in the optimization phase of BeUpstanding. The implementation trial is funded by a NHMRC of Australia Partnership Project Grant (#1149936) with partner funding provided by Safe Work Australia, Comcare, Queensland Office of Industrial Relations, VicHealth, and Healthier Workplace Western Australia. The NHMRC had no role in the design of the study and collection, analysis, and interpretation of data or in writing the manuscript. The partners were directly involved in the co-design of the study and the proposed measures and are included as co-authors or in the *Acknowledgments* section as appropriate. GH is supported by an NHMRC Career Development Fellowship (#108029); BC is supported through an NHMRC Early Career Fellowship (#1107168); DD is supported through an NHMRC Senior Research Fellowship (NHMRC APP1078360) and the Victorian Governments Operational Infrastructure Support Program; AG and EW are supported through an NHMRC Centre for Research Excellence Grant on Sitting Time and Chronic Disease Prevention—Measurement, Mechanisms and Interventions (#1057608); JB, JJ, and LU are supported by an NHMRC Partnership Project Grant (#1149936); LG is supported by an Alfred Deakin Postdoctoral Research Fellowship, Deakin University; and NO is supported by an NHMRC Senior Principal Research Fellowships (#1003960).

Authors' Contributions

GH and AG are primarily responsible for the development and optimization of the BeUpstanding program. The following authors (GH, AG, AA, JB, DD, EE, NG, LG, AL, MM, NO, LS, and PT) received funding for the implementation trial. All authors contributed to the study design and methods for the implementation trial. All authors reviewed and provided feedback for this manuscript.

Conflicts of Interest

The BeUpstanding toolkit includes paid consultancy options offered by The University of Queensland that are in addition to the free program reported on within this manuscript. All proceeds generated through the paid options are returned to the research program.

Multimedia Appendix 1
CONSORT-eHEALTH checklist (V 1.6.1).
[PDF File (Adobe PDF File), 4076 KB - resprot_v9i5e15756_app1.pdf]

Multimedia Appendix 2
Application assessment summary from Australian National Health and Medical Research Council (NHMRC).
[DOC File , 43 KB - resprot_v9i5e15756_app2.doc]

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Abbreviations

NHMRC: National Health and Medical Research Council
OSPAQ: Occupational Sitting and Physical Activity Questionnaire
RCT: randomized controlled trial

Edited by C Hoving; submitted 05.08.19; peer-reviewed by M Buman, J Manning, N Krause; comments to author 26.11.19; revised version received 22.12.19; accepted 06.02.20; published 04.05.20.

Please cite as:
Healy GN, Goode AD, Abbott A, Burzic J, Clark BK, Dunstan DW, Eakin EG, Frith M, Gilson ND, Gao L, Gunning L, Jetann J, LaMontagne AD, Lawler SP, Moodie M, Nguyen P, Owen N, Straker L, Timmins P, Ulyate L, Winkler EAH
Supporting Workers to Sit Less and Move More Through the Web-Based BeUpstanding Program: Protocol for a Single-Arm, Repeated Measures Implementation Study
JMIR Res Protoc 2020;9(5):e15756
URL: https://www.researchprotocols.org/2020/5/e15756
doi:10.2196/15756
PMID:32364513

Original Paper

The NASSS-CAT Tools for Understanding, Guiding, Monitoring, and Researching Technology Implementation Projects in Health and Social Care: Protocol for an Evaluation Study in Real-World Settings

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Abstract

Background: Projects to implement health care and social care innovations involving technologies are typically ambitious and complex. Many projects fail. Greenhalgh et al's nonadoption, abandonment, scale-up, spread, and sustainability (NASSS) framework was developed to analyze the varied outcomes of such projects.

Objective: We sought to extend the NASSS framework to produce practical tools for understanding, guiding, monitoring, and researching technology projects in health care or social care settings.

Methods: Building on NASSS and a complexity assessment tool (CAT), the NASSS-CAT tools were developed (in various formats) in seven co-design workshops involving 50 stakeholders (industry executives, technical designers, policymakers, managers, clinicians, and patients). Using action research, they were and are being tested prospectively on a sample of case studies selected for variety in conditions, technologies, settings, scope and scale, policy context, and project goals.

Results: The co-design process resulted in four tools, available as free downloads. NASSS-CAT SHORT is a taster to introduce the instrument and gauge interest. NASSS-CAT LONG is intended to support reflection, due diligence, and preliminary planning. It maps complexity through stakeholder discussion across six domains, using free-text open questions (designed to generate a rich narrative and surface uncertainties and interdependencies) and a closed-question checklist; this version includes an action planning section. NASSS-CAT PROJECT is a 35-item instrument for monitoring how subjective complexity in a technology implementation project changes over time. NASSS-CAT INTERVIEW is a set of prompts for conducting semistructured research or evaluation interviews. Preliminary data from empirical case studies suggest that the NASSS-CAT tools can potentially identify, but cannot always help reconcile, contradictions and conflicts that block projects' progress.

Conclusions: The NASSS-CAT tools are a useful addition to existing implementation tools and frameworks. Further support of the implementation projects is ongoing. We are currently producing digital versions of the tools, and plan (subject to further funding) to establish an online community of practice for people interested in using and improving the tools, and hold workshops for building cross-project collaborations.

International Registered Report Identifier (IRRID): DERR1-10.2196/16861

(JMIR Res Protoc 2020;9(5):e16861) doi:10.2196/16861

KEYWORDS

evaluation; complexity; theory-driven evaluation; diffusion of innovation; scale-up; sustainability; implementation; NASSS (nonadoption, abandonment, scale-up, spread, sustainability) framework; innovation adoption; project management

Introduction

Background

Technologies (which we define broadly as capabilities given by the practical application of knowledge) are often introduced in health care or social care settings as part of an attempt to improve services. Technology implementation projects (defined as active and planned efforts to mainstream a technology and associated changes to routines and services) have a high failure rate, especially when they are large, ambitious, and complex [1-4]. A previous study by our team explored the reasons why a very large, expensive, and centrally driven national program to implement an electronic patient record had failed to achieve its goals [5]. We concluded that such programs unfold as they do partly because nobody fully understands what is going on and that failure may result when this lack of understanding becomes mission-critical [6].

In that and other studies of large-scale innovation and technology implementation projects (see definitions), we have observed a tendency among policymakers and planners to employ bounded rationality—that is, to address an oversimplified and overly rationalized version of the challenge to make solutions seem more achievable [6-8]. Until recently, staff on many such projects had been trained in (and were expected to follow) the PRojects IN a Controlled Environment 2 approach [9], based on highly standardized procedures and a linear logic model with tightly stipulated goals and milestones. Significantly, we could find no health care or social care–based examples of such an approach in the academic literature. This is probably because the introduction of technology-supported change in health care and social care invariably involves not only technical implementation but also the ongoing judicious management of interacting subprojects characterized by competing values, goals, stakeholder interests, and local and national politics—all against a shifting contextual baseline [3,4,10-14].

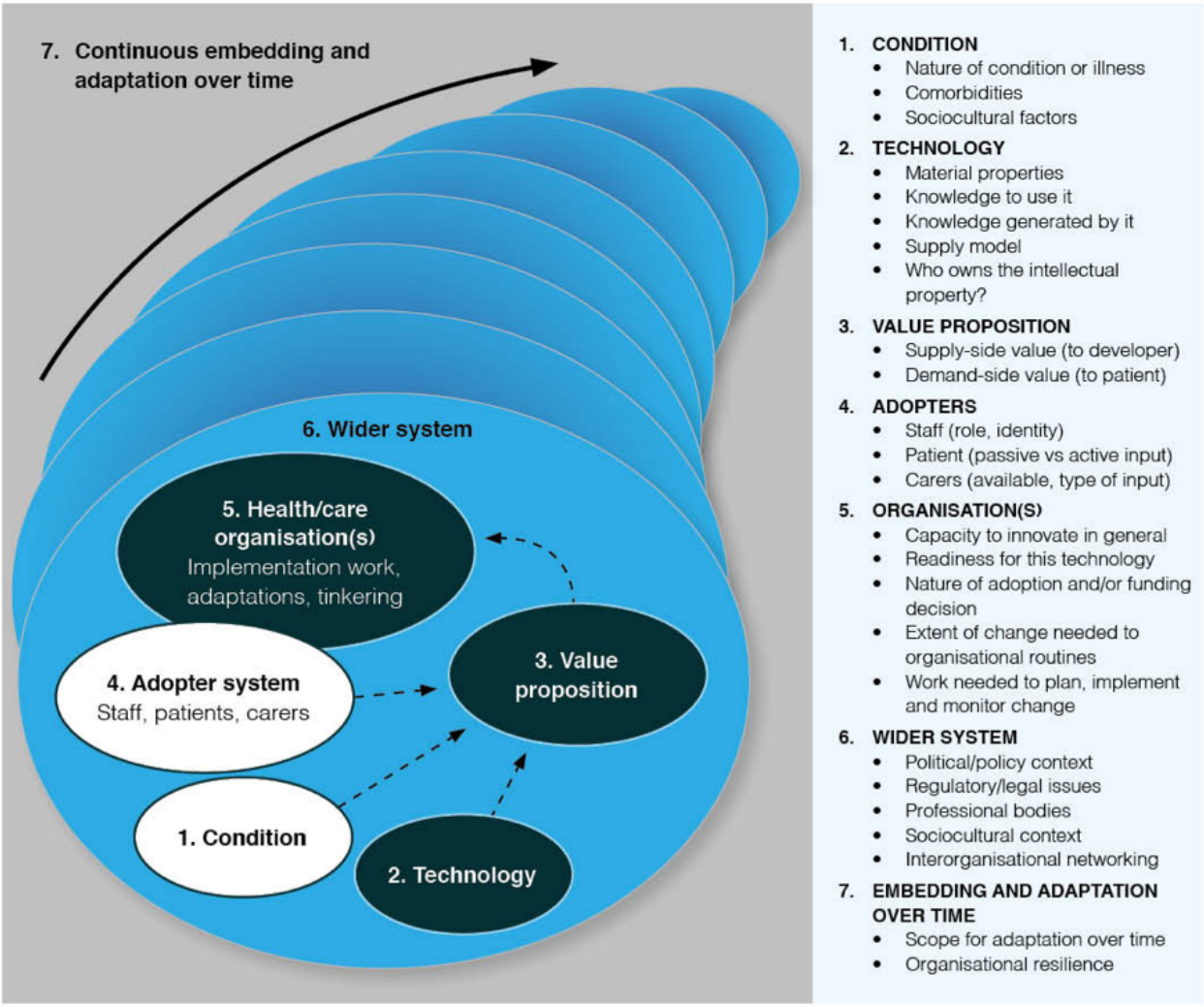
To the extent that technology implementation is a rational and predictable process, both strategic planning and project evaluation can be target-focused and follow a logic model format (what we are trying to do, who will do it, by when, and so on) [15]. However, the introduction of new health care and social care technologies in real-world settings (with concomitant changes in organizational roles and routines) is more typically a social and political process in which power is unevenly distributed and success is defined differently by different stakeholders [15]. In such circumstances, relationships, interstakeholder negotiation, and collective sensemaking are crucial; contextual influences (both anticipated and unanticipated) cannot simply be *controlled for* or stripped out of the analysis [11,16-19].

Complexity has been defined as "a dynamic and constantly emerging set of processes and objects that not only interact with each other, but come to be defined by those interactions" [20]. *Health care innovation* has been defined as a set of behaviors, routines, and ways of working (along with associated technologies), which are perceived as new, linked to the management of a condition or the provision of services, discontinuous with previous practice (ie, not just quality improvement), directed at improving outcomes for service users and/or staff, and implemented by means of planned and coordinated action [20]. *Adoption* is the decision by an individual to engage with, and make full use of, an innovation. Innovations may spread and be implemented by *diffusion* (a passive phenomenon of social influence, leading to adoption), *dissemination* (active and planned efforts to persuade target groups to adopt an innovation), and *implementation* (active and planned efforts to mainstream an innovation) [20].

Complex systems have fuzzy boundaries; their interacting agents operate on the basis of internal rules that cannot always be predicted; and they adapt, interact, and co-evolve with other systems [21]. Complexity is a feature of the system, not merely a characteristic of interventions [22,23]. So-called complex interventions in health care (eg, the introduction of a patient-facing technology aimed at supporting evidence-based behavior change) and the context in which they are expected to have an impact (eg, a community with low health literacy and overstretched primary and secondary care services with high staff turnover) will inevitably be interrelated and reciprocally interacting.

We applied complexity principles in our work on the nonadoption, abandonment, and challenges to scale-up, spread, and sustainability (NASSS) framework whose theoretical development [24] and empirical testing [25] have been described in detail earlier. Briefly, we conducted a systematic literature review alongside six diverse case studies, which were explored longitudinally for 3 years using ethnography, interviews, and document analysis. The NASSS framework (see Figure 1) allows researchers to surface and explain the multiple forms and manifestations of complexity in technology-supported change projects. It consists of six domains—the condition or illness, the technology, the value proposition, the adopter system (intended users), the organization(s), and the wider system (especially regulatory, legal, and policy issues); the seventh, cross-cutting, domain considers how all these interact and emerge over time.

Figure 1. The nonadoption, abandonment, scale-up, spread, and sustainability framework for studying nonadoption and abandonment of technologies by individuals and the challenges to scale-up, spread, and sustainability of such technologies in health and care organizations.



Although the NASSS framework has proved useful for illuminating and theorizing the successes, failures, and partial successes of technology implementation projects, it was designed for academic analysis, not as a practical tool for planning or managing technology projects prospectively. Such tools do, however, exist. Maylor et al [26], for example, developed a complexity assessment tool (CAT), on the basis that "[u]nderstanding and actively managing project complexity has the potential to identify better processes, staffing, and training practices, thereby reducing unnecessary costs, frustrations, and failures".

In developing their original CAT, Maylor et al [26] viewed complexity as something that was subjectively perceived and experienced by managers (as opposed to an abstract property of the system—though it may be that too, and as something that evolves dynamically and more or less unpredictably over time. In addition to a systematic review on complexity in project management [27], Maylor et al [26,28] asked over 120 managers *What makes your project complex to manage?* recognizing that there would inevitably be multiple answers to this question. They distinguished three broad kinds of complexity:

- Structural—related to scale, scope, level of interdependence of people or tasks, and diversity of user requirements
- Sociopolitical—related to the project's importance and its people, power, and politics (both within the project team and across wider stakeholders)
- Emergent—related to how stable the aforementioned issues are predicted to be over time

Maylor et al's [26] original CAT consisted of 32 items, each a statement with which the respondent could agree or disagree. Of the 32 items, 21 related to structural complexity (eg, *The scope can be well-defined*) and 11 to sociopolitical complexity (eg, *Your own senior management supports the work*). Emergent complexity was assessed for each item by the additional question *Do you expect this situation to remain stable over time?*

Maylor et al's [26] empirical work (undertaken across a wide range of companies outside the health care sector) showed that managers with limited domain knowledge typically did not experience a project as complex until their knowledge increased; managers on the same project often described the work quite differently (each identifying different elements of complexity but failing to recognize other elements); and they rarely considered a task to be complex unless or until they had some

personal responsibility for delivering on it. Although project complexity might, in general, be expected to fall over time as unknowns become known and uncertainties shrink, in reality, projects often became *more* complex because of major changes in requirements, abandonment of work by delivery partners, and technical challenges with integration [26].

Maylor et al's [26] rationale for producing the CAT was that if complexity could be better understood by project participants, it could often be reduced or actively managed. The CAT, which was field tested in 43 workshops involving over 1100 managers, was oriented toward a three-stage process—understand, reduce, and respond. These stages could be operationalized using CAT as a self-assessment and orientation tool, along with consultancy support, where needed [28]. The authors were surprised that in most cases, managers were able to identify strategies that allowed them to reduce the majority of complexities that they faced.

In sum, Greenhalgh et al's [24] NASSS and Maylor et al's [28] CAT, which were developed independently (one in health services research and one in business studies), for different purposes, and without knowledge of each other's work, were both centrally concerned with exploring complexity (eg, identifying challenges, uncertainties, and interdependencies) in technology projects. Both tools included questions about operational logistics and about the human and political aspects of projects, and both included a cross-cutting domain to assess emergence over time.

Objectives

In this new study, our aims are both methodological and empirical. Methodologically, we have sought to combine our programs of work to develop, validate, and extensively test a new instrument (NASSS-CAT) for understanding, reducing, and responding to complexity in the health (and health-related social care) sectors. Empirically, we are using NASSS-CAT to support, and generate lessons from, the implementation, routinization, spread, scale-up, and sustainability of technology-supported change in health care and social care.

Our research questions were as follows:

1. Is it feasible and helpful to combine the NASSS framework with CAT that will help with understanding, guiding, monitoring, and researching technology implementation projects in health care and social care?
2. To what extent can the use of NASSS-CAT tools enable the multiple aspects of complexity in health care and social care technology projects to be identified, reduced, and actively managed by policymakers, planners, and project teams?
3. How might the NASSS-CAT tools be used in practice (eg, who should complete the tool, when and how, and is a trained facilitator needed)?

We answer the first of these questions in the following sections, based on work completed to date. In addition, we describe a protocol for answering the second and third questions in a new set of case studies that are currently ongoing.

Methods

Origins, Management, and Governance of the Study

The initial groundwork to develop the NASSS framework was undertaken as part of our SCALS (Studies in Co-creating Assisted Living Solutions, 2015-2020) and VOCAL (Virtual Online Consultations–Advantages and Limitations, 2015-2017) research programs, whose methodology [29,30] and main findings [24,25,31,32] have been reported earlier. Co-design work to develop NASSS-CAT, described in the next section, was undertaken as part of SCALS. Recruitment of six case studies for prospectively testing NASSS-CAT was undertaken as part of a wider program of translational research within the Oxford Biomedical Research Centre [33]. All these programs have (or had) external steering groups with a lay chair and a wide range of stakeholders from UK National Health Service (NHS), social care, industry, academia, and patients. Steering groups meet six-monthly and receive a three-monthly interim report.

The study received research ethics approval from the Health Research Authority and Health and Care Research Wales on June 21, 2019, and from the National Research Service Permissions Coordinating Centre for Scotland on August 9, 2019 (IRAS no. 258679; REC no. 19/LO/0550). Many but not all research ethics committees have deemed the use of the NASSS-CAT *service evaluation* rather than *research*. This reflects an inherent ambiguity in the project: the tools are indeed designed to support service implementation, but there are also research questions (set out above), which seek to generate generalizable findings relating to their use in service evaluation.

Co-Design Phase: Developing and Refining the Nonadoption, Abandonment, Scale-Up, Spread, and Sustainability–Complexity Assessment Tools

This phase was undertaken in 2018-2019. TG and HM mapped Maylor et al's [26] original CAT questions to the seven NASSS domains, merging duplicates from the two instruments and eliminating those irrelevant to health care or social care. This resulted in an early draft of the NASSS-CAT instrument.

A nonprofit digital consultancy firm, mHabitat, which specializes in improving success of public sector technology projects, held six 3-hour workshops involving 42 participants drawn from health care, social care, patient organizations, technology suppliers, and wider stakeholders. They were involved in digital projects, which spanned all stages, from idea to implementation. Workshop participants used design techniques (1) to share examples of health and care projects for which technological solutions were being or had been developed, (2) to analyze these examples by applying a set of structured questions from the draft NASSS-CAT instrument, (3) to reflect on whether and to what extent the questions had helped them identify the complexities in their projects, and (4) to provide feedback about usability and suggest improvements. Written notes, flip charts, and photographic records from each workshop were retained and summarized. A seventh workshop of 2 hours was held with a panel of 8 patients and carers interested in

digital technologies in health care (see the Patient and Public Involvement section).

In response to multiple requests from PhD students and researchers, the NASSS-CAT tools were developed into a semistructured interview guide (NASSS-CAT INTERVIEW).

Selection of Case Studies for Testing the Nonadoption, Abandonment, Scale-Up, Spread, and Sustainability–Complexity Assessment Tools

At the time we were developing the NASSS-CAT tools, we were approached (usually by email and also in lectures or workshops where we were presenting our work) by around 20 teams seeking to use the NASSS framework to support technology implementation. This offered us the potential to test and further refine the NASSS-CAT tools on real-time, real-world projects. We did not have the capacity to support all these projects, so we defined a smaller, purposive sample to provide maximum variety in the following criteria: target population, nature (and system implications) of the condition and the technology, sector (health and/or social care), policy context (policy *push* vs policy negative or neutral), and geographical setting (including non-UK examples). All case studies selected for the testing phase were characterized by a successful proof-of-concept pilot or demonstration project and a strategic decision to attempt local scale-up or distant rollout, both with a view to achieving long-term sustainability.

The cases whose characteristics are summarized in Multimedia Appendix 1 (also see the Summary of Case Studies for more details) illustrate a wide range of challenges in digital health care and social care.

A final selection criterion for our sample of case studies was relevance to our interest in intervention-generated inequalities (IGIs). These arise when only the more digitally capable and digitally equipped members of the target group gain full access to the technology's benefits. As Veinot et al [34] have commented:

> *Many health informatics interventions may not themselves address social factors contributing to health disparities, such as poverty, residential segregation, and discrimination. However, they carry a risk of creating IGIs, and thus worsening underlying inequalities. We propose that such IGIs can be minimized or prevented through thoughtful decisions about access, uptake, adherence, and effectiveness.*

As we are committed to redressing the tendency of technology research to contribute to IGIs, we deliberately selected several case studies that seek to reduce such inequalities, for example, by extending the use of video consultations to underserved groups or adapting video technologies for the elderly *analog generation*.

Summary of Case Studies

Case Study 1: A Digital Dashboard to Increase Engagement in Evidence-Based Schizophrenia Care

This study is based in a secondary care psychiatry service in Gothenburg, Sweden. Schizophrenia is a serious and usually lifelong psychotic condition that typically begins in young adulthood. Treatment includes medication, psychological support, and social support, but compliance with all can be poor. A digital dashboard enabling visualization of key indicators of each patient's health and care status (including structured questionnaires to help evaluate care at medical encounters) was developed with a view to encouraging more active involvement of patients in their own care. Despite a strong coproduction component, scale-up and deployment of the dashboard proved difficult.

Case Study 2: Technology to Support the European Union Falsified Medicines Directive

Falsified and counterfeit medicines are a hazard and occur in every country [35]. With the aim of protecting health and also ensuring sustainability of the European pharmaceutical market, changes to European Union (EU) law were introduced by the Falsified Medicines Directive 2011 (FMD 201162/EC) [36,37]. EU countries, along with the United Kingdom, are committed to implementing the directive. This means introducing, in every pharmacy, a technological solution to support two obligatory safety features: (1) a unique identifier for every package of medicine, and (2) an antitampering device. It also means up-front investment by every pharmacy in hardware and software that can verify the end-to-end supply chain from the manufacturer to the point of supply to the patient. Use of these technologies will require substantial changes to organizational routines and procedures. Preliminary data indicate that few community pharmacies in the United Kingdom are fully prepared for this change. Successful implementation is likely to be influenced by numerous factors, including the attitudes and capabilities of individual pharmacists and the changing structure of pharmacy provision in the United Kingdom (eg, the move from owner pharmacists to corporate chains).

Case Study 3: Video-Mediated Social Connection Technologies

Loneliness (a subjective feeling of lack of social contact) and social isolation (weak or absent social networks) are increasing in older people, many of whom live alone [38]. This is addressed as a government priority in the United Kingdom [39]. Communication with family via a video link can reduce both loneliness and social isolation [38]. A number of technologies have been designed for the *analog generation* (eg, they resemble old-fashioned TV or radio sets and have one or two large buttons). Some are already in use by private purchasers, but as yet, no public sector provider has invested significantly in them. We have begun to work with two suppliers, along with selected social care providers and care homes in both the United Kingdom and Norway, to explore how video technologies may be used more widely as part of a strategy to reduce loneliness.

Case Study 4: Digital Support for Cancer Multidisciplinary Team Meetings

Multidisciplinary team (MDT) meetings are generally considered the gold standard in cancer services, but as workloads have increased in recent years, they have become overcrowded and inefficient [40,41]. A third-party digital solution offers *end-to-end* support for the MDT meeting, including organizing

data collection, visualizing materials (biopsies, scans, and blood test results) on-screen during the meeting, and inserting a summary and decision into the patient's electronic record. Research suggests that efficiency and safety gains could be considerable [42,43], but again, the technology appears disruptive and real-world implementation has been little studied.

Case Study 5: Extending Video Consultations to Become Business as Usual

Our previous research demonstrated the potential for some outpatient and primary care consultations to be undertaken effectively and safely by a video link [31,32]. However, it also showed that such consultations are only offered to a small percentage of eligible patients (often excluding those with limited English, low health literacy, complex health and social needs, or no internet connection at home). We are now working with various public sector and third-sector providers in England, Scotland, Wales, and Australia to support efforts to increase access to video consultations for patients with a much wider range of clinical conditions and also for underserved and underresearched groups whose various needs raise a range of logistical, technical, ethical, cultural, and clinical challenges.

Case Study 6: Digitization of Histopathology Services

This case addresses the introduction, mainstreaming, and regional spread of whole-slide imaging and related technologies in histopathology. Glass slides (eg, surgical biopsies) are scanned into a computer and viewed on screen; they can be retrieved easily and transmitted electronically for specialist opinions. Research suggests that substantial improvements in service efficiency and safety can occur [44,45], and it is hoped the change will help address a serious and worsening workforce crisis in pathology [46]. Due to major implications for workflows and staff roles, digitization of histopathology services is seen as a *disruptive* innovation, which poses daunting challenges for departments.

Early Piloting in Case Study 1

Earlier versions of the NASSS-CAT tools were used in case study 1 (conducted during 2018-2019 in Sweden; see Multimedia Appendix 1 and the Summary of Case Studies). Detailed methods and findings for that study have been published recently [47]. In short, the project goal was to develop a patient portal for people with psychosis. NASSS-CAT was used to structure a 1-day interprofessional workshop attended by 11 participants (line managers, department directors, organization developers, programmers, information technology developers, and clinical professions such as psychiatrists, psychologists, and occupational therapists). The day included both small breakout group sessions and large-group discussions. Outputs included free text mapping of different aspects of project complexity onto the NASSS domains. These were subsequently presented at two feedback sessions to senior and frontline staff involved in planning the future deployment of the technology and used to guide next-step planning.

Action Research in Case Studies 2 to 6

We are currently undertaking groundwork with five other project teams for a set of in-depth, longitudinal case studies in the United Kingdom using the principles of action research [48,49]. This comprises gaining access to the cases, building relationships and mutual understanding (especially of how the different versions of NASSS-CAT can be used to plan, guide, monitor, and evaluate the project), and agreeing on potential data sources and collection methods for monitoring process and outcomes (including data to populate costing models). The main method used at this stage is informal interviews and visits along with attendance at routine meetings; more formal audiotaped interviews will be undertaken where appropriate.

In the next phase, with different case studies commencing at different times over the next 3 to 12 months, we will work collaboratively with health care and social care teams and technology suppliers to support and monitor the implementation of the technological innovation and efforts to achieve sustained changes in work routines and system processes. This will include regular meetings for providing feedback on interim findings, responding to unforeseen events, and capturing learning. In this main action research phase, we will periodically administer the NASSS-CAT PROJECT instrument (see next sections for details) to a sample of project managers and other stakeholders and, following the approach developed by Maylor et al [26,28], generate quantitative data on how the perceived complexity of each project changes over time.

For each case, we plan to collect high-quality data to inform a quantitative before-and-after comparison (with and without the new technology). Metrics will be different in each case and iteratively adapted and will be described in detail in separate, detailed publications for each case. Quantitative data sources may include, for example, usage statistics, waiting times, and proportion of a defined denominator population who are confident users of the technology. All case studies have received some initial funding (see the Acknowledgments section). In some studies, continuation of data collection and analysis for the full study period will depend on securing additional research funding. We plan to follow these five case studies from 2019 to a planned completion date of 2022.

Stakeholder Interviews

We are also undertaking a wider (national and international) case study of the context for innovation. Building on our existing contacts, we will gain access to policymakers (including NHS England, NHS X, NHS Digital, and Health Education England), industries (both large and small technology companies), professional bodies (eg, Royal Colleges and General Medical Council), and patient and advocacy organizations. We will conduct background stakeholder interviews and maintain a two-way dialogue with these stakeholders throughout the study and link them with our dissemination efforts.

Analyzing and Theorizing

Principally, through the various theoretical perspectives that have been built into the NASSS-CAT instrument, we will apply relevant theories of technology adoption, implementation, spread and scale-up, and specific change and monitoring tools. These include theories of individual behavior change (to explain nonadoption and abandonment by individuals), organizational capacity to innovate and readiness for change, technologies as part of complex systems, and value creation. Using empirical

data and cross-case synthesis from the case studies, we will refine and extend the NASSS-CAT tools and linked resources, embracing additional approaches where appropriate.

Patient and Public Involvement

We are committed to patient and public involvement in all stages of this research. We have recently established a standing panel, Patients Active In Research on Digital health (PAIReD) with diversity in age, ethnicity, gender, and educational background. A member of PAIReD (JT) is a coauthor of this protocol. The action research process in each case study (still to be defined in detail) will include contextually appropriate methods for gaining input from patients and service users, including comments on data sources and input to data analysis and action planning. The PAIReD panel, and our wider online network of Patients Active In Research, will be consulted on dissemination activity, especially the preparation of lay summaries and a public-facing website.

Results

Co-Design Phase to Refine the Nonadoption, Abandonment, Scale-Up, Spread, and Sustainability–Complexity Assessment Tools

The co-design workshops generated a great deal of data that allowed us to refine the individual questions on NASSS-CAT. Most participants reported that they found the tools useful and felt that they had gained valuable insights into their technology project (or idea for a project) by using it. Specific issues raised that informed iterative refinement of the tools between workshops included:

- Rationale: Participants suggested an introductory section that explained what the tool was, how it had been developed, and how it was intended to be used.
- Terminology: Participants from different backgrounds were confused by terms used in different domains. For example, some people with a technical background had limited understanding of clinical terms, and many clinicians did not understand questions about business models. Not everyone knew what intellectual property was or what a value chain meant.
- Readability: The workshops identified long sentences, double negatives, and jargon, which were removed in subsequent iterations.
- Length: Adding the various explanations proposed by some participants made the tool very long; therefore, a later group proposed developing an additional short, *taster* version.
- Scoring: Earlier versions had a binary (yes or no) scoring system, but often, the response was *it depends* or *to some extent;* therefore, intermediate options were created.

Some of the co-design feedback was difficult or impossible to incorporate into paper (or PDF) versions of the tools, but we plan to address this issue in a future digital version which is now in production. For example:

- Order of questions: Stakeholders held different views about which order the domains should be listed in. A digital version could have multiple entry points designed for different users.
- Expandable format: The long version of the tool was off-putting and contained long sections that were irrelevant to some projects (eg, some technologies are not condition specific, so domain 1 is redundant). But the short version was too brief for a meaningful analysis of a real-world project. A digital version could be short but have hypertext links to be pursued if relevant.
- Use cases: The co-design workshops generated much discussion on *how* (ie, by whom) and *when* (ie, at what stage in the project) the NASSS-CAT tools might be used. People whose projects were advanced felt the version evaluated would have been useful at an earlier stage, as they felt it summed up the experience they had already gained. Those who had not yet begun felt what many of the questions were premature. A digital version of the tool could identify the phase of the project and take the user to an appropriate set of questions.
- Automatic score tally: Some participants did not want to add up the scores. A digital version could do this automatically and in real time.
- Visualization: Participants suggested various graphics, including histograms and radar charts, which could be incorporated into a digital version.
- Additional resources: The co-design workshops surfaced numerous existing resources, which (if included) would make a paper or PDF version of the tool unwieldy but to which a digital version could link. These include Web-based project management guides and templates, a digital assessment questionnaire designed to guide due diligence and risk assessment before investing in a technology, sources of information about specific diseases or conditions, regulatory standards, and co-design tools for incorporating the patient experience into the design of technologies and care pathways.

Four versions of NASSS-CAT have been produced to date as follows:

- NASSS-CAT SHORT (reproduced in Multimedia Appendix 2), a 3-page taster instrument, in paper (or PDF) format, designed to introduce the instrument and gauge interest. It is semiquantitative in that it seeks *agree/disagree a little/disagree a lot* responses on a range of questions relating to the different NASSS domains.
- NASSS-CAT LONG (Multimedia Appendix 3), a more detailed version of the tool, in paper/PDF and Web-based format (the last is still under development). This version is intended to be used at the stage when there is an idea, a suggestion, or a broad goal to introduce a technology, but there is no formal, agreed project yet. NASSS-CAT LONG can be used for detailed reflection and preliminary project planning, usually (though not necessarily) with support from a trained facilitator. It invites discussion among the project's many stakeholders across six domains, using interpretive (free-text) questions designed to generate a rich narrative and surface uncertainties and interdependencies and survey (closed-item) questions for systematically assessing different kinds of complexity. There is also an

action planning component aimed at shaping the early ideas into a formal project, including due diligence (eg, assessment of quality, safety, and regulatory issues) for the technology.

- NASSS-CAT PROJECT (Multimedia Appendix 4) is a 35-item instrument for monitoring the complexity of a technology implementation project (as perceived by project team members) over time. Five kinds of project-related complexity are considered: strategic, technical, operational, people related (eg, human resources), and political. Project teams may use this tool in a variety of ways—perhaps in an initial in-depth kick-off workshop followed by periodic reviews—and usually with a trained facilitator or project consultant.
- NASSS-CAT INTERVIEW (Multimedia Appendix 5) is a set of prompts for conducting semistructured interviews (eg, by someone doing research into the implementation of a technology).

Case Study 1: Patient Portal for People With Schizophrenia

In case study 1, the NASSS-CAT workshop generated rich data that informed the early stages of the project. Complexity mapping revealed, for example, that while intended adopters (staff and patients) were engaged and keen, there were high levels of complexity in all other domains, including the illness (schizophrenia is a heterogeneous condition with unpredictable course and often multimorbidity and associated social problems; the portal has significant interdependencies with systems controlled by third parties; the value proposition for the technology was uncertain; while departmental tension for change was high, the dashboard did not appear to be a strategic priority for the organization as a whole and the business plan was not considered persuasive; despite a strong pro-technology policy push in Swedish health care, the number of new products competing for attention may have overshadowed the portal project; and the practicalities of implementation appeared complex).

Although the mapping exercise did not generate easy fixes, workshop participants found that surfacing and talking through the complexities were extremely useful for clarifying and working through the project at a time when progress was slow. Recommendations stemming directly from the NASSS-CAT workshop in this case included (1) developing a clear value proposition with information on costs, benefits, and risks; (2) developing and disseminating a rolling shared vision of what the project is and keeping this updated; (3) strengthening project leadership and governance and allocating a dedicated budget to it; (4) focusing initially on the less complex components and functions of the technology; and (5) acting strategically in the wider context (eg, by seeking to rebrand the project to fit a policy initiative). Suggestions for improving the process included attention to detail in advance of the workshop to define each term in the NASSS-CAT tool more precisely in relation to the specific project being discussed. The participants also suggested including additional staff groups in the workshop.

Results of the other five (ongoing) case studies will be presented in subsequent publications.

Discussion

This protocol has described how we combined a theory-informed analytic framework to deepen understanding (NASSS) with a pragmatically focused planning tool to aid implementation (CAT) to produce the four versions of the NASSS-CAT tools and outlined the characteristics and data collection plans for a series of real-world case studies to test these tools. Our approach is based on the principle that if a project is complex, it is unlikely to be effectively managed using a linear, logic model methodology and technocratic progress metrics. On the contrary, the greater the uncertainties and interdependencies in a project, the more crucial it is to avoid oversimplifying and overrationalizing.

A limitation of the NASSS-CAT tools, according to those who favor a more rationalistic approach, is that they are relatively unstructured and likely to generate *messy* data. However, the strength of these tools, we believe, is that for the very reason that they are unstructured, they are particularly suited to addressing the hypercomplexity of many health and care technology projects.

In a recent theoretical paper entitled "Don't Simplify, Complexify," Tsoukas [50] warns against the temptation to produce a simplified and abstracted version of the challenge (an approach he calls *disjunctive theorizing*) and instead seeks to build a rich picture of the case in all its complexity by drawing together different kinds of data from multiple sources using a technique he calls *conjunctive theorizing*. Such an approach assumes an open-world ontology (ie, it sees the world as subject to multiple interacting influences, which must be captured in a rich and dynamic way), a performative epistemology (ie, it focuses on real-world action and on what becomes possible through action), and a poetic praxeology (ie, when writing up case studies, it seeks to produce descriptive details, an apt metaphor, and a narrative coherence) [50].

Our work to date on the NASSS-CAT tools has sought to embrace these features of conjunctive theorizing. The NASSS-CAT LONG, in particular, is designed to capture, through free-text narrative, the numerous interacting influences that could affect project success; to highlight the twists and turns as the project unfolds; and to foreground mundane issues that help explain why the project has stalled. The tool's action-planning section is directed at Tsoukas's [50] performative component (*what becomes possible through action*). Similarly, the NASSS-CAT INTERVIEW is designed to help a participant construct a sensemaking narrative of the (perhaps meandering) fortunes of a complex implementation project.

Another potential limitation of the NASSS-CAT tools is that people who do not understand the unresolvable nature of problems in complex systems may apply them in a rigid and deterministic way rather than—as we intend them to be used—flexibly and imaginatively to accommodate the wide differences between projects. In addition, the tools presented as appendices to this paper might be viewed as definitive rather than preliminary. We anticipate that as experience in using the NASSS-CAT tools accumulates, further refinements will be

made. At this stage, we strongly encourage implementation teams and implementation researchers to view these as *beta versions* and provide us feedback in the form of suggestions for improvements in their design or application.

In the dissemination phase of this study, we aim to produce a range of written and other outputs for academic and lay audiences, including standard academic outputs (peer-reviewed journal articles, conference presentations) plain-language versions of more definitive NASSS-CAT tools, resources (such as customizable templates and facilitator guides), and policy briefings.

In conclusion, we have presented the first iteration of a suite of tools designed to apply complexity principles to understand, guide, monitor, and evaluate technology projects in health and care. Academic and service teams are already using these tools to help achieve implementation, spread, and scale-up of various kinds of technology-supported change. We hope to report both empirical and theoretical findings from the case studies described here and additional cases as these come onstream. We also encourage teams working in low- and middle-income countries to use these tools in formal research or evaluation work, to extend their current scope of application.

Interested colleagues are also asked to note that (subject to further funding) we plan to establish, support, and nurture a community of practice that welcomes both academic, practitioner/policy, and lay members who share our interest in applying, improving, and learning from the NASSS-CAT tools. We are, in principle, interested in providing support to other research groups and implementation teams who seek to use NASSS-CAT in technology implementation, although, in practice, this will depend on our availability (and probably on securing additional external funding).

Acknowledgments

The authors would like to thank the workshop participants for their contributions to improving the NASSS-CAT tools. In addition, they would like to thank the patients and lay members of the PAIReD advisory group for advice on how to make the piloting of the NASSS-CAT tools more relevant to patients and Polly Kerr for support to this group. The VOCAL study was funded by the National Institute for Health Research Health Services and Delivery Research stream (HSDR 13/59/26). The SCALS program was funded by a Wellcome Trust Senior Investigator Award to TG (WT104830MA). Additional work to date has been funded by the Oxford National Institute for Health Research Biomedical Research Centre Partnerships for Health, Wealth, and Innovation Partnerships for Health, Wealth and Innovation theme (BRC-1215-20008) on which TG is the Principal Investigator and also by the Health Foundation (to support extension of video consultations in England, scale-up award to TG, SS, and NHS partners).

Additional funding for individual case studies has been provided by the following local funders as well as in-kind input from local providers: Aneurin Bevan Health Board, Pontypool, Wales (video consultations in Wales, small grant to TG); Scottish Department of Health (video consultations in Scotland, small contract research grant to JW); Oxford University NHS Foundation Trust (digital histopathology and digital MDT care, research capacity funding grant to TG); Academy of Medical Sciences (Springboard Leadership Award to CP); Oxford Economic and Social Research Council Knowledge Exchange Fellowship award to JW (industry engagement on video-mediated communication technology for health and social care); and Sahlgrenska University Hospital, Sweden, Department of Schizophrenia Spectrum Disorders (funding for AG and the digital dashboard pilots).

Authors' Contributions

TG conceptualized the study, co-led the work program with SS, and prepared the first draft of the manuscript. TG and HM produced the draft version of the NASSS-CAT tool. AG, AR, JW, CP, and MK were academic leads on different case studies. VB and NN ran six co-design workshops (TG and her team ran the patient workshop with the PAIReD group). NN worked with TG on iterations of NASSS-CAT. JT was a patient adviser and member of PAIReD. JW led the applications for ethical approval. All authors had input to revisions of the manuscript and approved the final manuscript.

Conflicts of Interest

NN and VB have used the NASSS-CAT tools in paid consultancy and facilitation work for mHabitat.

Multimedia Appendix 1
Characteristics of the six case studies.
[PDF File (Adobe PDF File), 53 KB - resprot_v9i5e16861_app1.pdf]

Multimedia Appendix 2
Nonadoption, abandonment, scale-up, spread, sustainability short.
[DOCX File , 696 KB - resprot_v9i5e16861_app2.docx]

Multimedia Appendix 3
Nonadoption, abandonment, scale-up, spread, and sustainability–complexity assessment tools long.

[DOCX File , 1157 KB - resprot_v9i5e16861_app3.docx]

Multimedia Appendix 4
Nonadoption, abandonment, scale-up, spread, and sustainability–complexity assessment tools project.
[DOCX File , 51 KB - resprot_v9i5e16861_app4.docx]

Multimedia Appendix 5
Nonadoption, abandonment, scale-up, spread, and sustainability–complexity assessment tools interview.
[DOCX File , 439 KB - resprot_v9i5e16861_app5.docx]

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Abbreviations

CAT: complexity assessment tool
EU: European Union
IGI: intervention-generated inequalities
MDT: multidisciplinary team
NASSS: nonadoption, abandonment, scale-up, spread, sustainability
NHS: National Health Service
PAIReD: Patients Active In Research on Digital health
SCALS: Studies in Co-Creating Assisted Living Solutions
VOCAL: Virtual Online Consultations–Advantages and Limitations

Edited by F Drozd; submitted 31.10.19; peer-reviewed by C May, K Beggs; comments to author 25.11.19; revised version received 06.12.19; accepted 13.12.19; published 13.05.20.

Please cite as:
Greenhalgh T, Maylor H, Shaw S, Wherton J, Papoutsi C, Betton V, Nelissen N, Gremyr A, Rushforth A, Koshkouei M, Taylor J
The NASSS-CAT Tools for Understanding, Guiding, Monitoring, and Researching Technology Implementation Projects in Health and Social Care: Protocol for an Evaluation Study in Real-World Settings
JMIR Res Protoc 2020;9(5):e16861
URL: https://www.researchprotocols.org/2020/5/e16861
doi:10.2196/16861
PMID:32401224

Protocol

Impact of Built Environments on Body Weight (the Moving to Health Study): Protocol for a Retrospective Longitudinal Observational Study

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Abstract

Background: Studies assessing the impact of built environments on body weight are often limited by modest power to detect residential effects that are small for individuals but may nonetheless comprise large attributable risks.

Objective: We used data extracted from electronic health records to construct a large retrospective cohort of patients. This cohort will be used to explore both the impact of moving between environments and the long-term impact of changing neighborhood environments.

Methods: We identified members with at least 12 months of Kaiser Permanente Washington (KPWA) membership and at least one weight measurement in their records during a period between January 2005 and April 2017 in which they lived in King County, Washington. Information on member demographics, address history, diagnoses, and clinical visits data (including weight) was extracted. This paper describes the characteristics of the adult (aged 18-89 years) cohort constructed from these data.

Results: We identified 229,755 adults representing nearly 1.2 million person-years of follow-up. The mean age at baseline was 45 years, and 58.0% (133,326/229,755) were female. Nearly one-fourth of people (55,150/229,755) moved within King County at least once during the follow-up, representing 84,698 total moves. Members tended to move to new neighborhoods matching their origin neighborhoods on residential density and property values.

Conclusions: Data were available in the KPWA database to construct a very large cohort based in King County, Washington. Future analyses will directly examine associations between neighborhood conditions and longitudinal changes in body weight and diabetes as well as other health conditions.

International Registered Report Identifier (IRRID): DERR1-10.2196/16787

(JMIR Res Protoc 2020;9(5):e16787) doi:10.2196/16787

KEYWORDS

electronic health records; obesity; built environment; Washington; geography; longitudinal studies

Introduction

Background

Residential context—the features of the neighborhoods we live in—affects our health behaviors and well-being [1,2]. Residential environments have been cross-sectionally linked to diet quality, body weight, and prevalence of obesity and obesity-related health conditions [3-7]. However, such study designs have limited causal interpretability owing to challenges isolating the impacts of a single neighborhood exposure and to the threat of reverse causality [8,9]. With a few notable exceptions [10,11], most studies of the impact of changing residential neighborhoods on health operated at the ecological level [12] or leveraged specific one-time changes such as a new transit system [13-15] or supermarket [16,17]. Meanwhile, studies assessing changes in weight among people who moved [18-20] have been limited by modest sample sizes. As neighborhood features often have only modest effects on behavior [21], studies with few participants frequently fail to identify robust and causally interpretable effects of residential environments [22].

Objectives

The Moving to Health Study, whose design and methods we present here, is using data from Kaiser Permanente Washington (KPWA; formerly Group Health Cooperative) to address this gap [23]. KPWA is a large integrated health insurance and care delivery system in Washington State, serving broad economic strata. By attaching a geographic context to more than a decade of anonymized electronic health records (EHRs) for more than 200,000 adults in King County, Washington (the central county of the Seattle-Tacoma-Bellevue metropolitan statistical area), the study will assess the longitudinal impact of baseline residential built environment, the effect of moving between environments, and the effect of changes in the built environment among those who did not move and on obesity and type 2 diabetes at a heretofore unparalleled scale.

Here, we describe the Moving to Health adult obesity study cohort design, the process of building a longitudinal epidemiologic cohort from health system data, the individual and neighborhood environment characteristics of adults aged 18 years and older in the cohort, and the residential moves that this cohort undertook during 11 years and 4 months of follow-up.

Methods

Setting

We constructed a retrospective observational cohort of adults and children in King County, Washington, using data from KPWA merged with publicly available data on the built environment compiled by the Urban Form Lab at the University of Washington. In this paper, we describe the adult cohort; details and analyses regarding the child cohort will be published separately. All study procedures were reviewed in advance and approved by the KPWA institutional review board, approved a waiver of consent, and the Health Insurance Portability and Accountability Act (HIPAA) authorization to identify and enroll study subjects.

KPWA has approximately 700,000 members in Washington, and 36% of these reside in King County. King County includes Seattle and is the most densely populated county in Washington State. KPWA enrollment in King County is similar to the county's population in terms of income, educational attainment, and representation of racial and ethnic minority groups.

Data Sources

Kaiser Permanente Washington Electronic Health Record

Overview

The majority of member care at KPWA is delivered using EHR databases, which also record the majority of clinical outcomes. KPWA medical centers have used the Epic (Epic Systems Corporation) EHR platform since 2005, the first year of our study. The data contained in the EHR data warehouse include the vital indicators of KPWA member health status. For example, biometric data such as heights, weights, and blood pressure values recorded at clinic visits are fully retrievable for analyses, rendering the available patient profiles more detailed than the *insurance claims only* data available from Medicaid, Medicare, or most health plans that contract with independent medical groups or networks of physicians. By combining KPWA EHR data with other extensive databases used in provision of insurance and care (ie, enrollment, outside claims, deaths, costs, outpatient visits, hospitalizations, emergency room care, pharmacy, radiology, and laboratory databases), we can document all medical and surgical care rendered during the period of their enrollment at KPWA for each study participant that was either delivered in (1) KPWA-owned and KPWA-operated medical centers or (2) in KPWA's contracted network facilities and providers and paid for by the health plan. Specifically, our cohort uses the following data features:

Membership

Dates and status of enrollment, types of insurance coverage, and drug coverage plan were used to determine the periods of eligibility as detailed below.

Residential Locations

Membership files also contain changes in mailing address, typically the home address (mailing address is confirmed every time a patient contacts KPWA, including clinical visits). We geocoded these home addresses to identify latitude and longitude values for residential locations that can be used to link with spatially referenced data from other sources. A total of 95% of members for whom we attempted to geocode all recorded addresses had at least one address matched successfully. Common sources of inability to geocode included the use of a post office box as a mailing address and a form of address too oblique to be *cleaned* such that the geocoder could find the relevant location. We identified residential relocation (hereafter called moves) by comparing successive address records, such that any change in the patient address that resulted in a different location for the geocoded home address constituted a move. We classified patients for whom we identified a move to another

location in the county as *movers* to compare available data for the population whose moves we can analyze to the population as a whole. Geocoding was performed in steps: first, we performed a crude but fast geocode using the SAS (SAS Institute) geocoder with US Census TIGER/Line files to rule out addresses clearly not in King County. Then, to get a more precise home location, we used a composite geocoding approach: we first looked for an exact match in the King County E-911 address points, and then, if no match was identified in the E-911 dataset, we used Esri Business Analyst (ESRI), requiring a *rooftop* match to consider the address successfully geocoded.

Demographics

Date of birth, gender, race, and ethnicity are available in the administrative datasets. These data were self-reported by patients as part of routine clinical practice.

Clinical Measures

Height and weight are measured by clinical staff and recorded in the EHR during clinical visits. These heights and weights have previously been used extensively for research purposes [4,24]. We excluded weight measurements that clinical expertise indicated were biologically implausible for adults (<70 pounds or ≥700 pounds). Smoking status was self-reported through patient questionnaires deployed during clinical visits.

Utilization, Diagnoses, and Procedures

The KPWA EHR includes dates and types of health care utilization for inpatient, emergency department, and outpatient settings. Using the baseline visit and all records dating to the previous 12 months, we constructed an Elixhauser comorbidity score [25,26]. As our baseline was 2005 and all subjects were aged 18 years or older at baseline, we consulted EHR records from as far back as 2004 and for patients as young as 17 years at the time of the visit to construct this score. We also used these records to assess the baseline prevalence of conditions of particular interest, including diabetes, hypertension, dyslipidemia, depression, and anxiety. Codes used to infer the presence of health conditions are available from the authors on request.

Measures of Neighborhood Context

As of December 2019, we have constructed six neighborhood environment measures (Table 1) and anticipate constructing more. These measures are drawn from publicly available geographic information systems (GIS) data layers and were selected to assess aspects of neighborhoods thought to influence physical activity behaviors and weight trajectory. Obtaining multiple GIS-based environmental measures for hundreds of thousands of point locations is challenging; to accomplish this, for each variable of interest, we first constructed SmartMaps [27], which are spatially continuous rasterized surfaces, where each raster cell contains the average value of the environmental feature of interest within a predetermined distance (Figure 1). The maps allow efficient estimation of environmental characteristics for large numbers of point locations. We used each SmartMap to assign the selected neighborhood measure to each subject home location at baseline and multiple follow-ups, based on historical GIS data temporally matched with the EHR. This approach avoids typical GIS workflows that require computing each environmental measure for each individual geocoded location. We used radial buffers rather than network buffers for most SmartMaps to minimize computational costs. An additional advantage of the SmartMap approach is that SmartMaps can be constructed by team members outside of KPWA without the need for HIPAA-protected home addresses. SmartMaps were developed using PostgreSQL, PostGIS, and R (R Foundation).

Table 1. Selected neighborhood built environment variables in the Moving to Health cohort study.

Domain and variable[a]	Data source	Median values for 1600 m buffer at baseline (first quartile, third quartile)	Years of data available	Radial buffer distance (m)
Neighborhood composition				
Residential density, units/hectare	King County Assessor's office	9 (6, 15)	2005-2017	800, 1600
Population density, residents/hectare	American Community Survey	21 (14, 31)	2005-2017	800, 1600
Property value per residential unit (US $), 2017	King County Assessor's office	282,949 (21,543; 373 470)	2005-2017	800, 1600
Transportation systems				
Street intersection density, intersections/hectare	TIGER/Line files	0.6 (0.5, 0.8)	2010-2018	800, 1600
Food environment				
Supermarket count	PHSKC[b]/UFL[c]	1 (0, 2)	2008, 2012, 2015	1600, 5000
Fast food retailer count	PHSKC/UFL	2 (0, 6)	2008, 2012, 2015	1600, 5000

[a]These variables have been constructed. Additional variables are planned as described in the manuscript text, and new variables can be added as data become available.

[b]PHSKC: Seattle/King County Public Health department.

[c]UFL: University of Washington Urban Form Lab.

Figure 1. SmartMaps of selected neighborhood measures used in the Moving to Health Cohort, 2005 to 2017. The top panel shows residential density in Western King County within 800 m (inset map of greater King County) in 2005. The bottom panel supermarket count within 1600 m in the same area in 2008.

We have constructed measures covering the following domains of neighborhood conditions; however, a key feature of our cohort design is that other measures of the built environment can be easily added in the future as the data become available:

Neighborhood Composition

The physical and social composition of a neighborhood may influence walkable access to retail and daily routine destinations, perceptions of the safety of outdoor physical activity, and other weight-relevant behavioral health norms. Our neighborhood composition measures included residential density (housing units/land area) [28-30] and population density (residents/land area) [6,31,32] to capture the intensity of neighborhood development and related mix of land uses, as well as residential property values as a dimension of neighborhood socioeconomic status [5]. We will develop a measure of employment density for use with this cohort.

Transportation Infrastructure

Transportation infrastructure affects a resident's ability to choose active transportation options, which, in turn, may prevent obesity. Street intersection density, a measure of walking connectivity, has been found to be negatively associated with obesity, albeit inconsistently [33,34]. Similarly, access to sidewalks and trails is also thought to encourage walking and prevent obesity, although findings focused on walking infrastructure have also been inconsistent [35-37]. We have measured street intersection density from King County GIS data and will measure trail density using King County GIS data and transit ridership per bus stop as reported by King County Metro, which operates the bus system within the county.

Food Environment

The food environment has been strongly correlated with obesity, but questions remain as to whether the relationship is causal [6,38,39]. Measures of the food environment for our cohort included densities of supermarkets and fast food restaurants as reported by King County Public Health and geoprocessed by the University of Washington Urban Form Lab [40], and we will construct a similar measure of convenience stores. As most King County residents drive to shop for food [41], the SmartMaps for food environment measures used network buffers to account for road network impacts on driving distances.

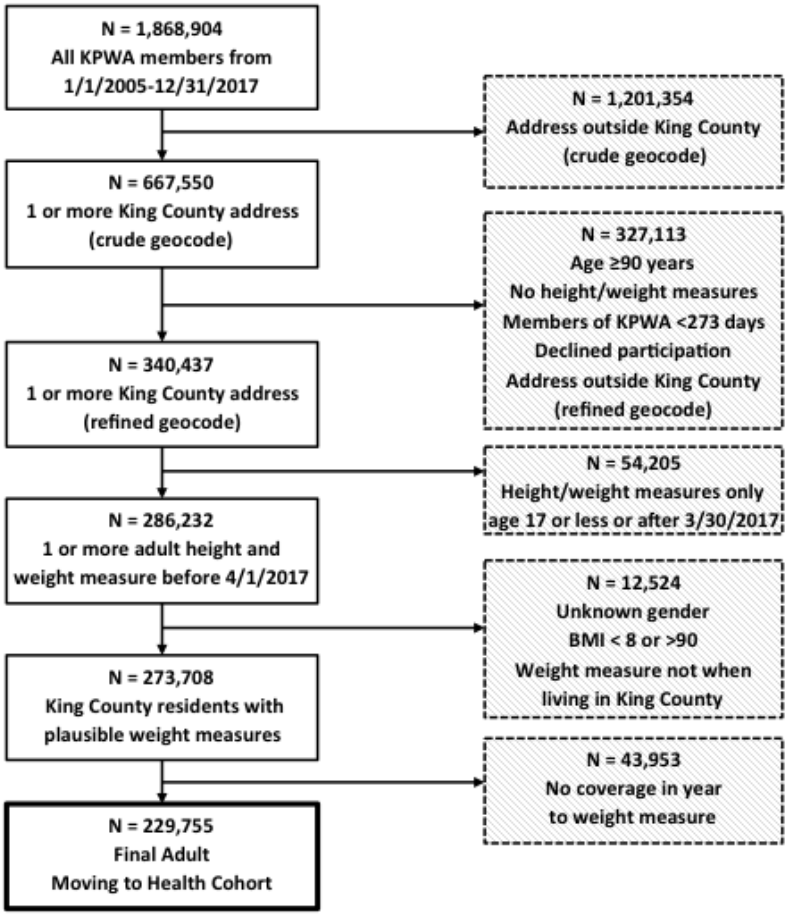
Recreational and Fitness Environments

Neighborhood parks are thought to encourage physical activity that prevents unhealthy weight gain [42,43]. We will compute the percent of land area dedicated to parks as reported by King County and local municipalities and compiled by the University of Washington Urban Form Lab [42]. Future analyses may also incorporate gyms, exercise studios, swimming pools, and other venues for recreational activity.

Identifying a Cohort From Electronic Health Record Data

To construct the study cohort, we initially identified KPWA members aged 18 to 89 years between January 1, 2005, and December 31, 2017, whose home addresses were successfully geocoded to a King County location and for whom height and weight data were available. We required a successful geocode because our goal was to assess the impacts of residential location. We excluded members older than 89 years owing to concerns that older age could be personally identifying. We later determined that an EHR system change rendered address changes after April 30, 2017 inconsistent and limited our data to records of visits before May 1, 2017. We included KPWA members who had a recorded weight measure while they were a resident of King County, Washington, after having been a KPWA member for at least 1 year to help ensure we had sufficient data to estimate the prevalence of comorbid health conditions before their weight measurement. Figure 2 is a flow diagram describing the identification of this cohort.

Figure 2. Flow diagram showing selection from the Kaiser Permanente Washington membership to the Moving to Health Cohort.

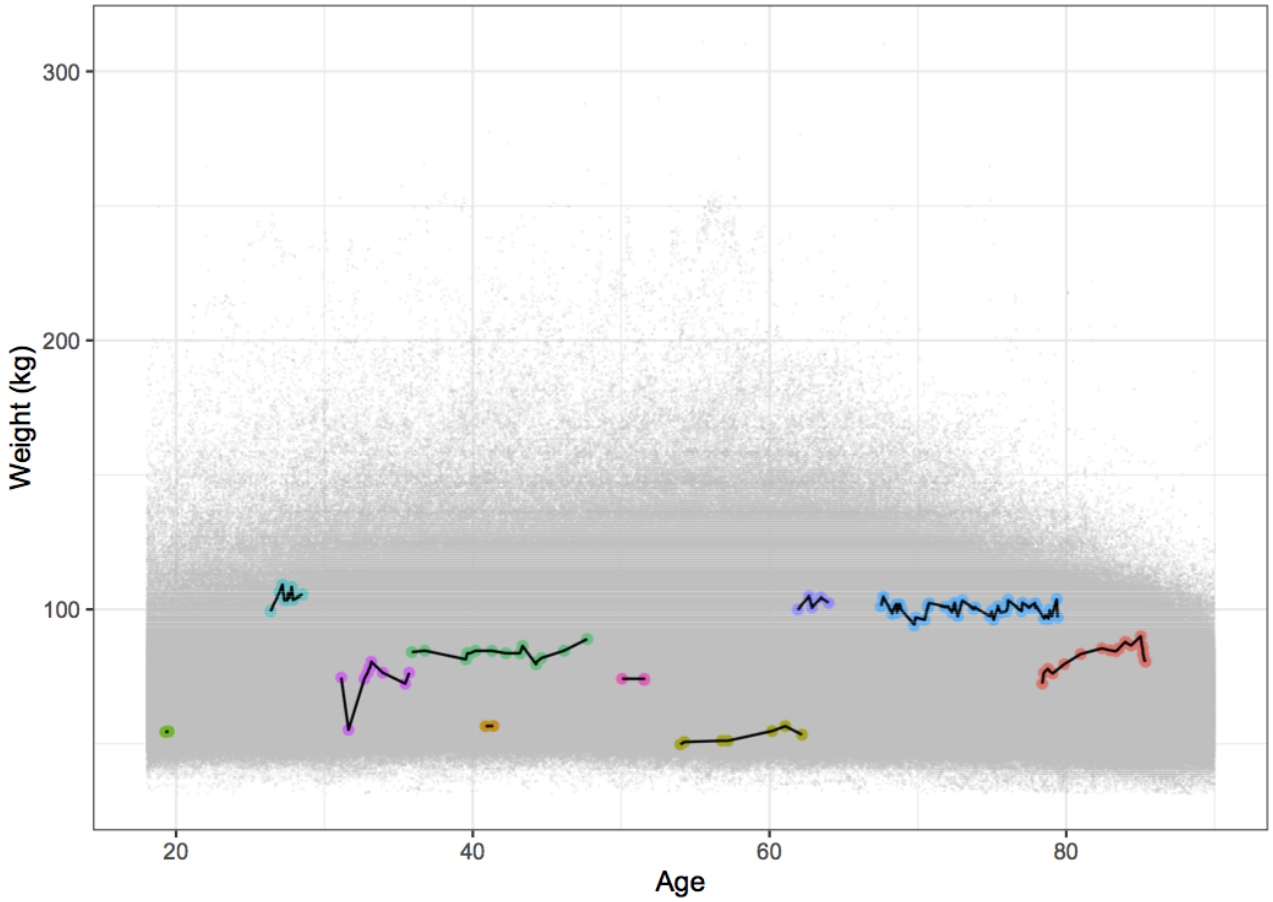


Follow-Up and Outcomes

We defined the first eligible weight measure of an individual in the cohort to be their *baseline* measure. We considered a member to be followed at each clinic visit after the baseline visit and censored before the end of follow-up if he or she moved out of King County or was not a member of KPWA for at least 13 months. Once censored, individuals did not rejoin the cohort even if they became KPWA members again. We did not censor women during pregnancy. This will allow us to conduct analyses incorporating pregnancy weight change; however, we anticipate that analyses not focused on pregnancy will need to handle pregnancy episodes appropriately.

The primary outcome of our future analyses will be weight change over time. We intend to focus on weight change rather than BMI change to minimize artifacts that could arise because of the height measurement error in this cohort of adults whose height change should be minimal. Figure 3 is a plot of weight measurements over time, with trajectories of selected study subjects highlighted as examples. There is substantial variability in weight trajectory, follow-up, and within-subject variability over time. Additional analyses will examine changes in glycemic control among patients with type 2 diabetes, as measured by the serum glycosylated hemoglobin test; these outcomes will be described in future manuscripts.

Figure 3. Weight values recorded in the Moving to Health adult cohort, 2005 to 2017, with selected individual weight trajectories highlighted to demonstrate the range of within-subject follow-up, variability, and weight trajectory over time.



Analyses

The analyses for this cohort description manuscript focused on baseline characteristics of the study cohort, comparison of movers with nonmovers to the full cohort, and exploration of the characteristics of residential moves undertaken by cohort members. All analyses were descriptive and conducted in R for Windows version 3.5.2 (Vienna, Austria).

Results

Exclusions

The records of 4,208,674 clinic visits that included a weight assessment among 286,232 unique adults met initial inclusion criteria. After applying the exclusion and censoring criteria as depicted in Figure 2, 3,061,603 visits by 229,755 adults remained. Most exclusions (43,953/229,755, 19.1%) of the adults identified in the initial data extraction) were subjects for whom a baseline weight measure could not be identified because the EHR included no weight measure during a time window in which the subject had been a KPWA member for the prior year.

Population Characteristics

The final study population was a broad cross-section of King County adults (Table 2). Nearly 58.0% (133,326/229,755) of the study population was female, the mean age was 45.0 years, and approximately 59.5% (136,793/229,755) reported non-Hispanic white race/ethnicity. The mean BMI at baseline was 27.7 kg/m^2, and about 70.1% (161,246/229,755) of the participants were in the 18.5 to 30 kg/m^2 BMI range typically associated with the lowest mortality risk. The IQR for BMI at baseline was 23.2 to 30.7.

Table 2. Baseline characteristics of participants in Moving to Health Cohort Study, King County, Washington, 2005 to 2017.

Characteristic	Total (N=229,755)	Moved within county (n=55,152)	Never moved within county (n=174,603)
Years of follow-up, mean (SD)	5.0 (3.7)	6.1 (3.5)	4.6 (3.7)
Year of cohort entry, n (%)			
2005-2007	101,543 (44.2)	26,501 (48.1)	75,042 (43.0)
2008-2010	38,487 (16.8)	11,308 (20.5)	27,179 (15.6)
2011-2013	49,410 (21.5)	11,692 (21.2)	37,718 (21.6)
2014-2017	40,315 (17.5)	5651 (10.2)	34,664 (19.9)
Age in years at cohort entry, mean (SD)	45.0 (17.3)	41.5 (17.1)	46.2 (17.2)
Age categories (years), n (%)			
18-29	55,624 (24.2)	17,519 (31.8)	38,105 (21.8)
30-44	62,861 (27.4)	17,504 (31.7)	45,357 (26.0)
45-54	42,030 (18.3)	7991 (14.5)	34,039 (19.5)
55-64	38,212 (16.6)	5940 (10.8)	32,272 (18.5)
65-89	31,007 (13.5)	6194 (11.2)	24,813 (14.2)
Gender, n (%)			
Male	96,429 (42.0)	21,658 (39.3)	74,771 (42.8)
Race/ethnicity, n (%)			
Asian	27,573 (12.0)	6496 (11.8)	21,077 (12.1)
Black	13,420 (5.8)	4096 (7.4)	9324 (5.3)
Hawai'ian/Pacific Islander	2278 (1.0)	694 (1.3)	1584 (0.9)
Hispanic	11,275 (4.9)	3127 (5.7)	8148 (4.7)
Native American/Alaskan Native	2585 (1.1)	671 (1.2)	1914 (1.1)
Other	2797 (1.2)	726 (1.3)	2071 (1.2)
Unknown	33,034 (14.4)	6745 (12.2)	26,289 (15.1)
Non-Hispanic white	136,793 (59.5)	32,597 (59.1)	104,196 (59.7)
Height (m), mean (SD)[a]	1.69 (0.1)	1.69 (0.1)	1.69 (0.1)
Weight (kg), mean (SD)	79.3 (21.0)	78.6 (21.1)	79.5 (21.0)
BMI (kg/m^2), mean (SD)	27.7 (6.4)	27.5 (6.5)	27.8 (6.4)
BMI categories (kg/m^2), n (%)[a]			
<18.5	3399 (1.5)	873 (1.6)	2526 (1.5)
18.5-25.0	85,572 (37.4)	22,114 (40.2)	63,458 (36.6)
25.0-29.9	75,674 (33.1)	17,325 (31.5)	58,349 (33.6)
30.0-34.9	36,745 (16.1)	8266 (15.0)	28,479 (16.4)
≥35.0	27,056 (11.8)	6395 (11.6)	20,661 (11.9)
Weight measurements			
Number of BMI measures, mean (SD)	13.3 (17.8)	17.0 (19.4)	12.2 (17.2)
Any BMI measures 1+ years apart, n (%)	154,040 (67.0)	46,868 (85.0)	107,172 (61.4)
Any BMI measures 3+ years apart, n (%)	103,314 (45.0)	33,847 (61.4)	69,467 (39.8)
Any BMI measures 5+ years apart, n (%)	72,726 (31.7)	23,798 (43.2)	48,928 (28.0)
Any BMI measures 9+ years apart, n (%)	37,612 (16.4)	10,971 (19.9)	26,641 (15.3)
Elixhauser score, mean (SD)	0.7 (1.2)	0.7 (1.1)	0.7 (1.2)
Comorbidities prior to baseline, n (%)			

Characteristic	Total (N=229,755)	Moved within county (n=55,152)	Never moved within county (n=174,603)
Diabetes	13,345 (5.8)	2786 (5.1)	10,559 (6.0)
Hypertension	30,182 (13.1)	5907 (10.7)	24,275 (13.9)
Dyslipidemia	17,964 (7.8)	3165 (5.7)	14,799 (8.5)
Depression	23,385 (10.2)	6166 (11.2)	17,219 (9.9)
Anxiety	18,636 (8.1)	5016 (9.1)	13,620 (7.8)
Smoking status, n (%)[b]			
Current	23,920 (13.2)	6237 (14.4)	17,683 (12.8)
Former	35,915 (19.7)	8198 (19.0)	27,717 (20.0)
Never	120,654 (66.3)	28,511 (66.0)	92,143 (66.5)
Did not respond	1362 (0.7)	265 (0.6)	1097 (0.8)
Property value per unit at home address, 2017 (US $), mean (SD)[c]	354,464 (265,517)	313,455 (263,759)	366,932 (264,795)

[a]Modal height missing from 0.5% of the cohort.

[b]Smoking status missing from 20.9% of the cohort who never received survey.

[c]Property values at home address missing from 9.8% of the cohort.

Follow-Up

The baseline visit for approximately 44.1% (101,543/229,755) of the final analytic cohort was in the first 3 years of study enrollment, between January 1, 2005, and December 31, 2007. The mean follow-up was slightly less than 5 years, and follow-up ranged from 1 day to 12 years and 118 days, 3 days shy of the full follow-up period. Weight measures at least 1 year apart were available for 67.0% (154,040/229,755) of subjects, measures at least 5 years apart were available for 31.6% (72,726/229,755) of subjects, and measures at least 9 years apart were available for 16.3% (37,612/229,755) of subjects. In addition, 43.9% (101,053/229,755) of subjects were still enrolled at the end of study follow-up; the most common (87,116/229,755, 37.9%) reason for censoring was that the subject disenrolled from KPWA for at least 13 months.

Moves

Approximately 24.0% (55,152/229,755) of the cohort moved at least once during follow-up. Movers were a somewhat younger subcohort (mean age 41.5 years among movers compared with 45.0 overall) and tended toward longer follow-up (54% followed for 5 years or more compared with 39% overall). This may be because those who remained a member with KPWA for longer had a greater probability of their membership time overlapping with a move. In addition, 67.8% (37,388/55,152) of movers moved only once during the follow-up. Figure 4 is a histogram of residential tenure at each address tracked in the study.

In total, the 55,152 movers made 84,698 moves (Table 3). A total of 45.9% (38,911/84,698) of these moves were less than 5 km in distance, and destinations had residential densities and property values more like origins than would be expected by chance (χ^2 test $P<.001$). For example, although only 19.8% (16,803/84,698) of moves were initiated from residential locations with densities of 18.7 units/hectare (roughly that of a 1920's era *streetcar suburb* neighborhood) or more, 53.5% (8962/16,803) of those moves were to destinations that also had residential densities of 18.8 units/hectare or above (Figure 5, top panel).

Figure 4. Histogram of location-specific follow-up (residential tenure) in the Moving to Health cohort, 2005 to 2017. The peak around 13 years corresponds to people who were enrolled throughout the full study period without moving.

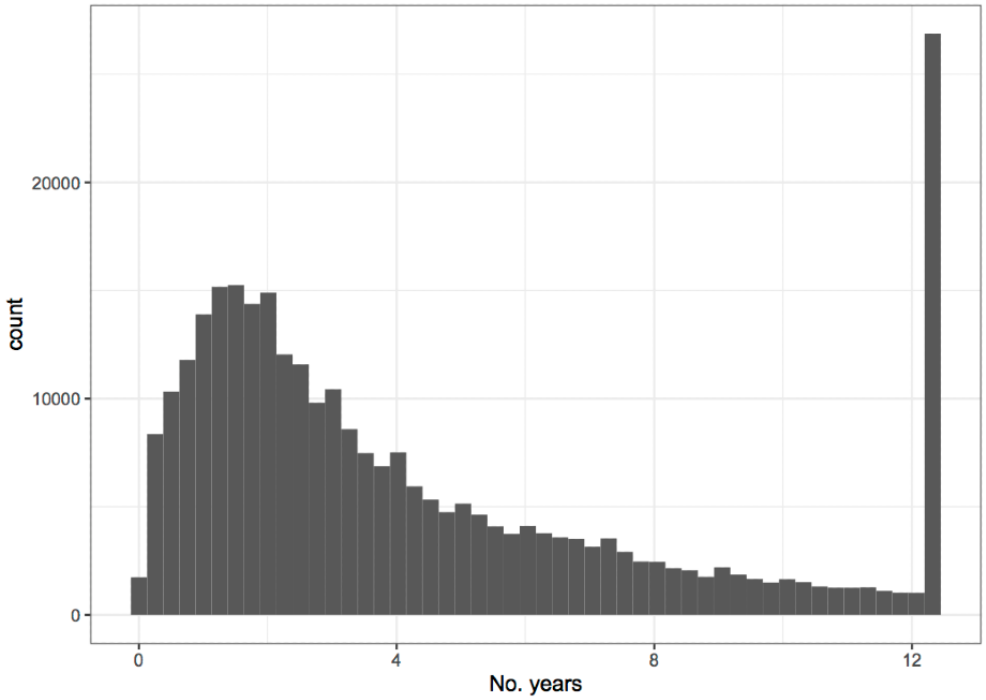
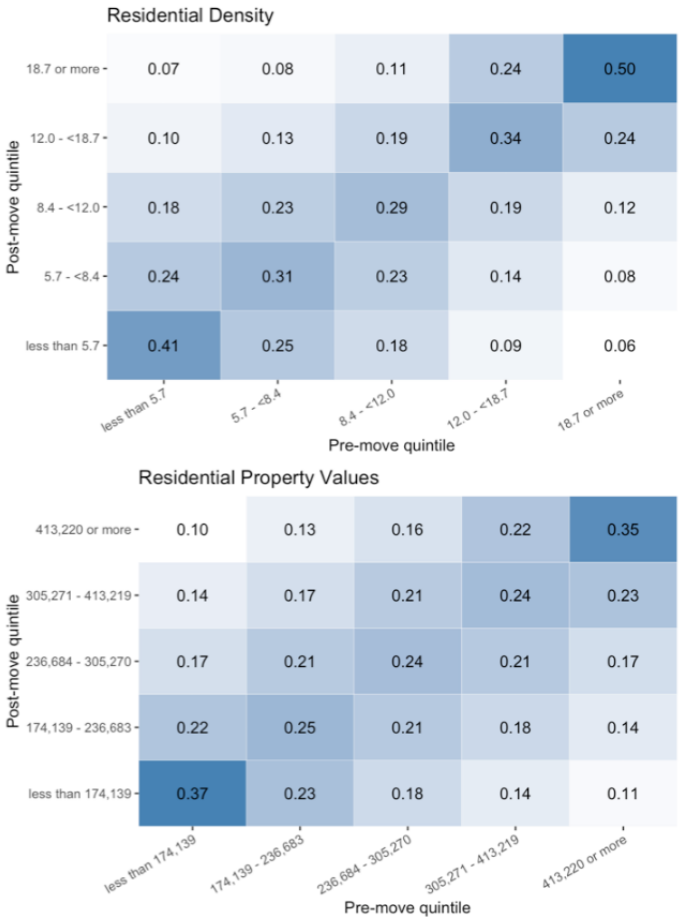


Table 3. Selected characteristics of the 84,698 residential moves within King County, Washington, occurring during Moving to Health Cohort follow-up, 2005 to 2017.

Characteristic	Change
Order of move, n (%)	
First move for this member	55,152 (65.1)
Second move for this member	17,764 (21.0)
Third or more move for this member	11,782 (13.9)
Year of move, n (%)	
2005-2007	16,443 (19.4)
2008-2010	20,118 (23.8)
2011-2013	23,365 (27.6)
2014-2017	24,772 (29.2)
Distance between residential locations in the move (km), n (%)	
<1	11,003 (13.0)
1-4.9	27,908 (33.0)
≥5.0	45,787 (54.1)
Change in selected neighborhood characteristics, median (first quartile, third quartile)	
Residential density within 800 m, housing units/hectare	0.1 (−4.1, 4.2)
Population density within 800 m, population/hectare	−0.5 (−9.4, 7.5)
Street intersection density within 800 m, intersections/hectare	0 (−.19, .15)
Mean residential property value within 800 m ($), 2017	−9173 (−113 805, 8 9 537)
Supermarket count within 1600 m	0 (−1, 1)
Fast food restaurant count within 1600 m	0 (−3, 2)

Figure 5. Heat maps showing quintiles of neighborhood residential density and property value within 800 m across moves among persons in the Moving to Health cohort, 2005 to 2017. Numbers in grid cells indicate the proportion of those in the premove quintile whose move destination was in the associated postmove quintile. For example, the top right corner of the top panel indicates that 50% (9519/19,107) of those living in locations where residential densities were 18.7 units/hectare or more before a move moved to locations with residential densities of 18.7 units/hectare or more.



Discussion

Principal Findings

In this population-based, retrospective cohort constructed from KPWA medical records, we have identified 229,755 adults aged 18 to 89 years who lived in King County, Washington, who were continuously enrolled in KPWA for at least 1 year, and for whom at least one weight measure is available for analysis. Of these adults, an average of about 5 years of follow-up was available, and 55,152 moved within the county at least once.

To the best of our knowledge, this is the first large-scale EHR-based cohort developed to assess the impact of residential moves on the health of adults [44]. However, there is prior work assessing neighborhood influences on BMI change in children using EHR data [45], and there is a substantial literature on the reasons that people change the residential location and the process by which movers select residential locations [23,46-48]. Our finding that nearly half of our recorded moves were within 5 km of the initial residential location is consistent with prior findings that moves in Western Washington and elsewhere tend to be within corridors or neighborhoods [49,50]. As short distance moves imply limited changes to neighborhood built environments, substantial statistical power is needed to assess the impacts of moves.

Strengths and Limitations

Indeed, the sample size and considerable follow-up time available are key strengths of this cohort [10,11]. Individual health impacts of built environments are likely to be small in general, but because many people are affected by the same characteristics, impacts that may be small at the individual level can still have large population impacts [1]. Another key strength of our design is our use of EHR cohorts for population inferences [51]; our design may act as a template for future similar studies in other populations in other geographic contexts. The sample size is large for examining health outcomes such as obesity, type 2 diabetes, and hypertension, and data on health outcomes are comprehensive in that they include all diagnoses and treatments paid for by Kaiser Permanente insurance during the study period. More generally, our work was possible only because of a foresighted health system decision to treat residential address as patient data to be recorded longitudinally rather than contact information to be updated without maintaining the old value.

Studies using our cohort will also be subject to several limitations. First, this is an EHR cohort, and the research team is not interacting with study subjects directly, which precludes collecting some data that may be readily available in more conventional cohort designs. For example, there are no available measures of the behaviors through which exposure to

neighborhood environments might affect weight change, such as physical activity or diet. Second, because the data were not initially collected for research purposes, some potentially relevant covariates are missing (eg, race/ethnicity, particularly in the early years of the cohort), and we cannot verify whether those data are missing at random. Third, weight change, which captures not only changes in fat mass but also changes in lean mass, can be challenging to interpret as an indicator of health [52]. Fourth, our cohort excludes members who listed a post office box address or whose address otherwise could not be geocoded, who may be different from other members. Fifth, residential address recorded in the EHR does not fully capture a subject's environment, both because residential environment is only a subset of environment encountered and because address in the dataset may only partially reflect the true home location of some members, such as students attending college. Finally, although King County is large and geographically diverse and our cohort demographics resemble those of the county as a whole, county residents are wealthy relative to the rest of Washington State, and the region has fewer African American and Hispanic residents than the country as a whole.

Conclusions

In conclusion, the Moving to Health Cohort is a very large, EHR-based cohort that offers novel potential for identifying neighborhood effects on obesity and obesity-related conditions.

Acknowledgments

This study was funded by a grant from the National Institute for Diabetes and Digestive and Kidney Diseases, 5R01DK114196. SM was supported by 1K99LM012868. The authors would like to thank Chris Mack for his assistance with geocoding our cohort.

Conflicts of Interest

None declared.

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Abbreviations

EHR: electronic health record
GIS: geographic information systems
HIPAA: Health Insurance Portability and Accountability Act
KPWA: Kaiser Permanente Washington

Edited by G Eysenbach; submitted 24.10.19; peer-reviewed by N Bhavsar, YH Yaw; comments to author 06.12.19; revised version received 20.12.19; accepted 07.01.20; published 19.05.20.

Please cite as:
Mooney SJ, Bobb JF, Hurvitz PM, Anau J, Theis MK, Drewnowski A, Aggarwal A, Gupta S, Rosenberg DE, Cook AJ, Shi X, Lozano P, Moudon AV, Arterburn D
Impact of Built Environments on Body Weight (the Moving to Health Study): Protocol for a Retrospective Longitudinal Observational Study
JMIR Res Protoc 2020;9(5):e16787
URL: https://www.researchprotocols.org/2020/5/e16787
doi:10.2196/16787
PMID:32427111

Protocol

Assessing the Real-Time Mental Health Challenges of COVID-19 in Individuals With Serious Mental Illnesses: Protocol for a Quantitative Study

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Abstract

Background: The outbreak of coronavirus disease 2019 (COVID-19) has caused significant stress and mental health problems among the general public. However, persons at greatest risk for poor mental health outcomes, such as people with serious mental illness, have been largely overlooked.

Objective: This paper presents the protocol for a study that aims to examine the mental health impact of COVID-19 and social distancing behaviors in people with serious mental illness and the behaviors undertaken to prevent COVID-19 infection in this group.

Methods: Participants will include individuals with serious mental illness (eg, schizophrenia, bipolar disorder) and nonpsychiatric control participants who are currently participating in or have previously participated in several ongoing parent observational studies. Data will be collected from April 2020 through August 2020. Participants will complete phone interviews at 2 time points to assess their current emotional functioning and discuss the measures they have taken to prevent COVID-19 infection. Baseline (pre-COVID-19) mental health, sampled by ecological momentary assessment over an extended period, will be compared with current mental health, also sampled by ecological momentary assessment over an extended period. Demographic, cognitive, and psychosocial factors at baseline will be used to examine risk and resilience to current mental health and coping.

Results: The inclusion of participants for the first round of telephone assessments started on April 3, 2020 and will be completed by May 31, 2020. As of April 30, 2020, 101 individuals had completed these first-round assessments. The second round of telephone assessments will likely occur between June 1, 2020, and August 31, 2020. Study results will be published in peer-reviewed scientific journals.

Conclusions: Our findings will have broad implications for understanding the psychological consequences of COVID-19 among vulnerable persons with serious mental illness and will provide the opportunity to identify targets to reduce negative outcomes in the future. We also hope our efforts will provide a roadmap and resources for other researchers who would like to implement a similar approach.

International Registered Report Identifier (IRRID): DERR1-10.2196/19203

(JMIR Res Protoc 2020;9(5):e19203) doi:10.2196/19203

KEYWORDS

mental disorders; technology; telemedicine; pandemic; psychology; stress; social distancing; coping; COVID-19; public health

Introduction

Coronavirus disease 2019 (COVID-19) has created a global pandemic and disrupted our society and daily lives. Americans have been forced to separate from their workplaces and their friends, engage in previously foreign behaviors including "social distancing" and "sheltering in place," and unemployment rates have jumped to unprecedented highs. The media have mainly focused on the psychological effects of COVID-19 in the general public, largely overlooking its impact on the most vulnerable groups in our society. The aim of this paper is to present the protocol for a study that will examine the effect of the pandemic on people with serious mental illness (SMI).

A recently published review in Lancet Psychiatry outlined the heightened risk of COVID-19 transmission among people with mental health disorders [1]. In addition to increased risk for infection, people with mental health disorders, and particularly those with SMI, could experience greater susceptibility to emotional responses to the pandemic, such as fear, anxiety, stress, depression, as well as risk of relapse or worsening of positive (eg, paranoia, hallucinations) and negative (eg, anhedonia, apathy) psychotic symptoms. This could be due to several reasons, including higher vulnerability to stress compared to the general population [2,3], reduced access to resources to permit ongoing mental health treatment and services [4,5], greater job or food insecurity [6,7], and additional restrictions in existing congregated situations such as group homes [8]. Social isolation or distancing may be less discrepant from daily living in some people with SMI than the general population. Moreover, some people with SMI may be less engaged in social networks and standard news media. Thus, the hypothesis of reduced subjective stress compared to the population in general needs to be considered.

On the other hand, health messages and awareness of the crisis are quite likely to not be well disseminated to people with SMI, creating a public health risk for individuals with SMI and others with whom they may have contact. An additional issue is challenges in the ability to understand and comply with complex directives and precautionary measures. People with SMI represent about 2%-3% of the population, and COVID-19 may result in collective increases in symptom severity, which, in turn, could result in expansive increases in mortality, emergency care utilization, and distress. Thus, it is critical to understand the influences of the COVID-19 pandemic on people with SMI. Further, our previous research has suggested that people with SMI are particularly challenged in self-assessments of both their emotional states and of their ability to engage in productive behaviors targeting their everyday functioning and self-management [9,10].

Our research team has two ongoing studies centered around Strategy 3.1 of the National Institute of Mental Health's (NIMH) strategic plan to "identify and validate new targets for treatment development that underlie disease mechanisms" [11]. Both studies are multisite collaborations between the University of Texas at Dallas, University of California San Diego, and the University of Miami. Study 1 (principal investigator [PI]: author AEP, R01MH112620) assesses the construct of introspective accuracy, or the ability to correctly judge one's own skills and abilities. The goals of this study are (1) to learn how impaired introspective accuracy in individuals with serious mental illness contributes to difficulties in real-world functioning, (2) to understand how introspective accuracy differs from other types of self-awareness, and (3) to discover how clinical symptoms affect the amount and direction of introspective accuracy impairments among outpatients with serious mental illness. To date, 189 participants aged 18-60 years have completed the study protocol (101 with schizophrenia or schizoaffective disorder, 72 with bipolar disorder, 16 controls; see Table 1 for baseline demographic and clinical characteristics of the sample), which includes an in-person, lab-based assessment followed by 30 days of at-home symptom tracking and cognitive testing via smartphone-based ecological momentary assessment (EMA). The goals of study 2 (PI: author CAD, R01MH116902) are to understand, over a 1-year period, how cognitive biases in the ways that outpatients with psychotic disorders (eg, schizophrenia, bipolar disorder with psychosis) perceive other people impact suicidal ideation and behavior. Ninety-seven participants aged 18-65 years have completed baseline assessments (38 with schizophrenia, 41 with schizoaffective disorder, 16 with bipolar disorder with psychosis, 2 with major depressive disorder and psychosis; see Table 2 for baseline demographic and clinical characteristics of the sample). Similar to study 1, the baseline assessments for study 2 include an in-person, lab-based assessment followed by 10 days of in-the-moment reports of symptoms and performance-based social cognition assessments via smartphone-based EMA.

Table 1. Participant demographic and clinical characteristics from parent study 1.

Characteristic	Patients (n=196)	Controls (n=16)
Sex (male), n (%)	88 (45)	11 (69)
Race, n (%)		
Caucasian	79 (40)	10 (63)
African American	82 (42)	4 (25)
Native American	3 (2)	0 (0)
Asian	6 (3)	1 (6)
Native Hawaiian/Pacific Islander	2 (1)	0 ()
Other	24 (12)	1 (6)
Ethnicity, n (%)		
Hispanic	51 (26)	3 (19)
Non-Hispanic	145 (74)	13 (81)
Diagnosis, n (%)		
Schizophrenia	60 (31)	N/A[a]
Schizoaffective disorder	52 (27)	N/A
Bipolar disorder (with psychotic features)	45 (23)	N/A
Bipolar disorder (without psychotic features)	38 (19)	N/A
Employment status[b], n (%)		
Employed, full time	22 (11)	13 (81)
Employed, part time	25 (13)	1 (6)
Unemployed	29 (15)	1 (6)
Stay-at-home parent	2 (1)	0 (0)
Part-time student	5 (3)	0 (0)
Full-time student	6 (3)	2 (13)
Receiving disability	96 (49)	0 (0)
Receiving disability, part-time work	13 (7)	0 (0)
Retired	6 (3)	0 (0)
Residential status[c], n (%)		
Independent, financially responsible	136 (69)	16 (100)
Independent, not financially responsible	38 (19)	0 (0)
Residential facility, unsupervised	8 (4)	0 (0)
Residential facility, supervised	13 (7)	0 (0)
Age (years), mean (SD)	41.30 (10.97)	35.56 (9.06)
Education (years), mean (SD)	13.30 (2.57)	15.13 (1.09)
Maternal education (years)[d], mean (SD)	13.11 (3.57)	13.75 (3.97)
Paternal education (years)[e], mean (SD)	13.59 (3.74)	14.69 (2.56)
Positive and Negative Syndrome Scale, mean (SD)		
Positive total	15.64 (5.08)	N/A
Negative total	12.29 (3.91)	N/A
General total	30.14 (7.03)	N/A
Montgomery-Asberg Depression Rating Scale total, mean (SD)	10.70 (10.65)	N/A
Young Mania Rating Scale total, mean (SD)	1.89 (4.35)	N/A

[a]N/A: not applicable.

[b]Categories were not mutually exclusive.

[c]Missing for 1 patient.

[d]Missing for 29 patients.

[e]Missing for 55 patients and 3 controls.

We also have one study that responds to NIMH Strategic Aim 2.2 [12] to develop novel behavioral assessments to evaluate domains relevant to mental illness. This is a single-site study at UCSD (PI: author RCM, R21MH116104) with the goals of understanding the real-time effects of mood on real-world cognitive performance and discovering how real-world cognition relates to real-time daily functioning among individuals with bipolar disorder. Sixty-six participants aged 18-65 years have completed this study (36 with bipolar disorder I, 10 with bipolar disorder II, 20 controls; see Table 3 for baseline demographic and clinical characteristics of the sample), which included a baseline assessment followed by 14 days of smartphone-based EMA and mobile cognitive testing (administered 3 times per day for a total possibility of 42 EMAs per participant).

For the present study, we will follow up with these previously enrolled research participants to assess their current mental health and psychosocial functioning with the exact same questions that were utilized during their previous participation. This study design will allow us to directly compare participants' prepandemic mental health functioning, based on dense sampling of their momentary responses regarding symptoms, functioning, and self-evaluations with mental health functioning during the acute phase of the COVID-19 pandemic. We will also be positioned to examine demographic, cognitive, and psychosocial factors that may be predictive of better and worse mental health outcomes in this unprecedented time. Therefore, the aims of this study are to learn about (1) the mental health impact of COVID-19 and social distancing behaviors among at-risk populations and (2) prevention behaviors taken to reduce the risk of COVID-19 infection among persons with SMI. In so doing, we will use a comprehensive and detailed set of previously collected EMA data (up to 90 observations per patient collected over a 30-day sampling period) and ask those same questions again in two telephone reassessments: the first round of telephone assessments will occur between April 3, 2020, and May 31, 2020; the second round will occur 1 month after reopening. Although this will differ by state, we anticipate a date between June 1, 2020, and August 31, 2020. Our results should provide vital information regarding the overall level of awareness individuals with SMI have regarding the health risks of COVID-19 and how it is currently impacting their daily lives.

Table 2. Participant demographic and clinical characteristics from parent study 2 (note: this study includes only individuals with a diagnoses of mental illness).

Characteristic	Suicidal ideation (n=48)	No suicidal ideation (n=49)
Sex (male), n (%)	22 (47)	23 (47)
Race, n (%)		
Caucasian	14 (29)	17 (35)
African American	17 (36)	28 (57)
Native American	0 (0)	0 (0)
Asian	3 (6)	1 (2)
Native Hawaiian/Pacific Islander	0 (0)	1 (2)
Other	14 (29)	2 (4)
Ethnicity, n (%)		
Hispanic	16 (33)	7 (14)
Non-Hispanic	32 (67)	42 (86)
Diagnosis, n (%)		
Schizophrenia	14 (29)	23 (47)
Schizoaffective disorder	24 (50)	18 (37)
Bipolar disorder (with psychotic features)	8 (18)	7 (14)
Major depressive disorder (without psychotic features)	1 (2)	1 (2)
Employment status[a], n (%)		
Employed, full time	2 (4)	0 (0)
Employed, part time	6 (13)	7 (16)
Unemployed	5 (12)	4 (9)
Part-time student	1 (2)	0 (0)
Full-time student	1 (2)	0 (0)
Receiving disability	26 (59)	30 (68)
Receiving disability, part-time work	2 (4)	3 (7)
Retired	2 (4)	0 (0)
Residential status[b], n (%)		
Independent, financially responsible	31 (69)	30 (68)
Independent, not financially responsible	10 (22)	11 (25)
Residential facility, unsupervised	0 (0)	1 (2)
Residential facility, supervised	4 (9)	2 (4)
Age (years)[c], mean (SD)	44.04 (12.20)	44.6 (11.02)
Education (years)[d], mean (SD)	12.40 (2.84)	12.81 (1.86)
Maternal education (years)[e], mean (SD)	11.74 (4.13)	12.63 (3.44)
Paternal education (years)[f], mean (SD)	13.83 (3.52)	13.14 (3.55)
Montgomery-Asberg Depression Rating Scale total[g], mean (SD)	21.95 (11.2)	9.68 (9.86)
Young Mania Rating Scale total[h], mean (SD)	2.30 (3.85)	1.21 (3.38)

[a]Not available (ie, data not entered prior to shelter-in-place orders and unavailable at this time) for 3 patients with suicide ideation and 5 patients without suicide ideation.

[b]Not available for 3 patients with suicide ideation and 5 patients without suicide ideation.

[c]Not available for 3 patients with suicide ideation and 5 patients without suicide ideation.

[d]Not available for 2 patients with suicide ideation and 5 patients without suicide ideation.

[e]Missing for 10 patients with suicide ideation and 11 patients without suicide ideation.

[f]Missing for 14 patients with suicide ideation and 16 patients without suicide ideation.

[g]Total not available for 4 patients with suicide ideation and 5 patients without suicide ideation.

[h]Total not available for 2 patients with suicide ideation and 5 patients without suicide ideation.

Table 3. Participant demographic and clinical characteristics for parent study 3.

Characteristic	Bipolar disorder (n=46)	Controls (n=20)
Sex (male), n (%)	16 (35)	6 (30)
Race, n (%)		
Caucasian	26 (57)	8 (40)
African American	4 (9)	2 (10)
Asian	2 (4)	5 (25)
Native Hawaiian/Pacific Islander	3 (7)	1 (5)
Other	11 (24)	4 (20)
Ethnicity[a], n (%)		
Hispanic	8 (18)	2 (10)
Non-Hispanic	37 (82)	18 (90)
Diagnosis, n (%)		
Bipolar disorder I	14 (30)	N/A[b]
Bipolar disorder II	10 (22)	N/A
Bipolar disorder I (with psychotic features)	22 (48)	N/A
Employment status, n (%)		
Employed, full time	13 (28)	12 (60)
Employed, part time	4 (9)	4 (20)
Unemployed	6 (13)	0 (0)
Stay-at-home parent	0 (0)	0 (0)
Part-time student	0 (0)	0 (0)
Full-time student	1 (2)	1 (5)
Receiving disability, unemployed	16 (35)	0 (0)
Receiving disability, part-time work	5 (11)	1 (5)
Retired	1 (2)	2 (10)
Residential status, n (%)		
Independent, financially responsible	36 (78)	16 (80)
Independent, not financially responsible	8 (17)	4 (20)
Residential facility, unsupervised	1 (2)	0 (0)
Residential facility, supervised	1 (2)	0 (0)
Age (years), mean (SD)	42.72 (11.42)	41.03 (14.56)
Education (years), mean (SD)	14.91 (2.52)	15.65 (2.74)
Maternal education (years)[c], mean (SD)	14.20 (3.93)	12.83 (3.62)
Paternal education (years)[d], mean (SD)	15.22 (3.04)	15.24 (3.07)
Montgomery-Asberg Depression Rating Scale total, mean (SD)	11.20 (8.50)	N/A
Young Mania Rating Scale total, mean (SD)	6.44 (5.64)	N/A

[a]Missing for 1 participant with bipolar disorder.

[b]N/A: not applicable.

[c]Missing for 1 participant with bipolar disorder and 2 controls.

[d]Missing for 9 participants with bipolar disorder and 3 controls.

Methods

Design

This study involves 2 telephone interviews during which participants will be readministered psychiatric symptom–related questions that they received during the parent study via EMA, with the major modification being that the questions for the present study will be administered via a telephone survey. These items are presented in Multimedia Appendix 1 as a combination of the three surveys (please note that each parent study had a slightly different EMA survey). Participants will also be asked new questions about how they are currently feeling, thinking about, and dealing with COVID-19. The survey will take approximately 30 minutes to complete.

Study Population and Inclusion and Exclusion Criteria

All participants who are currently or have previously participated in one of our ongoing parent studies (N=352 participants to date; approximately 24% participants overlap between studies), and who consented to being contacted for future studies, will be called and invited to participate. In general, participants include adults between the ages of 18 and 65 years who have a diagnosis of schizophrenia, schizoaffective disorder, bipolar disorder (I or II), or major depression with psychotic features. All individuals are receiving only outpatient care and are free from neurological and/or neurodegenerative disorders. A small sample of psychiatrically healthy individuals is also included (n=35).

Questionnaires

The parent study EMA questionnaires were developed by authors CAD, PDH, RCM, and AEP. All three questionnaires include items about engagement in daily activities and social interactions (Where are you? Who are you with? What are you doing?), mood (in the moment or since the past alarm), symptoms (eg, “since the past alarm, how often have you heard voices”), and other behavioral indicators of health (eg, sleep, substance use).

The newly developed COVID-19 exposure and prevention behavior questionnaire includes 16 items on exposure and prevention behaviors (Multimedia Appendix 2). We will also be administering open-source scales to assess the psychological impacts of COVID-19, including the Center for Epidemiologic Studies Depression Scale [13], National Institutes of Health PROMIS (Patient-Reported Outcomes Measurement Information System) emotional distress-anxiety scale [14], Perceived Stress Scale [15], 3 items from the UCLA Loneliness Scale [16], modified to be specific to COVID-19, the 6-item Lifetime Orientation Test-Revised (LOT-R; measure of optimism) [17], Satisfaction with Life Scale [18], Duke Social Support Scale-Social Interaction Subscale (4 items) [19], and an 11-item brief coping scale [20]. The corresponding author can be contacted to request a complete packet of these measures.

Consent

This study was approved by each participating university’s Institutional Review Board. Participants will provide verbal consent on the phone and will be compensated for their participation.

Data Analysis Plan

The estimated sample size is 200. For aim 1, the primary outcome will be change in average mood ratings (sadness, relaxed, energized, happiness, anxious) from the previous EMA surveys to now (spring 2020, when shelter-in-place orders are effective), then again during the summer of 2020 (unknown if shelter-in-place orders will be effective or if people have returned to a “normal” life). Changes in these outcomes will be evaluated using a mixed-models repeated measures analysis of variance with restricted maximum likelihood estimation. Group membership (schizophrenia, schizoaffective disorder, bipolar disorder) and assessment point (baseline, follow-up) will be treated as fixed effects and participants will be treated as a random effect. The group-by-time interaction will be the fixed effect of interest. Secondary analyses will be conducted to evaluate (1) the predictors of change from baseline, with a focus on diagnosis and psychotic symptoms, examined with regression models, and (2) group differences at each time point and differences in change scores between controls (n=35) and patient groups.

For aim 2, the primary outcome will be characterization of prevention behavior by group. For studies and participants where we have this information, we will also relate these data to assessments of insight, including clinical insight, self-monitoring ability collected during EMA, and the results of a comprehensive assessment of the ability to evaluate one’s own performance on an array of neurocognitive, social cognitive, and functional measures. These analyses will be examined with correlational statistics, including regression models.

Results

The inclusion of participants for the first round of telephone assessments started on April 3, 2020 and will be completed by May 31, 2020. As of April 30, 2020, 101 individuals had completed these first-round assessments. The second round of telephone assessments will likely occur between June 1, 2020, and August 31, 2020. Study results will be published in peer-reviewed scientific journals in a timely fashion at completion of data collection. Data addressing non-COVID-19 topics from the sample collected to date are already being submitted for publication to scientific journals.

Discussion

Principal Findings

This study will shed light on the direct impact of the COVID-19 pandemic on the well-being of people with serious mental illness, a largely overlooked yet vulnerable population during this pandemic. Individuals with mental illness are often burdened not only by their illness but also by social isolation, under- or unemployment, lower socioeconomic status, cognitive impairments, and limited access care. Such individuals may therefore represent a particularly vulnerable and important group in whom we must strive to understand the effects of COVID-19. Findings from this study have the potential to characterize the

degree of distress among persons with SMI during this pandemic and will also help to clarify whether individuals with SMI are able to protect themselves and others from infection. These findings can also help us identify risk and resiliency factors predictive of positive and negative outcomes to this high-stress situation, which could provide targets for early intervention in the (likely inevitable) event that another pandemic occurs and/or that social distancing measures are necessary in the future. Lastly, we hope this protocol paper will provide a roadmap and resources for other researchers who would like to implement a similar approach in their studies.

Authors' Contributions

All authors contributed extensively to the work presented in this paper. RCM designed the protocol and wrote the paper; CAD, PDH, and AEP wrote the paper. RCM, CAD, and AEP are the PIs on the parent grants of which this study is an extension of.

Conflicts of Interest

RCM is a cofounder and vice president of research of KeyWise AI, Inc. She has a research grant from Gilead Sciences. PDH has received consulting fees or travel reimbursements from Acadia Pharma, Alkermes, Bio Excel, Boehringer Ingelheim, Minerva Pharma, Otsuka Pharma, Regeneron Pharma, Roche Pharma, and Sunovion Pharma during the past year. He receives royalties from the Brief Assessment of Cognition in Schizophrenia. He is chief scientific officer of i-Function, Inc. He had a research grant from Takeda and the Stanley Medical Research Foundation. The remaining authors declare that they have no conflicts of interest pertinent to this study.

Multimedia Appendix 1
Psychiatric symptom EMA questions from parent studies (combined), adapted for a telephone follow-up assessment. Includes skip-logic.
[DOCX File , 51 KB - resprot_v9i5e19203_app1.docx]

Multimedia Appendix 2
COVID-19 exposure and prevention behavior questionnaire.
[DOCX File , 17 KB - resprot_v9i5e19203_app2.docx]

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Abbreviations

COVID-19: coronavirus disease 2019
EMA: ecological momentary assessment
NIMH: National Institute of Mental Health
PI: principal investigator
SMI: serious mental illness

Edited by G Eysenbach; submitted 08.04.20; peer-reviewed by E Weizenbaum, N Zhao, K Aguirre, J Olalla; comments to author 24.04.20; revised version received 01.05.20; accepted 04.05.20; published 22.05.20.

Please cite as:
Moore RC, Depp CA, Harvey PD, Pinkham AE
Assessing the Real-Time Mental Health Challenges of COVID-19 in Individuals With Serious Mental Illnesses: Protocol for a Quantitative Study
JMIR Res Protoc 2020;9(5):e19203
URL: http://www.researchprotocols.org/2020/5/e19203/
doi:10.2196/19203
PMID:32365043

Protocol

Dietary Intake Nutritional Status and Lifestyle of Adolescent Vegetarian and Nonvegetarian Girls in New Zealand (The SuNDiAL Project): Protocol for a Clustered, Cross-Sectional Survey

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Abstract

Background: Anecdotally, vegetarian eating patterns seem to be increasing in parallel with growing concerns about environmental sustainability. While this pattern of eating is widely believed to be associated with benefits for the planet and individual health, it may increase the risk of inadequate intakes and nutrient deficiency if not planned carefully. Adolescent girls may be particularly at risk, as they have increased requirements for nutrients such as iron, zinc, calcium, and vitamin B12 during growth and development.

Objective: The objective of the SuNDiAL Project (Survey of Nutrition, Dietary Assessment, and Lifestyles) is to compare the dietary intakes and habits, nutrition status, motivations, attitudes, and physical activity of a sample of vegetarian and nonvegetarian adolescent girls in New Zealand.

Methods: A clustered, cross-sectional, nationwide study of adolescents aged 15-18 years was conducted. Secondary schools were recruited throughout New Zealand, and pupils (n=290) were invited to participate in data collection in either the first (February to April) or third (August to October) school term of 2019 (New Zealand schools operate on a 4-term year). Sociodemographic and health information; vegetarian status; dietary habits; and attitudes, motivations, and beliefs regarding food choices were assessed via an online self-administered questionnaire. Dietary intakes were collected via two 24-hour diet recalls on nonconsecutive days and will be adjusted for within-person variation using the Multiple Source Method, to represent usual intakes. Nutrient adequacy will be assessed by the estimated average requirement cut-point method or probability approach as appropriate. Height and weight were measured, and blood and urine samples collected for micronutrient status assessment. Participants wore an accelerometer for 7 days to assess 24-hour activity patterns (time spent asleep, sedentary, or engagement in light-intensity or moderate-to-vigorous intensity physical activity).

Results: Recruitment and data collection were conducted in 2019. Data are currently being cleaned and analyzed, with publication of the main results anticipated at the end of 2020.

Conclusions: The SuNDiAL Project will provide a meaningful and timely description of diet, nutrition status, and motivational factors associated with vegetarianism and identify any risks this pattern of eating may pose for female adolescents. The results of this study will support the development of targeted recommendations and interventions aimed at enhancing the health, growth, and development of adolescent girls.

Trial Registration: Australian New Zealand Clinical Trials Registry ACTRN12619000290190; https://tinyurl.com/yaumh278

International Registered Report Identifier (IRRID): DERR1-10.2196/17310

(JMIR Res Protoc 2020;9(5):e17310) doi:10.2196/17310

KEYWORDS

vegetarianism; teenagers; women; iron; zinc; calcium; B12; physical activity; attitudes motivations, beliefs

Introduction

Background

Few, if any, robust estimates of the prevalence of vegetarianism in populations exist, although plant-based and vegetarian diets (defined as not consuming any red meat, poultry, or seafood for the purposes of this article) appear to be growing in popularity. Increasing concern regarding the importance of environmental sustainability may explain this apparent rise; however, health is reported as a significant motivator for many vegetarians [1]. Indeed, vegetarians tend to have a body mass index that is 1-2 kg/m^2 lower than their otherwise comparable nonvegetarian peers and exhibit less weight gain during adulthood [2]. Vegetarians also have a slightly lower risk of some cancers [2] and as much as a 24% lower risk of ischemic heart disease [2], presumably because they tend to have lower total and low-density lipoprotein cholesterol concentrations [2]. However, much of the data that underpin our understanding of how vegetarianism may affect disease incidence was collected from adult populations prior to the 1990s [3,4] or in the early 2000s [5]. Much less is understood about the foods and nutrient intake of vegetarian adolescents. Recent advances in food technology, food fortification, and the widespread availability of products designed to be plant-based substitutes for meat and milk imply that vegetarians can now choose from many commercially produced food products [6]. However, consistent with older research, more recent studies indicate that vegetarian or vegan eating patterns score higher on the healthy eating index due to a lower sodium and saturated fat intake and higher intakes of fruits and vegetables [7].

A well-planned vegetarian diet containing vegetables, fruits, whole grains, legumes, nuts, and seeds can provide adequate nutrition for most members of the population [8]. In general, vegetarian diets provide large amounts of phytate, dietary fiber, folate, vitamins C and E, and magnesium, but without planning, they may have low protein, vitamins D and B12, iron, zinc, and calcium (particularly among vegans who do not consume animal products of any kind) [8,9]. Additionally, while the iron and zinc content of a vegetarian diet may be similar to that of a nonvegetarian diet, the high phytate content, absence of heme iron from cellular animal sources, and lower animal protein intake reduces the bioavailability of iron and zinc, significantly increasing the risk of deficiency [10]. The risk of vitamin B12, calcium, iron, and zinc deficiency may be greater in certain sex and life-stage groups such as young female adults [10-12]. The pubertal growth spurt, sexual maturation, and the onset of menarche increase requirements for vitamin B12, calcium, iron, and zinc in adolescent girls [12]. Increased autonomy over food intake and reductions in energy intake due to a desire to lose weight or achieve a certain body type may further contribute to the risk of nutrient deficiencies in this age group that could be exacerbated in vegetarians without careful food choice. Indeed, the latest representative data collected in New Zealand over a decade ago indicates that 88% of female adolescents have inadequate intakes of calcium, and 34% have inadequate intakes of iron, with 11% being identified as having iron deficiency and a further 5% as having anemia [13], despite the estimation that less than 9% of this age group was likely to be vegetarian at the time of data collection [14].

Reasons for following a vegetarian diet include health [1], ethical and environmental concerns [1,15,16], animal welfare [1,15,16], and religious beliefs [16]. However, adolescent girls in New Zealand, who are already at risk of low calcium intakes and iron status, may be further increasing that risk if they do not follow a carefully planned vegetarian diet. It is crucially important to develop guidelines that mitigate the risk and maximize potential benefits, such as reducing saturated fat and increasing fiber intakes. Understanding the motivations, attitudes, and beliefs that underpin food choices is important to inform the development of appropriate and effective guidelines, in particular, to understand why some people choose to be vegetarian and others do not. Other lifestyle behaviors, such as physical activity, that may go hand-in-hand with food choices, should also be examined in relation to health risks and benefits of a vegetarian diet. This knowledge can then be used to appropriately and effectively communicate lifestyle recommendations for those following a vegetarian diet.

Objectives

Anecdotally, vegetarianism appears to be increasing in popularity. While this increase in popularity may confer some health benefits to the population, adolescent girls in New Zealand are already at an increased risk of inadequate intakes of iron and calcium, which would clearly be exaggerated if animal products were avoided. A poorly planned vegetarian diet can increase the risk of some nutrient deficiencies that may be exacerbated in female adolescents. Therefore, it is critical that the nutrient intake and status of vegetarian adolescent girls are assessed. Furthermore, assessing motivations, attitudes, and beliefs will further our understanding of dietary choices and inform the development of health promotion materials and programs targeted to this age group.

The aim of the SuNDiAL Project (Survey of Nutrition, Dietary Assessment and Lifestyles) is to compare the dietary intakes and habits, nutrition status, motivations, attitudes, and physical activity of a sample of vegetarian and nonvegetarian adolescent girls in New Zealand. The objectives of this study are to describe and compare the following between vegetarians and nonvegetarians:

- Dietary intakes of macronutrients, free and added sugars, phytate, fiber, and key micronutrients (iron, zinc, vitamin B12, folate, iodine, and calcium)
- Biochemical status of key micronutrients (iron, zinc, vitamin B12, and folate)
- Attitudes toward and motivations for food choice (eg, the environment, animal welfare, health)

- Twenty-four–hour activity patterns (sleep, sedentary behavior, and physical activity)
- Dietary habits
- Weight loss intentions

Methods

Study Design

The SuNDiAL project is a nationwide cross-sectional survey of female adolescents aged 15-18 years. Nationwide data collection was achieved by utilization of a cohort of postgraduate research students. At the University of Otago, second-year Master of Dietetics students are required to undertake a 6-month research project in addition to 6 months of clinical placement. These student researchers are trained in dietary assessment and clinical skills, making them ideal data collectors for this study. In groups of 2-4 students, they collected data in locations convenient to their clinical placement or home city in New Zealand. In total, data were collected in 8 locations throughout New Zealand. The goal was to recruit at least one secondary school in each of Dunedin, Christchurch, Wanaka, Nelson, Wellington, Tauranga, Whangarei, and New Plymouth. These locations cover a range of cities from small (Wanaka) to large (Christchurch), from the south (Dunedin) to the north (Whangarei) of New Zealand. Data were collected in the first (February to April) or third (August to October) term of school in 2019 (New Zealand secondary schools operate on a 4-term year). The underlying ethnic makeup of the female population aged 15-18 years living in these areas is 70% New Zealand European, 17% Māori, 8% Pacific, and 15% Asian. Socioeconomic status information for this age group is not readily available in New Zealand. However, because we used a convenience sample, the final study population may differ from the overall population. This study has been approved by the University of Otago Human Ethics Committee (Health) (H19/004) and is registered with the Australian New Zealand Clinical Trials Registry (registration number: ACTRN12619000290190). Informed consent was obtained electronically from all participants via an online questionnaire [Research Electronic Data Capture (REDCap), production server version 9.3.3]. In addition, parental consent was obtained via email for participants who were under 16 years of age.

Selection of Schools

Initially, secondary schools in the predetermined locations were selected to be invited to participate. Initial selection was made by selecting 2-5 schools per location, with a female roll number of at least 200. Lower decile schools (a measure of the socioeconomic status of the school) were preferentially selected for this round of invitation to ensure representation (Figure 1). The selected schools received emails and follow-up phone calls inviting them to participate. If the required number of schools was not reached through this method, other schools in the area were contacted and invited to participate. Schools that were interested provided written consent to participate (signed by an appropriate representative from the school).

Recruitment of Participants

A brief information session (10-15 min) was delivered by the Master of Dietetics students to eligible pupils at each consenting school. At the session, pupils were given detailed information about the study and the required commitment. An expression of interest form was distributed for individuals to indicate their interest in participating by providing their email address. Individuals were also able to indicate interest on the study website [17]. Electronic and print information about the study was distributed at the school for anyone who required further information about the study. Individuals who provided their email address were sent a link to an online questionnaire (hosted on REDCap), on which they completed consent forms and answered a series of sociodemographic and general health questions. Participants who were under 16 years of age were asked to provide a parent's email address and did not receive the link to the online questionnaire until a parent or guardian had consented to their participation.

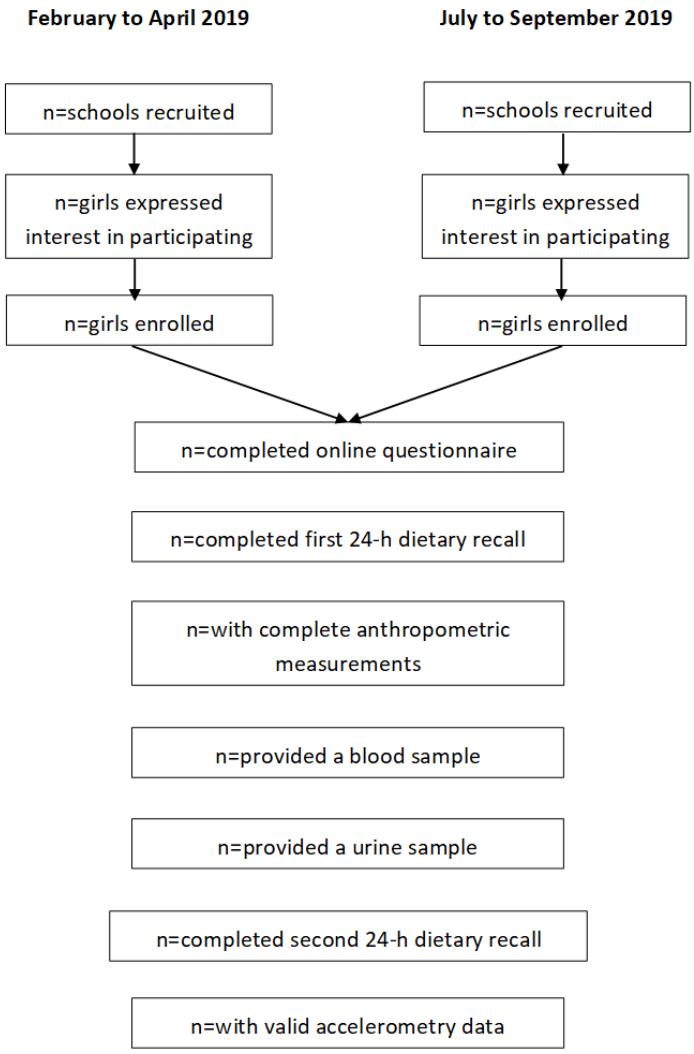
Inclusion Criteria

Adolescents who identify as female, are aged between 15 and 18 years, are enrolled in one of the selected secondary schools, can speak and understand English, and are not pregnant were eligible to participate.

Sample Size

A sample size of 300 adolescent girls from 13 secondary schools will have 80% power to the P=.05 level to detect a 0.5 standard deviation difference (a "moderate" difference) in continuous outcome variables between vegetarians and nonvegetarians, assuming a prevalence of vegetarianism of 20% and a design effect (for school clusters) of 1.5. If the prevalence of vegetarianism is much less than 20%, then purposeful sampling of vegetarians was planned in the second half of the recruitment year.

Figure 1. Study Design.



Outcome Measures

Online Questionnaire

Once participants completed enrollment, they were asked to complete an online questionnaire that follows from the enrolment questions on REDCap. This questionnaire is divided into three sections. The health and demographics section consists of 29 questions about sociodemographic characteristics and health status including current menstrual status, and food allergies or intolerances. It also asks participants if they identify as vegetarian. Initially, this was done by simply asking them, "Are you a vegetarian or vegan?" If they answered in the affirmative, they were asked to identify which of the following foods they eat: *Eggs, Milk, Fish or seafood, Chicken or poultry, Meat/red meat occasionally,* or *None of the above*. If they selected *None of the above*, they were asked if they identify as vegan. Participants were asked how long they have been following this way of eating, to which they could select options ranging from *less than a month* to *my whole life.* Adaptive questioning is used in this section so that, for example, if a participant answered "no" to "Are you a vegetarian?" they then moved on to the next question and did not see the questions pertaining to identifying as vegan or how long they have been following that eating pattern. The attitudes and motivations section includes 4 previously validated questionnaires [18-21] (Table 1) that, combined, consist of a total of 81 questions. In this section, questions that ask about similar concepts have been randomly distributed within each of the 4 questionnaires. Responses will be scored according to the published instructions [18-21]. The Dietary Habits section consists of 73 questions from the Dietary Habits Questionnaire that was used in the New Zealand Adult Nutrition Survey 2008/2009, which includes questions about weight loss intentions [22]. Each participant completed the questions from all sections in the same order, and an answer was required for each question. There was no timeframe limitation on completion. Participants were able to go back to previously answered questions and change their answers but there was no review step, and once the questionnaire was completed, they could not access it again. However, participants could leave the questionnaire at any point without completing it. A code was provided to participants so they could log back in and complete the questionnaire later, and reminders were sent to encourage them to do this. Incomplete questionnaires will be included in analysis on a case-by-case basis, depending on the outcome of interest.

Table 1. Summary of outcome measures to be collected in the SuNDiAL Project.

Outcome	Assessment Method
Online Questionnaire	
Demographics and health status	Self-report
Vegetarian/vegan status	Self-report
Dietary Habits	Dietary Habits Questionnaire
Attitudes and motivations towards food choice	Rationalizing meat consumption: The 4Ns Questionnaire [19]
	The Food Choice Questionnaire [21] Ethical Food Choice Motives [18]
	Dietarian Identity Questionnaire [20]
School visit	
Estimated usual dietary intake	Two 24-hour recalls, with adjustment of usual intake using MSM[a]
Height	Stadiometer
Weight	Body weight scales
Ulna Length	Steel measuring tape
Blood sample	
Hemoglobin	Cyanide-free photometry
Plasma ferritin	Immunoassay
Soluble transferrin receptor	Immunoassay
C-reactive protein	Immunoassay
Alpha-glycoprotein	Immunoassay
Zinc	ICP-MS[b]
Selenium	ICP-MS
Vitamin B12	Electrochemiluminescence immunoassay
Folate	Microbiological Assay
Urine Sample	
Iodine	ICP-MS
Accelerometry	
Average daily 24 h Activity	ActiGraph GT3x+, and accompanying wear time and sleep diary.
Average daily sleep	
Average daily sedentary time	
Average daily light intensity activity	
Average daily moderate to vigorous intensity physical activity	

[a]MSM: Multiple source method

[b]ICP-MS: Inductively couple plasma mass spectrometry

Usual Dietary Intake

Dietary intake was assessed using two 24-hour diet recalls. The first recall was completed face-to-face by a Master of Dietetics student during the in-school data collection visit. The recall was performed using a multiple-pass technique. In the first pass, a "quick list" of all foods and beverages consumed during the previous day (midnight to midnight) is obtained. In the second pass, a detailed description is added to each food and beverage, including cooking methods, recipe information (where appropriate), and brand and product information. In the third pass, the amounts of each food and beverage consumed are obtained. Participants were asked to estimate the amount consumed for each food and beverage using standard household measures (cups, tablespoons, etc), food photographs, shape dimensions, food portion assessment aids (dried beans), and information from packaging. Finally, the full food list was reviewed and any additions or changes were recorded. Upon completion of the recall, participants were asked if salt was added to any of the food consumed, and if so, whether it was iodized. A second recall was completed over video call on a nonconsecutive day, with preference given, where possible, to

performing the second recall on a weekend day. All 24-hour diet recalls were entered into FoodWorks dietary analysis software (version 9, Xyris Software) using the New Zealand Food Composition Database, FOODfiles (2016; The New Zealand Institute for Plant and Food Research Limited and the Ministry of Health) and nutrient data for commonly consumed recipes collated in the 2008/09 New Zealand Adult Nutrition Survey [22]. Dietary intake estimated for each nutrient of interest will be adjusted to represent usual intakes based on the estimated within-person variance of vegetarians and nonvegetarians using the Multiple Source Method [23]. Individual daily intakes from supplements will then be calculated and added to the usual intakes. The median (IQR) (for data that are not normally distributed) or mean (SD) (for data that are normally distributed) of daily intakes of energy and key macro- and micro-nutrients, and the main food sources of these nutrients will then be calculated. Molar ratios of phytate:zinc will be calculated to provide estimates of absorbable zinc. The estimated average requirement (EAR) cut-point method will be applied to the usual intake distribution to assess the prevalence of inadequate intakes with the exception of iron, for which the full probability approach will be used because of the skewed iron requirements as a result of menstruation in this population. [24].

Anthropometric Assessments

Body weight was measured to the nearest 0.1 kg using calibrated body weight scales. Standing height was measured to the nearest 0.1 cm using a calibrated stadiometer and standardized protocols. Both these measurements were taken with participants wearing light clothing and no footwear. Ulna length was measured on the nondominant arm between the point of the elbow and the midpoint of the prominent bone of the wrist, using a nonexpandable steel measuring tape, with the arm positioned across the torso with the hand resting on the front of the opposite shoulder. Wrist watches and jewelry were removed for this measurement. All anthropometric measurements were performed in duplicate, with a third measurement performed if the difference between the initial two measurements was ≥0.5 units, and the mean of the two closest measurements used as the "true" value. BMI was calculated by weight (in kg) divided by height (in m) squared. BMI z-scores for age and sex will be calculated using the World Health Organization child growth standards [25].

Biochemical Assessment

Participants were able to opt-out of providing the blood and urine samples while still participating in the other components. A nonfasting venous blood sample was collected by a trained phlebotomist, using trace element free equipment. A spot urine sample was also collected. Time of collection and time of the last meal were recorded, and all blood and urine samples were transferred in a cooler to an accredited testing laboratory where hemoglobin and vitamin B12 concentrations were analyzed within 8 hours of collection. The remaining blood sample was centrifuged and the serum aliquoted and frozen at –80°C. Frozen serum and urine samples were transferred on ice to the Department of Human Nutrition at the University of Otago where they are stored for later analysis (outlined in Table 1).

Twenty-four–hour Activity

Average daily 24-hour activity (sleep, sedentary time, light activity, moderate-to-vigorous physical activity) was measured via a triaxial GT3x+ accelerometer (ActiGraph) among those who consented to accelerometry. Participants were asked to wear the accelerometer continuously for 7 days (except for water-based activities or during full contact sports) on an elasticated belt around their waist, so that the accelerometer was situated over their right hip. The raw accelerometer data were collected at 30 Hz. A daily wear time diary was used to record bedtime, sleep, and wake times and any times when the device was removed. If the device was removed for the purpose of engaging in water-based physical activity or full contact sports, then participants were asked to record the duration and intensity of this activity. Customized Stata (Release 16; StataCorp) code will be used for both accelerometer and log data, to differentiate nonwear and wear time. Time spent asleep will be identified using the Sadeh algorithm [26], and time spent in sedentary behavior and in light intensity and moderate-to-vigorous intensity physical activity will be identified using Freedson cut points [27].

Statistical Analysis

Statistical analyses will be carried out using Stata (StataCorp). School clusters will be accounted for in all analyses using appropriate methodology (for example, with a sandwich estimator or as a random effect). Estimates of prevalence and means will be reported with 95% confidence intervals. A binary variable for vegetarianism will be created, and comparisons between vegetarians and nonvegetarians will be carried out using regression models: linear regression for continuous outcomes and logistic regression for binary outcomes.

Results

Recruitment and data collection were conducted and completed with 290 participants in 2019. Data are currently being cleaned and analyzed, with publication of the main results anticipated at the end of 2020.

Discussion

Anecdotal reports suggest that the popularity of plant-based and vegetarian eating patterns may be rising in parallel with growing concerns about environmental sustainability. This pattern of eating is associated with some positive health outcomes [2,3,9]. Nonetheless, without careful planning, a vegetarian diet can increase the risk of inadequate intakes of bioavailable iron, zinc, calcium, and B vitamins [9,28]. The pubertal growth spurt combined with sexual maturation [12] increases the requirements for these nutrients, and therefore, we propose that female adolescents adopting a vegetarian diet may be at particular risk of nutrient inadequacy and deficiency.

The SuNDiAL project will provide a well-timed investigation into the dietary intakes, micronutrient status, physical activity, motivations, and beliefs of New Zealand adolescent girls. This project will also assess whether the current vegetarian diet consumed by adolescent girls in New Zealand offers substantial benefits or risks over a nonvegetarian eating pattern. The

collection of biochemical data, dietary intakes, and 24-hour activity patterns will provide additional important details on benefits associated with vegetarianism, and the identification of individuals "at risk." The results of this study will support the development of targeted interventions and recommendations aimed at enhancing the health, growth, and development of adolescent girls.

Acknowledgments

This SuNDiAL project is funded by a Lotteries Health Research Grant and funds from the Department of Human Nutrition, University of Otago, Dunedin, New Zealand. MP is supported by a National Heart Foundation Research Fellowship that is partly funded by the Southland Medical Association. In advance, we also thank the Master of Dietetics students enrolled in HUND 5B in 2019 who worked as the data collectors on this study.

Conflicts of Interest

None declared.

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Abbreviations

REDCap: Research electronic data capture

Edited by C Hoving; submitted 04.12.19; peer-reviewed by B Turner-McGrievy, R Quigg; comments to author 17.02.20; revised version received 15.03.20; accepted 20.03.20; published 27.05.20.

Please cite as:
Peddie M, Ranasinghe C, Scott T, Heath AL, Horwath C, Gibson R, Brown R, Houghton L, Haszard J
Dietary Intake Nutritional Status and Lifestyle of Adolescent Vegetarian and Nonvegetarian Girls in New Zealand (The SuNDiAL Project): Protocol for a Clustered, Cross-Sectional Survey
JMIR Res Protoc 2020;9(5):e17310
URL: http://www.researchprotocols.org/2020/5/e17310/
doi:10.2196/17310
PMID:32459178

Original Paper

An Ecologically Valid, Longitudinal, and Unbiased Assessment of Treatment Efficacy in Alzheimer Disease (the EVALUATE-AD Trial): Proof-of-Concept Study

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Abstract

Background: The current clinical trial assessment methodology relies on a combination of self-report measures, cognitive and physical function tests, and biomarkers. This methodology is limited by recall bias and recency effects in self-reporting and by assessments that are brief, episodic, and clinic based. Continuous monitoring of ecologically valid measures of cognition and daily functioning in the community may provide a more sensitive method to detect subtle, progressive changes in patients with cognitive impairment and dementia.

Objective: This study aimed to present an alternative trial approach using a home-based sensing and computing system to detect changes related to common treatments employed in Alzheimer disease (AD). This paper introduces an ongoing study that aims to determine the feasibility of capturing sensor-based data at home and to compare the sensor-based outcomes with conventional outcomes. We describe the methodology used in the assessment protocol and present preliminary results of feasibility measures and examples of data related to medication-taking behavior, activity levels, and sleep.

Methods: The EVALUATE-AD (Ecologically Valid, Ambient, Longitudinal and Unbiased Assessment of Treatment Efficacy in Alzheimer's Disease) trial is a longitudinal naturalistic observational cohort study recruiting 30 patients and 30 spouse coresident care partners. Participants are monitored continuously using a home-based sensing and computing system for up to 24 months. Outcome measures of the automated system are compared with conventional clinical outcome measures in AD. Acceptance of the home system and protocol are assessed by rates of dropout and protocol adherence. After completion of the study monitoring period, a composite model using multiple functional outcome measures will be created that represents a behavioral-activity signature of initiating or discontinuing AD-related medications, such as cholinesterase inhibitors, memantine, or antidepressants.

Results: The home-based sensing and computing system has been well accepted by individuals with cognitive impairment and their care partners. Participants showed good adherence to the completion of a weekly web-based health survey. Daily activity, medication adherence, and total time in bed could be derived from algorithms using data from the sensing and computing system. The mean monitoring time for current participants was 14.6 months. Medication adherence, as measured with an electronic pillbox, was 77% for participants taking AD-related medications.

Conclusions: Continuous, home-based assessment provides a novel approach to test the impact of new or existing dementia treatments generating objective, clinically meaningful measures related to cognition and everyday functioning. Combining this

approach with the current clinical trial methodology may ultimately reduce trial durations, sample size needs, and reliance on a clinic-based assessment.

International Registered Report Identifier (IRRID): DERR1-10.2196/17603

(JMIR Res Protoc 2020;9(5):e17603) doi:10.2196/17603

KEYWORDS

mild cognitive impairment; Alzheimer disease; mobile health; clinical trial; health information technology

Introduction

Background

The current clinical trial methodology for testing dementia treatments relies on the time-honored approach of assessing enrolled individuals with a combination of self-report measures (eg, function, mood, adverse events), cognitive and physical function tests (eg, psychometric batteries, timed walks), and biomarkers (eg, neuroimaging-, cerebrospinal fluid-, plasma-based). These measures are typically collected at a baseline visit, followed by randomization of patients to a placebo or treatment arm. Patients are sent home until their next appointment, which may occur at varying time intervals depending on the phase and design of the study. In cases where follow-up is frequent (eg, every 2 weeks), the protocol needs to be modified to cover information carry-over, including practice effects, especially with regard to cognitive tests. Recency effects are also a particular concern, considering that people tend to report what they most recently experienced in the last few days as opposed to the overall quality of change for the entire period or may forget events which occurred during the period closest to the last visit. Across a wide range of behaviors and activities, self-report assessments have been shown to have weak correlations with objective measures [1-4]. In general, the amount of information that can be obtained is restricted by limits on how much testing a patient may be reasonably asked to complete at a single appointment, and by the frequency of appointments as the accuracy of information gained decreases as the testing intervals become more widely dispersed. In all cases, key data related to cognition and functions are rarely ecologically valid. Patients are asked to perform tasks that they typically never do in real life (eg, memorize a list of words, copy figures) or to describe how well they perform a task at home, although it may vary from the reported actual daily performance on those tasks.

The limitations of such an assessment paradigm result in data that is inherently variable, episodic, and proxy based. The cardinal features of change in patients with mild cognitive impairment (MCI) and early Alzheimer disease (AD) are a slow decline in cognition and function punctuated with acute, unpredictable events. This trajectory is challenging to assess with conventional tools and methods that lack sensitivity to subtle changes. Thus, for definitive efficacy trials, large samples followed for long periods of time are needed to determine if there is a meaningful change in cognition or function. In earlier phase trials, it is generally not possible to detect a clinical signal of change in these patients unless the treatment has a substantial effect size.

This state of affairs may be transformed by fundamentally changing the assessment paradigm [5-9]. If data can be collected continuously as opposed to episodically and infrequently, then the data lends itself to improving the precision of the estimate of the trajectory of change (ie, the slope of a line composed of only a few points is less certain than a line composed of hundreds or thousands of points) as well as intraindividual estimates of change (as opposed to the conventional group change dichotomy) [10]. High-dimensional, high-frequency data capture can be achieved by taking advantage of advances in in-home remote sensing, pervasive computing, and high dimensional data analytics. The objective sensed data also provides outcomes that are ecologically valid with immediate tangible clinical meaning. These outcome metrics collectively referred to as *digital biomarkers* include precise, time-stamped measures of physical activity, medication-taking behavior, sleep, socialization, and everyday cognitive function (eg, using a computer, driving). In addition, the approach employs relatively frequent (weekly) direct queries via email regarding internal states that inherently require direct reporting (eg, pain, mood states) as well as the opportunity to capture adverse events and health economic data (eg, falls, emergency department visits, clinic appointments).

Objectives

Over the past decade, these digital biomarkers have been studied in relevant populations (healthy elderly and those with early MCI), demonstrating that they are sensitive to change and that the technology to capture these changes is feasible to deploy in older adults' homes [7,8]. However, the specific use of this multisensor methodology in dementia-specific clinical trials is yet to be evaluated. To begin to understand how these technologies and digital biomarkers may be best employed in dementia clinical trials, we established a longitudinal research study to examine the relative feasibility and sensitivity of this approach in patients taking typical symptomatic treatments for AD (eg, cholinesterase inhibitors and other central nervous system active medications). This study, EVALUATE-AD (Ecologically Valid, Ambient, Longitudinal and Unbiased Assessment of Treatment Efficacy in Alzheimer's Disease), is currently underway to determine the feasibility of capturing these more continuous and objective everyday measures at home, to assess the comparability of these novel measures to conventional outcome metrics, and to develop a composite model from these functional measures that can detect changes related to initiating and discontinuing common treatments employed in AD-related care. This paper describes the methodology behind the assessment protocol, presents preliminary results of feasibility measures, and provides examples of preliminary data from home-based system sensors.

Methods

Study Design

EVALUATE-AD is a longitudinal, naturalistic observational cohort study. Thirty patients and 30 spouse coresident care partners (a total of 60 participants in 30 households) will be enrolled and monitored continuously for up to 24 months with the home-based computing and sensor system. The participants are recruited from an existing cohort of patients followed at the National Institute on Aging (NIA)−Layton Oregon Aging and Alzheimer's Disease Center (OADC). Additionally, new patients seen at the Aging and Alzheimer's clinic and participants referred from community physicians are enrolled if they meet the inclusion criteria. All participants sign informed consent forms (Oregon Health and Science University, OHSU Institutional Review Board number 16515).

Participants with MCI or AD living in the Portland metropolitan and surrounding areas, together with a coresident considered as a care partner are invited to participate in the study. The inclusion criteria for the participants with cognitive impairment and their coresidents include the following: NIA and the Alzheimer's Association clinical criteria for MCI [11] or probable AD [12] and have a Mini-Mental State Examination (MMSE) [13] score of 15 to 30, inclusive; the coresident care partner is functionally independent and has an MMSE of 24 to 30, inclusive; any gender; aged 50 to 90 years; consents to enrollment in the protocol; The coresident care partner is computer literate, defined as being able to send and receive an email; the household owns and uses a desktop or laptop computer; households have a reliable, broadband internet connection; and live in a larger than 1-room apartment.

The exclusion criteria are as follows: Significant neurologic diseases other than MCI or early AD, such as multi-infarct dementia or vascular cognitive impairment, Parkinson's disease, normal pressure hydrocephalus, brain tumor, or a history of significant head trauma with subsequent persistent neurologic deficits; major psychiatric disorders such as major depression, bipolar disorder (Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; DSM-IV criteria) within the past year, or history of schizophrenia (DSM-IV); psychotic features, agitation, or behavioral problems within the last 3 months, which could lead to difficulty complying with the protocol; history of alcohol or substance abuse or dependence within the past 2 years (DSM-IV criteria); any uncontrolled medical condition that is expected to preclude completion of the study, such as late-stage cancers; and more than 2 people live in the participant's residence (overnight visitors are acceptable).

Participants have dementia screening laboratory studies (complete blood count, chemistry panel, thyroid function, vitamin B-12), and brain imaging (magnetic resonance imaging or computed tomography) as part of their initial diagnostic work-up. An in-home screening visit is conducted by a research coordinator where consent is obtained, self-report questionnaires are completed, and neurocognitive tests are administered. A baseline assessment is then performed by a clinician at the participants' residence with a physical and neurological exam and neurocognitive tests. At 12 months and at the end of the study, the self-report questionnaires, physical and neurological exam, and neurocognitive tests are repeated during separate home visits by the research coordinator and clinician. The full assessment protocol, including baseline and follow-up assessments are shown in Table 1.

Table 1. Study schedule of assessments.

Assessment type	Week 0 (screening visit)	Week 0 (baseline assessments)	Week 1 (technology installation visit)	Week 52 (12-month assessments)	Week 104 (24-month assessments)
Consent	X[a]	—[b]	—	—	—
Personal and Family History Questionnaire	X	—	—	X	X
Subject Memory and Health Rating	X	—	—	X	X
MMSE[c] [13]	X	—	—	X	X
ADAS-Cog[d] [14]	X	—	—	X	X
Geriatric Depression Scale [15]	X	—	—	X	X
ISAAC[e] Technology Use Survey	X	—	—	X	X
Handedness Inventory	X	—	—	—	—
Technology and Computer Experience and Proficiency Questionnaires	X	—	—	X	X
Functional Assessment Questionnaire [16]	X	—	—	X	X
Neuropsychiatric Inventory Questionnaire [17]	X	—	—	X	X
Zarit Burden Interview–Short [18]	X	—	—	X	X
Pittsburgh Sleep Quality Index [19]	X	—	—	X	X
WRAT[f] reading level	X	—	—	—	—
Neurobehavioral Cognitive Status Examination [20]	—	X	—	X	X
Clinical Dementia Rating [21]	—	X	—	X	X
Neurological examination	—	X	—	X	X
Modified Unified Parkinson Disease Rating Scale [22]	—	X	—	X	X
Medical history and comorbid conditions	—	X	—	X	X
Tinetti gait	—	X	—	X	X
Tinetti balance	—	X	—	X	X
Sensor system installation	—	—	X	—	—
ORCATECH[g] Health and Life Activity Form	—	—	Assessed weekly	Assessed weekly	Assessed weekly
Total activity: mobility, steps, gait speed, and time in locations	—	—	Assessed continuously	Assessed continuously	Assessed continuously
Socialization and caregiving: time out, time alone or with partner, and time on internet	—	—	Assessed continuously	Assessed continuously	Assessed continuously
Medication taking: adherence (also weekly)	—	—	Assessed continuously	Assessed continuously	Assessed continuously
Cognition: computer activity, time on; session times, and complete forms	—	—	Assessed continuously	Assessed continuously	Assessed continuously
Sleep: time up, time in bed, times up at night, restlessness, and sleep latency	—	—	Assessed daily	Assessed daily	Assessed daily
Physiology: BMI and pulse	—	—	Assessed daily	Assessed daily	Assessed daily

[a]X: Assessment performed at this visit.

[b]Assessment not performed at this visit.

[c]MMSE: Mini-Mental State Examination.

[d]ADAS-Cog: Alzheimer Disease Assessment Scale–Cognitive Subscale.

[e]ISSAC: Intelligent Systems for Detection of Aging Changes.

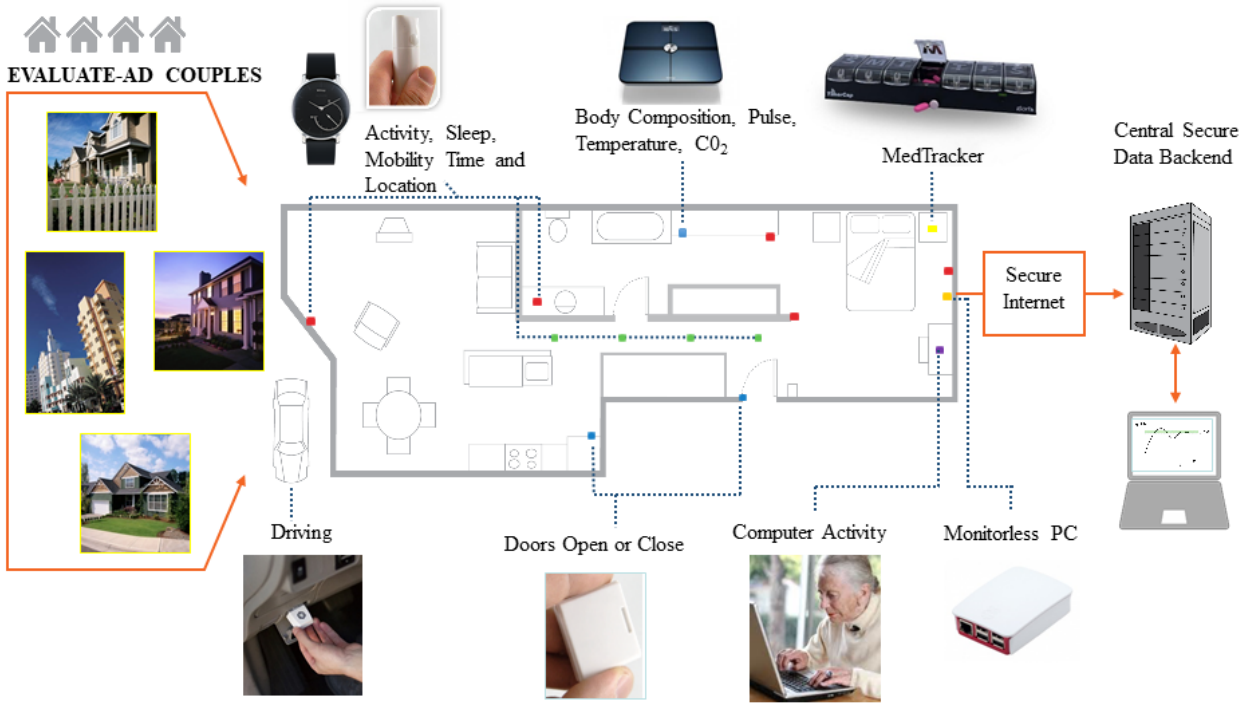
[f]WRAT: Wide Range Achievement Test.

[g]ORCATECH: Oregon Center for Aging and Technology.

Components of the Assessment System

After the screening and baseline clinician visits are complete, the sensor system is deployed at the participants' residence by a technology deployment field team according to the established Oregon Center for Aging and Technology (ORCATECH) Life Laboratory protocols [7-9] and the Collaborative Aging Research using Technology (CART) initiative [23]. Initial data are recorded with regard to the layout of the home to label the use of various spaces (eg, kitchen, bathroom, bedroom, etc). To facilitate deployment of the system in the community, where each home typically has a unique layout, a tablet-based graphing tool is used to automatically record where various sensors are located and their physical adjacencies to other sensors. A schematic of the overall home-based setup is shown in Figure 1; specific details of each component are described in Multimedia Appendix 1 [24-34] and are available on the CART initiative website [35].

Figure 1. Schematic of the home-based sensor system. EVALUATE-AD: Ecologically Valid, Ambient, Longitudinal and Unbiased Assessment of Treatment Efficacy in Alzheimer's Disease.



The components are described briefly as follows:

1. Hub computer:
   A monitorless computer (Raspberry Pi) functions as a data hub for all the sensors. Data are collected via standard wireless communications protocol (eg, Bluetooth, Zigbee, Wi-Fi) and transferred securely to servers at OHSU.
2. Activity sensing:
   Passive infrared (PIR) motion sensors using the Zigbee wireless communication protocol (NYCE Control) are placed in each room in the home and sense participants' motion at home and transitions between rooms. A line of four PIR sensors with more restricted fields of view are placed on the ceiling in an area where the participant walks regularly to detect walking speed. Each participant will also wear an activity-monitoring wristwatch (Withings Steel) to measure individual mobility and sleep measures.
3. Medication-taking behavior:
   An electronic pillbox (TimerCap iSort) records the times when specific lids (marked by the days of the week) are opened and closed. The electronic pillbox is provided to the participants with cognitive impairment to track their medication usage. Care partners do not use the pillbox. However, care partners can assist or remind the patient to take medications if this is part of their normal routine.
4. Physiological monitoring:
   Participants are asked to weigh themselves daily using a digital bioimpedance scale (Withings Body Cardio).
5. Driving assessment:
   An on-board telematic device (Automatic Pro) records data on multiple aspects of driving behavior and connects to the on-board diagnostic (OBD-II) port in each participant's vehicle.
6. Computer-based monitoring:
   WorkTime software (Nestersoft) is installed on the computers of each participant, which records data on

computer use (eg, time spent using the computer, number of sessions on the computer per day).

Medication Changes

To provide a conventional measure of changes in cognition that occur when patients transition on or off AD-related medications (cholinesterase inhibitors, memantine, antidepressants, hypnotics), the Telephone Interview for Cognitive Status (TICS) [36] is administered to participants within 1 week of a change in these medications and then subsequently at 6 and 12 weeks. Scores from the TICS are highly correlated with the MMSE [36]. Prior studies of cholinesterase inhibitors in individuals with AD administered the MMSE at baseline, 6, and 12 weeks and found a significant difference in MMSE scores at 12 weeks [37,38]. Changes in medication are identified using the weekly self-report survey, and an alert is sent from the ORCATECH home-participant management system to a research coordinator when participants indicate a medication change.

Analytic Considerations

This study is a proof of concept designed to construct a composite model of sensor-derived outcome measures that correlate with changes in conventional cognitive test scores seen when individuals start or stop cholinesterase inhibitors, memantine, or other medications, such as antidepressants, that are commonly used for managing AD. As this is an observational study, participants with MCI and AD are followed longitudinally, but medication changes are not dictated or restricted by the study; the participants' primary clinician prescribes these medications according to their practice. Therefore, participants may start, increase the dose, discontinue, or never be on AD-related medications. The Alzheimer Disease Assessment Scale–Cognitive Subscale (ADAS-Cog 11) was chosen for comparison to previous trials that found significant improvements in cognitive function with cholinesterase inhibitors [37-40] and memantine [41,42] relative to placebo. The ADAS-Cog is performed at baseline, 1 year, and 24 months (study end). The continuous sensor-based measures will be compared with the ADAS-Cog test scores. The effect of changes in dementia-related medications will be analyzed in a subset of participants where those changes occur. Our hypothesis is that changes in medications can be detected by high frequency, in-home monitored data with higher sensitivity (ie, high signal-to-noise ratio) than cognitive test scores, based on a previous study where we could reduce intraindividual variability and thereby reduce the required sample size [10].

Analysis

Feasibility Measures (Adherence and Dropout)

The first objective of this study is to assess the feasibility of using home-based pervasive computing systems to identify changes in meaningful outcomes in patients across the spectrum of MCI through early AD. Accordingly, the focus of analysis is on measures of adherence, retention, and report of experience with the technologies and protocol. Primary measures are the percentages of completed weekly web-based health and activity forms and dropout at 24 weeks and at the end of the study. Criterion measures are >80% adherence to completion of the weekly web-based survey and 0 dropout (for nonmedical reasons). In addition, information on each participant's experience with respect to the home sensor will be collected using a modified home monitoring technology attitudes and beliefs survey administered at the study end or early discontinuation.

Description of Sensor-Based Measures

The measures from nine individual functional/health domains evaluated are summarized in Table 2. The sensors collect data on a daily or continuous basis that provides information on the core functions and measures. Sensor-derived outcome measures from each domain will be compared with the corresponding conventional assessment measures in subsequent analyses at the completion of study data collection.

Table 2. Core functions and measures collected and types of sensors used to collect data. Metrics may be event driven (eg, medication taking) or unscheduled (eg, minutes to days of total activity).

Core functions and measures (continuous, daily, or weekly)	Sensors or devices used	Conventional assessment measures (at baseline, 12- and 24-months follow-up)
Physical capacity and personal mobility: Total daily activity, number of room transitions, median weekly walking speed from multiple daily walks, daily steps, and time out of home	PIR[a] motion sensors and door contact sensors; wearable activity tracking wristwatch	Walking speed (with a stopwatch). Self-report of activity from the OADC[b] Personal and Family History Questionnaire (Paffenbarger scale [43], for example, *estimate how many hours per day you spend in moderate activity*)
Sleep and nighttime behavior: Time of awakening in the morning, time spent in bed at night, wake after sleep onset, times up at night, and sleep latency	PIR motion sensors; wearable activity tracking wristwatch	Pittsburgh Sleep Quality Index and Sleep Disturbance Symptom Questionnaire [19] (part of the OADC Personal and Family History Questionnaire)
Physiologic health: daily BMI, pulse	Biofunction scale (AM pulse)	Vital signs (height, weight, pulse)
Medication adherence: Percentage of doses missed in a 7-day period, relative to the prescribed schedule.	Electronic pillbox	Self-report of adherence to medication-taking regimen (visual analog scale: ranging from 0% to 100%)
Socialization and engagement: Time out of home, time alone or with spouse, and computer activity	PIR motion sensors, contact sensors; wearable activity tracking wristwatch; personal computer	Self-report of eight social activities from the OADC Personal and Family History Questionnaire (eg, how often do you have visitors: rarely/never, daily, weekly, monthly, yearly)
Cognitive function: Time to complete online tasks (eg, weekly web-based online health forms), mouse movements, prospective memory for medication, and AM weighing protocol.	Personal computer or tablet; electronic pillbox; biofunction scale.	ADAS-Cog[c] 11 score [14], MMSE[d] score [13], NCSE[e] scores [20], TICS[f] [36] (completed if participant has an AD[g]-related medication change)
Community mobility: Driving time and distance driving, hard braking, hard accelerations, and most frequent locations out of home	Home sensors (exit door contact sensors); automobile data port telematic sensor	FAQ[h] [16] rating of ability: traveling out of neighborhood, driving, arranging to take buses
Health and life events: online self-report (ie, ER[i], doctor, or hospital visits, home visitors, mood, pain, loneliness, falls, injuries, change in home space, home assistance received, change in medications)	Personal computer or tablet (online reporting)	Mood: Geriatric Depression Scale (15-item) [15] and Neuropsychiatric Inventory [17]; self-report of health events from the OADC Personal and Family History Questionnaire
Care partner engagement: Time alone or time with cognitively impaired partner, time in bathroom together	PIR motion sensors; door contact sensors; wearable activity tracking wristwatch	Zarit Caregiver Burden Scale [18]

[a]PIR: passive infrared.

[b]OADC: Oregon Aging and Alzheimer's Disease Center.

[c]ADAS-Cog: Alzheimer Disease Assessment Scale–Cognitive Subscale.

[d]MMSE: Mini-Mental State Examination.

[e]NCSE: Neurobehavioral Cognitive Status Examination.

[f]TICS: Telephone Interview for Cognitive Status.

[g]AD: Alzheimer disease.

[h]FAQ: Functional Assessment Questionnaire.

[i]ER: emergency room.

Results

Participant Characteristics

Thirty homes have been enrolled and had the home assessment system installed (Figure 1), as of February 2020. Here, we present the preliminary data from the first 10 dyads with over first 6 months of monitoring after enrollment, composed of 5 participants with AD and 5 participants with MCI and their respective care partners (20 participants total). Participants with cognitive impairment were, on average, 74.7 years old with 17.7 years of education (Table 3). Mean scores on the MMSE were 24.9 and 13.7 on the ADAS-Cog. Care partners were, on average, 71.1 years old with a mean MMSE score of 29.7. The mean total duration of monitoring for the first 10 homes was 14 months.

Table 3. Demographics for participants from 10 homes (N=20).

Baseline variable	Patient (n=10)	Care partner (n=10)
Age (years), mean (SD)	74.7 (7.5)	71.1 (8.5)
Female, n (%)	2 (20)	8 (80)
Education (years), mean (SD)	17.7 (3.0)	16.3 (2.4)
MMSE[a], mean (SD)	24.9 (5.0)	29.7 (0.7)
ADAS-Cog[b] (n=9), mean (SD)	13.7 (10.4)	N/A[c]
CDR[d], mean (SD)	0.7 (0.2)	N/A
GDS[e], mean (SD)	2.2 (2.3)	1.5 (1.6)
ZBI-12[f], mean (SD)	N/A	10.0 (7.5)
NPI-Q[g], mean (SD)	3.3 (3.2)	N/A
FAQ[h], mean (SD)	8.4 (9.5)	N/A
Dementia-related medications, n (%)	6 (60)	N/A

[a]MMSE: Mini-Mental State Examination.

[b]ADAS-Cog: Alzheimer Disease Assessment Scale–Cognitive Subscale.

[c]N/A: not applicable.

[d]CDR: Clinical Dementia Rating.

[e]GDS: Geriatric Depression Scale.

[f]ZBI-12: Zarit Burden Interview–Short.

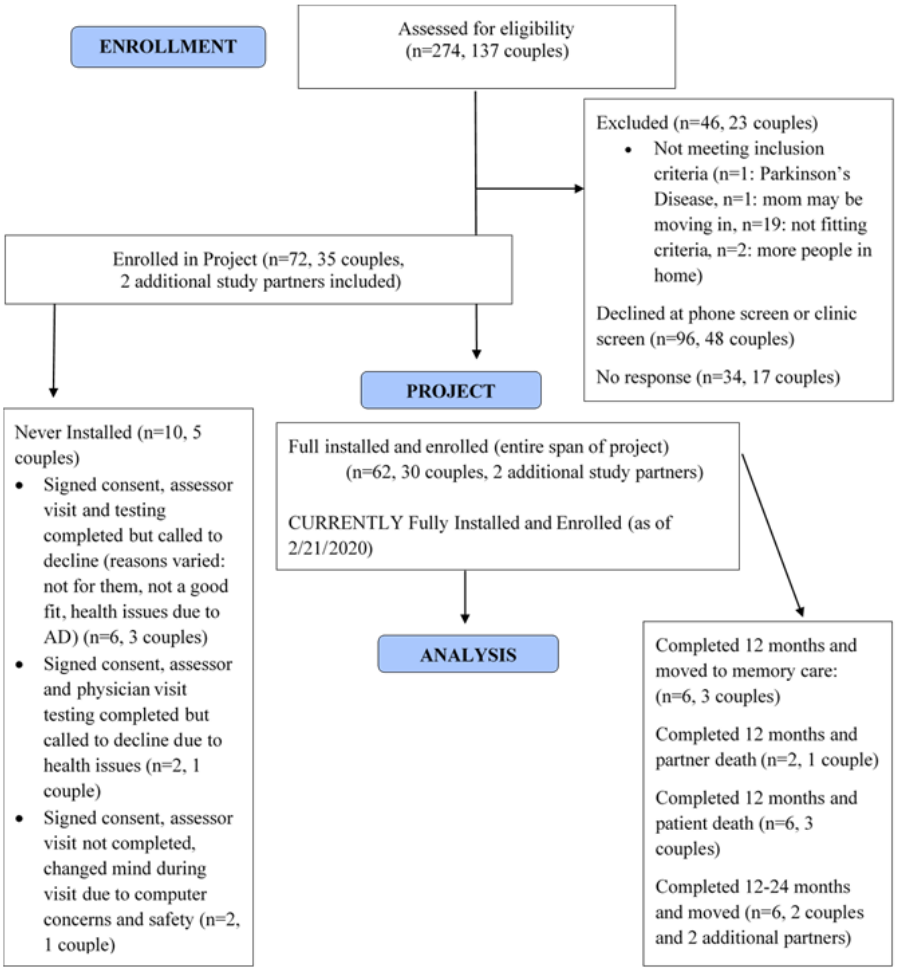
[g]NPI-Q: Neuropsychiatric Inventory Questionnaire.

[h]FAQ: Functional Assessment Questionnaire.

Recruitment

The screen failure rate was approximately 68.04% (132/194 individuals) for eligible participants (Figure 2). A total of 274 participants were assessed for eligibility, with 46 not meeting criteria and 34 not responding to messages left about participation in the trial. Other individuals who were contacted declined participation for a variety of reasons. The majority of individuals that declined indicated they were not interested in participating in a clinical trial at the time of contact. Some individuals were more interested in participation in an interventional trial, and others declined because their study partner did not agree to be involved in the trial. The installation of a home assessment system or having to wear an activity monitoring wristwatch was offered as another reason for declining participation in the study.

Figure 2. Participant enrollment and follow-up summary. Two homes were enrolled with a third additional study partner in the home, who also wore an activity monitoring wristwatch. AD: Alzheimer disease.



Feasibility Measures

Acceptance of the Home Assessment System

The home-based pervasive computing system is well tolerated by participants. There have been no withdrawals from the study after the system has been deployed in the home. Exit survey responses were available from the care partners of the two homes that completed the study due to the individual with cognitive impairment transitioning to long-term care. The exit surveys are shown in Multimedia Appendices 2 and 3. Both care partners strongly agreed with the statements *I do not mind being monitored unobtrusively in my home*, and *I did not find the sensor system was an extra source of stress.*

Adherence

Adherence to completion of the weekly web-based health survey was 75% for participants with cognitive impairment (n=6, independently completing on the web) and 84% for care partners (n=10; Table 4), with the longest enrollment in the study being 396 days. The completion rate was good for the care partners; however, the completion rate for participants with cognitive impairment was slightly lower than the criterion rate. A total of 4 of the 5 participants with AD required assistance with the completion of the survey each week from their care partner.

Table 4. Summary of sensor-based measures in patient participants and care partners.

Sensor system outcome measure	Patient (n=10)	Care partner (n=10)
Follow-up time (months), mean (SD)	14.6 (3.0)	13.9 (4.1)
Mean daily total steps, mean (SD)	3709 (3245)	4089 (2230)
Daily watch compliance (%), mean (SD)	75 (15)	72 (12)
Mean nightly sleep time (hours), mean (SD)	7.2 (0.8)	7.8 (0.6)
Nightly watch compliance (%), mean (SD)	60 (23)	65 (14)
Electronic pillbox compliance (%; n=6), mean (SD)	77 (26)	N/A[a]
Independently completing online weekly health form, n	6	10
Weekly health form compliance (%), mean (SD)	75 (27)	84 (16)

[a]N/A: not applicable.

Instances of Missing Data

A few technical issues were encountered during the enrollment and data collection of the first few participants. This was mainly due to a major upgrade in the home monitoring system that included, in part, the addition of new devices (eg, activity monitoring wristwatch and new electronic pillbox). These issues were quickly identified and resolved using a series of software and firmware updates.

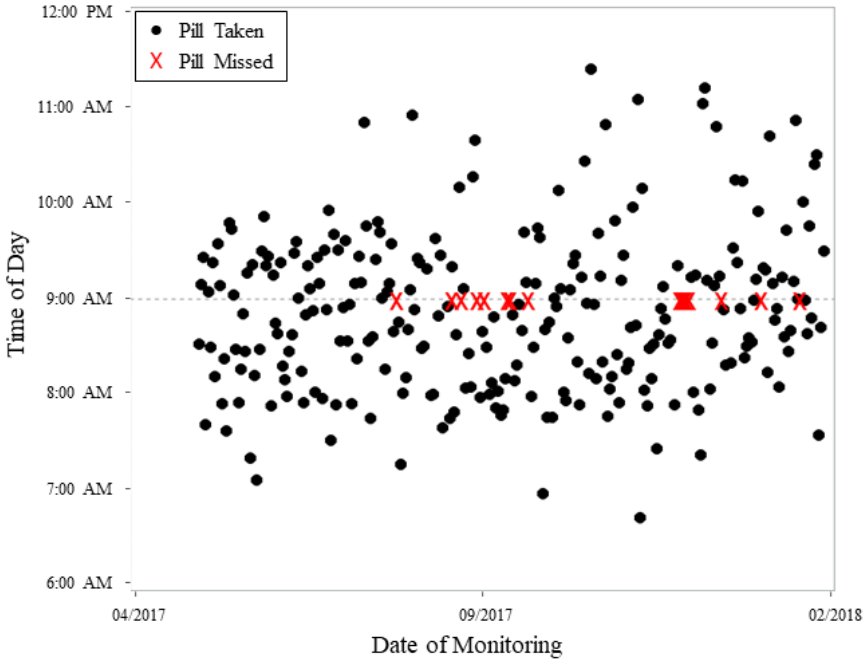
Sensor-Based Outcome Measures

Table 4 shows a summary of a sample of sensor-based outcome measures comparing care partners with participants with cognitive impairment.

Medication-Taking Behavior

Of the 10 participants with cognitive impairment, 6 (5 with AD, 1 with MCI) were taking AD-related medications (cholinesterase inhibitors, memantine, antidepressants, or sleep aids) and using the electronic pillbox. Overall compliance for the group was 77% (Table 4). Figure 3 shows adherence for a single participant over 7 months for a once-daily medication (venlafaxine).

Figure 3. Time of day that medication was taken for each day over 7 months of monitoring by a participant with mild Alzheimer disease. The dots indicate the times at which the pill was taken, and an X indicates when a pill was missed. Overall, participant adherence was 94% over 9 months.



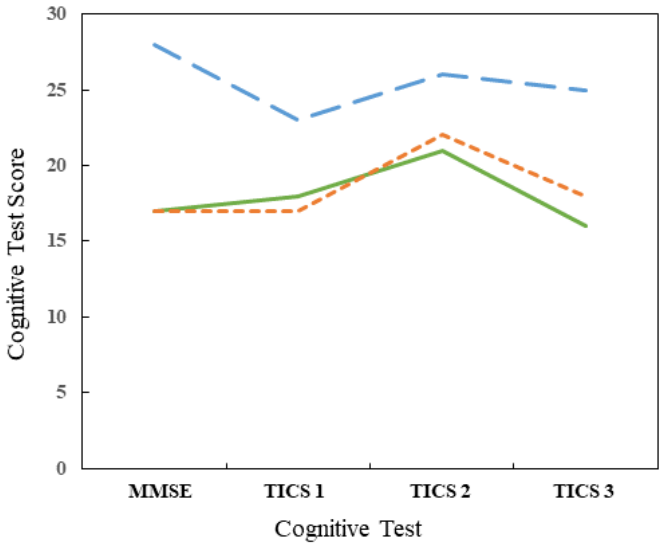
Activity Sensing and Sleep Behavior

Preliminary data collected from the activity monitoring are presented from a mean of 14.6 months of monitoring in participants with cognitive impairment. In this sample, participants with cognitive impairment (n=10) had a mean step count of 3709 and a mean total sleep time of 7.2 hours per night. Care partners (n=10) had a mean step count of 4089 and a mean total sleep time of 7.8 hours per night. Compliance to wearing the watch ([number of days with watch data]/[total number of days]×100) for both groups is shown in Table 4.

Changes in Medications

Changes in AD-related medications occurred in 3 participants. The changes were all related to antidepressant medications used to treat behavioral symptoms associated with AD. Two participants had the dose of their medication increased and 1 was started on a new antidepressant medication. Figure 4 shows the results of TICS at the time of medication change (TICS 1), at 6 weeks (TICS 2), and at 12 weeks (TICS 3). In addition to the cognitive testing performed after medication changes, the weekly health report form also collects information that may be relevant to medications treating behavioral and psychiatric symptoms of dementia. Participants are asked if they have felt *blue* or *lonely* in the past week. In 1 participant, reports of feeling *blue* decreased from 33% (7/21) of weekly responses before the medication change to 10% (3/30) afterward, and reports of feeling *lonely* decreased from 24% (5/21) to 3% (1/30). In the other 2 participants, reports of feeling *blue* or *lonely* did not change significantly. In the second participant, there were no reports of feeling *blue* and only one report of feeling *lonely* after the medication change. In the third participant, there was one report of feeling *blue* before the medication change, with none afterward, and only one report of feeling *lonely* after the medication change.

Figure 4. Cognitive test scores in the 3 participants with medication changes. The MMSE was completed at the baseline study visit. The Telephone Interview for Cognitive Status were completed over the phone after a change in medication and subsequently at 6 and 12 weeks. MMSE: Mini-Mental State Examination; TICS: Telephone Interview for Cognitive Status.



Discussion

Initial Findings

The EVALUATE-AD trial aims to determine the feasibility of detecting changes in everyday health and functional domains that are related to cognitive impairment in individuals with MCI and AD. In order to properly utilize remote sensing approaches in clinical trials, potentially more sensitive, objective, and ecologically valid measures digital biomarkers need to be longitudinally acquired and analyzed in real-world environments. Although individuals with MCI have been studied with home-based sensing systems for extended periods of time [44,45], people with early AD and their care partners have not. The collection of digital biomarkers in more natural settings provides the opportunity to collect data on novel outcomes related to daily functioning that cannot be ascertained with conventional clinic-based methods. Additionally, the data collection occurs unobtrusively and with little involvement of the participants, thereby avoiding the addition of potential stress and burden to individuals with cognitive impairment and their care partners.

Preliminary results from this study demonstrate that the deployment of the home-based computing and sensing system is well received by participants. There has been no dropout after study enrollment. Adherence to completion of the weekly health survey is above the expected criterion value for care partners, but slightly below the criterion for individuals with cognitive impairment. The difference between groups may be in part related to the need for assistance in completion of the form in some individuals with AD. Outcome metrics comprising multiple functional and health-related domains are being collected and analyzed from multiperson homes. Examples from preliminary data show how medication adherence, activity levels, and sleep behavior can be collected longitudinally by the home-based system. The use of an electronic pillbox has potential limitations, as the opening and closing of a daily compartment does not guarantee that the medication was ingested. However, daily monitoring of medication-taking behavior with this sensor should provide greater accuracy than the current practice of relying on study participants to bring unused medication to study visits for tabulation. Compliance with wearing the activity-monitoring wristwatch was higher during the day than at night and was collected for 60% of the nights in participants with cognitive impairment. This demonstrates the potential shortcoming of wearable technologies in everyday long-term use. Participants may not feel comfortable wearing the watch during sleep. Additionally, if the device is removed during the day, individuals may forget to put it back on. The activity watch provides the advantage of detecting activity levels even when the participant is outside of the home, but for monitoring sleep, unobtrusive sensors (eg, PIR sensors

and movement-sensitive bed mats) may provide more reliable methods for longitudinal monitoring.

Technical issues that arose initially during the study demonstrated problems that can arise as new sensors are integrated into a platform. To ensure that all sensors were functioning, modifications to the alert system in the home monitoring platform were designed. An automated program was created to summarize the data from each sensor in each home on a weekly basis. Sensors that may not have collected data on a specific day still generate a regular *check-in* signal to ensure that they are functioning properly. This system also provides frequent data reviews to identify issues that arise with data collection as early as possible. Any issues that were detected by the program were identified by the study coordinator and the technology field team for the study, and a solution to the problem was provided either remotely or with a home visit if necessary. The technical solutions to these issues can be applied as new sensors continue to be integrated into research platforms and will help improve the reliability of data collection and prevent loss of data.

Future Analysis

The second objective of the project is to compare the outcome measures of the automated system in different functional and health domains with conventional clinical outcome measures in AD. As part of the evaluation of these novel approaches, comparison to current standards need to be conducted, and three approaches will be applied. Data from the continuous sensor-based measures will be aggregated from 2-month periods anchored on the date of conventional measure acquisition. This is done because the frame of reference of the conventional measure comparator is restricted to a single day and is a method used in previous studies [24]. For these comparisons, simple correlations will be calculated between the objective, continuous sensor-derived variables, and the conventional test domains in the total cognitively impaired sample regardless of diagnosis and then in a secondary analysis dividing the group into MCI and early AD. The second approach examines the trajectories of change in continuously collected sensor-based measures, using a previously established procedure to determine these trajectories [10]. A subject-specific distribution is calculated for each metric using the data collected during the first month, and an individual-specific threshold of low and high activity is created. The change (or shift) in individual-specific distributions over time can then be examined by tracking how often individuals move below or above their own threshold determined at baseline (ie, during the first 3 months). This approach, which utilizes individual-specific distributions instead of group means, was found to be sensitive to changes even among those with presymptomatic MCI, where detection of change is often quite difficult. Finally, using generalized mixed effects models, the likelihood of having low functional days that differs by diagnostic group (MCI or early AD) and medication status (eg, taking anticholinesterase medication vs not taking them) is determined. Before applying the above approach, we ensure that the trajectories for each metric are reasonable in terms of ranges, direction, and the amount of change using conventional approaches, such as examination of spaghetti plots, linear mixed effects models with or without nonlinear terms, and latent trajectory models (an approach successfully employed in previous work [25]).

The third goal of the project is to develop an objective behavioral-functional signature of patients on cholinesterase inhibitors and related therapies. This measure will be derived from a composite model composed of sensor-based outcome measures that are found to be significant in detecting differences in trajectories by cognitive impairment group as well as those on or off symptomatic AD treatments. The ultimate goal is to examine whether those initially without treatment or adjustment to treatment show changes (ie, improvement) in the derived digital composite score over time when they are on the medication. High-frequency, multidomain data afforded by the pervasive computing environment deployed affords the ability to identify contrasting dynamic changes in relevant functions between different pharmacologic agents. Those relevant to current, approved therapy form a baseline of activities and behaviors to contrast for future trials. This pharmacologic behavioral fingerprinting and, ultimately, the generation of more meaningful composite measures can be generalized to future randomized control trials using new agents. This objective is not the focus of this preliminary report and will be reported in a subsequent publication once data collection for the trial is complete.

Although a focus of this research is to detect treatment-specific changes, the sample size is small, and not all participants in the study will transition on or off a cholinesterase inhibitor, memantine, or a symptom-management medication. Nevertheless, we anticipate that a composite digital biomarker composed of multiple outcome measures derived from the home monitoring system will detect sensitive changes in the digital biomarker signal with increased statistical power. Unlike the presymptomatic subjects enrolled in prior studies [7], the MCI and AD patients recruited in this study are anticipated to experience greater cognitive decline (ie, MMSE declines by 0.02 points per year among presymptomatic subjects or over 5 years of change≈1 MMSE point), with MMSE declines of 2 or 3 points per year observed for AD patients (ie, a >10-fold faster decline) [46]. Given that we would see an approximately 8-fold steeper decline in outcomes than previously shown, using this intraindividual approach, we would achieve 80% power to detect a 30% treatment effect size with 30 subjects (20 subjects with medication and 10 subjects without) over 2 years (alpha=.05, 2-tailed). The automated sensor-based measures collected in EVALUATE-AD for up to 24 months will provide important measures of variance and trajectory of change data needed for future power estimates.

Conclusion

The use of high-frequency, longitudinal data acquisition appears more sensitive to change than conventional, episodic in-clinic testing. The measures lend themselves to more direct translation to meaningful outcomes for patients and care partners (eg, improved mobility, computer use, better sleep, better medication adherence). These digital biomarkers can be used in combination with conventional clinical assessment methods. A behavioral-pharmacologic signature composed of multiple digital biomarkers could be used to detect changes in cognition

and functional status in individuals with cognitive impairment initiating or discontinuing symptomatic treatments. This methodology has the potential to reduce the size and/or length of clinical trials by more precisely estimating the true trajectory of change in participants with high-frequency in-home data and individual-specific distributions. The ultimate goal will be to use these longitudinal and person-specific measures to more effectively test new therapeutics and guide individual responses to therapies in patients.

Acknowledgments

This research was supported by grants from the Merck Investigators Study Program, the NIA-Layton OADC (Grant No. P30-AG008017), and ORCATECH (Grant No. P30-AG024978). Technical guidance was provided in part by the CART initiative (National Institutes of Health, NIH, Grant No. U2C-AG0543701; Department of Veteran Affairs Health Services Research and Development, Grant No., IIR 17-144), the Oregon Clinical Translational Research Institute award (National Center for Advancing Translational Sciences, Grant No. UL1 TR002369). CART is funded by the Office of The Director, NIH, National Center for Advancing Translational Sciences, National Institute of Biomedical Imaging And Bioengineering, National Institute of Nursing Research, NIA, National Institute of Neurological Disorders And Stroke, National Cancer Institute, and the Departments of Veteran Affairs Health Services Research and Development.

Conflicts of Interest

NT is the primary author on this manuscript. He was involved in the implementation of the study, and drafted the manuscript. NT is compensated for assessments performed within clinical trials sponsored by Genentech. ZB was involved in development of components of the data management system and data analysis. He made substantive contributions to revising the manuscript for intellectual content. He has no disclosures. JM was involved in coordination of the study. She made substantive contributions to revising the manuscript for intellectual content. She has no disclosures. KW was involved in coordination of the study, participant study assessment and data analysis. She has no disclosures. NS was involved in the design, conceptualization, and implementation of the study. She has no disclosures. NM was involved in the design and conceptualization of the study, and statistical analysis. She has no disclosures. HD contributed to the design and conceptualization, and made substantive contributions in data analysis and in revising the manuscript for intellectual content. She receives research support from the NIH (R01 AG033581, R01AG051628, R01AG056102, P30 AG008017, P30AG024978, U2CAG054397, R01AG043398, U2CAG057441). KW made substantive contributions to revising the manuscript for intellectual content. She has no disclosures. JK was involved in the design and conceptualization of the study and drafting of the manuscript. He receives research support from the NIH (U2C AG054397, P30 AG008017, R01 AG024059, P30 AG024978, P01 AG043362, U01 AG010483) and Merck. He directs centers at Oregon Health & Science University that receives research support from the NIH, and the Department of Veterans Affairs, AbbVie, Novartis, and Eisai. In the last 36 months, he has been compensated for serving on Data Safety Monitoring Committees for Eli Lilly and Suven. He is also compensated for serving on the Scientific Advisory Board for Sage Bionetworks and receives reimbursement through Medicare or commercial insurance plans for providing clinical assessment and care for patients and serves on the editorial advisory board and as Associate Editor of the journal, Alzheimer's & Dementia and as Associate Editor for the Journal of Translational Engineering in Health and Medicine.

Multimedia Appendix 1
Components of the assessment system.
[DOCX File , 25 KB - resprot_v9i5e17603_app1.docx]

Multimedia Appendix 2
Participant exit survey examining attitudes and perceptions towards the home-based sensor system.
[DOCX File , 16 KB - resprot_v9i5e17603_app2.docx]

Multimedia Appendix 3
Care partner exit survey examining attitudes and perceptions towards the home-based sensor system.
[DOCX File , 16 KB - resprot_v9i5e17603_app3.docx]

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Abbreviations

AD: Alzheimer disease
ADAS-Cog: Alzheimer Disease Assessment Scale–Cognitive Subscale
CART: Collaborative Aging Research using Technology
DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, 4th Edition
EVALUATE-AD: Ecologically Valid, Ambient, Longitudinal and Unbiased Assessment of Treatment Efficacy in Alzheimer's Disease
MCI: mild cognitive impairment
MMSE: Mini-Mental State Examination
NIA: National Institute on Aging
NIH: National Institutes of Health
OADC: Oregon Aging and Alzheimer's Disease Center
OHSU: Oregon Health and Science University
ORCATECH: Oregon Center for Aging and Technology
PIR: passive infrared
TICS: Telephone Interview for Cognitive Status

Edited by G Eysenbach; submitted 27.12.19; peer-reviewed by C Consel, A Piau, C Homan; comments to author 10.02.20; revised version received 24.02.20; accepted 26.02.20; published 27.05.20.

Please cite as:
Thomas NWD, Beattie Z, Marcoe J, Wright K, Sharma N, Mattek N, Dodge H, Wild K, Kaye J
An Ecologically Valid, Longitudinal, and Unbiased Assessment of Treatment Efficacy in Alzheimer Disease (the EVALUATE-AD Trial): Proof-of-Concept Study
JMIR Res Protoc 2020;9(5):e17603
URL: http://www.researchprotocols.org/2020/5/e17603/
doi:10.2196/17603
PMID:32459184

Original Paper

Patient-Reported Outcome Measures of Utilizing Person-Generated Health Data in the Case of Simulated Stroke Rehabilitation: Development Method

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Abstract

Background: Person-generated health data (PGHD) are health data that people generate, record, and analyze for themselves. Although the health benefits of PGHD use have been reported, there is no systematic way for patients to measure and report the health effects they experience from using their PGHD. Patient-reported outcome measures (PROMs) allow patients to systematically self-report their outcomes of a health care service. They generate first-hand evidence of the impact of health care services and are able to reflect the real-world diversity of actual patients and management approaches. Therefore, this paper argues that a PROM of utilizing PGHD, or PROM-PGHD, is necessary to help build evidence-based practice in clinical work with PGHD.

Objective: This paper aims to describe a method for developing PROMs for people who are using PGHD in conjunction with their clinical care—*PROM-PGHD*, and the method is illustrated through a case study.

Methods: The five-step qualitative item review (QIR) method was augmented to guide the development of a PROM-PGHD. However, using QIR as a guide to develop a PROM-PGHD requires additional socio-technical consideration of the PGHD and the health technologies from which they are produced. Therefore, the QIR method is augmented for developing a PROM-PGHD, resulting in the PROM-PGHD development method.

Results: A worked example was used to illustrate how the PROM-PGHD development method may be used systematically to develop PROMs applicable across a range of PGHD technology types used in relation to various health conditions.

Conclusions: This paper describes and illustrates a method for developing a PROM-PGHD, which may be applied to many different cases of health conditions and technology categories. When applied to other cases of health conditions and technology categories, the method could have broad relevance for evidence-based practice in clinical work with PGHD.

(JMIR Res Protoc 2020;9(5):e16827) doi:10.2196/16827

KEYWORDS

patient monitoring; patient reported outcome measures; patient generated health data; person generated health data; questionnaire design; telemedicine

Introduction

Understanding the Effects of Person-Generated Health Data

Person- or patient-generated health data (PGHD) are health, wellness, and other biometric data that people generate, record, and analyze for themselves [1]. Examples of technologies that support PGHD include Web-based journaling tools, activity-tracking devices or mobile apps, networked health data–gathering devices such as weighing scales, and simulated rehabilitation technologies. Patients who use PGHD-enabled technologies may experience positive, negative, or nil effects. PGHD use has been reported to increase patients' interest in

their own health care processes [2-4] and the management of their own health status [5]. It is known that when patients understand their illness, they may become active problem solvers and improve their health behavior [6]. However, PGHD use can also cause feelings of frustration and discouragement [7], and may even make some patients feel excluded from the benefits of PGHD use [5].

Although such varying health effects of PGHD use have been reported for a variety of health conditions and technology types, there is no systematic way for patients to measure and report health effects that they experience from utilizing their PGHD—whether positive, negative, or nil. This may hamper the integration of PGHD into clinical workflows [1]. In addition, PGHD technologies may be designed to support clinicians' utilization of these data at the expense of functionality that supports patients to use their data for self-management and shared decision making [8]. Thus, it is necessary to consider the patient's perspective in the design and development of health technologies [9], particularly those that generate PGHD [8].

Patient-Reported Outcome Measures

In health care services and interventions in general, the measurement of effects on patients, by patients themselves, is not new. Patient-reported outcomes are self-reported status updates of a patient's health condition, experience with an illness, or treatment without additional interpretation of the report, for example, by clinicians [10-12]. They may be used to indicate health status, such as state of a disease, at a single point in time, and any changes over time from previous patient-reported outcomes [10,13].

Standardized instruments that measure patient-reported outcomes, Patient-Reported Outcome Measures (PROMs) contribute to a more precise evaluation of the effects of a variety of health interventions and improve the evidence base in many areas of clinical care [14,15]. PROMs are used to determine the effectiveness of health care practices and to set standards for health care providers' performance, and their importance is highlighted by several national projects [15,16].

PROMs are developed systematically [10,11,13], and this formalism makes PROMs valuable to complement clinician-reported outcome measures used in reporting as part of standardized treatment assessments, such as clinician assessments of patient health, health outcome indicators collected routinely by health care organizations, and physiological or other biomedical indicators [15]. Their utility in generating first-hand evidence of the impact of health care services enables them to reflect the real-world diversity of actual patients and management approaches [17,18]. Thus, PROMs may provide a more comprehensive and accurate assessment of patient outcomes and the effectiveness of health care services and interventions [11,15,19,20].

Patient-Reported Outcome Measures of Utilizing Person-Generated Health Data

A systematic way for patients to measure and self-report the health effects they experience from utilizing their PGHD is lacking. A PROM of utilizing PGHD, or PROM-PGHD, is necessary to help build evidence-based practice (EBP) in clinical work with PGHD. Measuring outcomes of PGHD utilization using PROMs has been suggested [21]. Patient participation is considered essential in developing PROMs [10,22,23], with nearly three-quarters of PROM-development papers including patients during the process [24]. Given PGHD's person- or patient-centric approach to health data, it is useful and appropriate to involve patients in developing a standard way of using PROMs to capture the effects of PGHD. The participatory health paradigm recognizes the value of having patients contribute to the creation of knowledge in such ways [25].

PROMs-PGHD may deepen our understanding of how PGHD impact the health status and quality of life of patients, in an era of mobile and wearable remote patient monitoring [26]. PROMs-PGHD could also be used as a complement to existing clinician-reported and patient-reported outcomes, similar to how many PROMs are used alongside other health outcome indicators [15]. While many PROMs allow patients to report outcomes that correlate with their quantifiable PGHD [26], specific PROMs-PGHD would allow more direct self-reporting of the effects on patient health of utilizing PGHD. PROMs-PGHD could contribute to a more holistic and accurate assessment of whether and how patients' use of PGHD from health self-monitoring technologies actually has health benefits. This would provide a triangulated measurement of patients' experiences and outcomes resulting from their use of health information technology.

Objective

The aim of this paper was to describe and illustrate a method for developing PROMs for people who are utilizing PGHD in conjunction with their clinical care—*PROM-PGHD*.

Methods

This section reviews practices for developing PROMs, provides a rationale for the selection of the qualitative item review (QIR) method to develop a PROM-PGHD, and explains the need to augment QIR considering the socio-technical domains of health technologies.

Patent-Reported Outcome Measure Development Practices

PROMs are developed in many different ways, but generally accepted elements in the process can be discerned [15]. Reviewing recognized methods for PROM development (Table 1) and their commonalities put into context the selection of a particular method to guide PROM-PGHD development.

Table 1. Patient-reported outcome measure (PROM) development: the best practice activities.

Number	Phases (review paper [23])	Steps (US Food and Drug Administration Guide [10])	Stages (Scientific Advisory Committee of the Medical Outcomes Trust [21,22,26])
1	Establish correct health outcomes to measure	Hypothesize conceptual framework • Concepts hypothesized • Target population and application of the PROM identified • Literature or expert review conducted	Conceptual model for the PROM and its Initial Items are developed • Includes literature review to identify existing PROMs within the target domain • Interviews and/or focus groups with the target population, condition, or disease • Identification of relevant areas as a basis for PROM development • Pilot testing of initial PROM items on a small cohort of patients
2	Develop PROM items	Adjust conceptual framework and draft instrument • Patient input obtained • New PROM items generated • Method of data collection/administration determined • PROM draft items pilot tested	Revised PROM items from stage I are field-tested on a larger cohort of patients • Results in further item revisions to improve item validity • Reductions to eliminate redundancy, endorsement frequency, and absent data
3	Test the PROM items on comprehensibility and a range of psychometric criteria, for example, acceptability, internal consistency, and reliability	Confirm conceptual framework and assess other measurement properties • Developed conceptual framework confirmed via a scoring rule • PROM items assessed using psychometric criteria and finalized for content and format	Psychometric field-testing of the PROM being developed • Resulting PROM administered to a large cohort of patients and tested based on a psychometric criterion, for example, acceptability, internal consistency, and reliability
4	N/A[a]	Collect, analyze, and interpret data • Protocol and statistical plan for PROM data collection and analysis developed • Product treatment responses evaluated and benefits interpreted	N/A
5	N/A	Modify instrument • PROM items revised again using psychometric criteria • PROM items translated and adapted culturally for multiple languages; this fifth step then leads back iteratively to the first step	N/A

[a]N/A: not applicable.

We found a scoping review of 189 PROM development papers from 1980 to 2014 that outlined the development processes of 193 PROMs retrieved from the PubMed, Cochrane Methodology, MEDLINE, and EMBASE databases [24]. This review noted that PROM development follows three broad, distinct phases, as shown in Table 1, although the review paper itself provided limited information on those phases. One of the included papers was the highly cited US Food and Drug Administration (FDA) industry guide to use PROMs for medical product labeling [10]. Many of the suggested activities in its first three steps align with the three phases described in the review paper [24]. However, the FDA guide suggests a more detailed, 5-step iterative process for developing PROMs [10], as shown in Table 1.

Another highly cited guide for PROM development, not included in the review paper, is that of the Scientific Advisory Committee (SAC) of the Medical Outcomes Trust [22]. This defines a set of attributes for developing and assessing instruments for measuring health status and quality of life, and recommends a 3-stage process for developing PROMs [23,27], as shown in Table 1.

We observed that the steps of the FDA guide [10] align with many of the activities outlined by the SAC [23,27], and consequently both align with the three phases described in the review paper (Table 2) [24]. This indicated consensus on the best practice in PROM development and gave us an understanding of what the developers of a PROM-PGHD must do so as to adhere to the best practice.

Table 2. Parallels between patient-reported outcome measure (PROM) development processes in the literature.

Phases (review paper [23]) and steps (US Food and Drug Administration Guide [10])	Stages (Scientific Advisory Committee of the Medical Outcomes Trust [21,26])
Phase 1: Establish correct health outcomes to measure	
Step 1: Hypothesize conceptual framework	Stage I: Conceptual model for the PROM and its initial items are developed
Phase 2: Develop PROM items	
Step 2: Adjust conceptual framework and draft instrument	Stage I: Conceptual model for the PROM and its initial items are developed
Phase 3: Test the PROM items on comprehensibility and a range of psychometric criteria	
Step 3: Confirm conceptual framework and assess other measurement properties	Stage III: Psychometric field-testing of the PROM being developed
Step 4: Collect, analyze, and interpret data	Stage III: Psychometric field-testing of the PROM being developed
Step 5: Modify instrument	All stages: PROM item revision activities
Iteration back to Step 1, with further testing	Stage II: Revised PROM items from Stage I are field-tested on a larger cohort of patients

Qualitative Item Review

The systematic QIR process was designed to develop PROM items for the Patient Reported Outcomes Measurement Information System (PROMIS), a US National Institutes of Health initiative to provide a PROMs infrastructure for clinical research and practice [15,16]. QIR was intended to identify and develop items that could precisely estimate the traits being measured, and to represent the range of experiences relevant to the domains of interest. QIR is based on the best practices of PROM development and is committed to involving patients in the process, as described below. All of these factors make it suitable as a foundation for developing a PROM-PGHD.

PROM development falls within the participatory health paradigm, as the patient's perspective is central to the value of PROMs [14]. Thus, patient participation should be deliberate in the development of a PROM-PGHD. QIR was developed with a commitment to involving patients, with a reference to the recommendation in the FDA guide [10]. It specifically suggests when and how patients are included in the development process. It also examines how patient perspectives influence the concepts measured and the items constructed, and aims to bridge gaps between them. Moreover, it gathers patient input to increase the suitability of the items so that they reflect patient experiences closely, facilitating the correct understanding and interpretation of patients' responses to the items [16]. QIR provides the necessary attention to patient participation to make it a sound choice as a method for developing a PROM-PGHD.

QIR was specifically designed to optimize a set of PROM items in preparation for field testing. It was meant to develop an initial set of PROM items qualitatively and revise them by eliciting patient participation. Quantitative field testing, for example, using psychometric criteria, may then follow QIR, according to good practice guidelines [16].

Comparing QIR with the PROM development process described in the literature reveals that it closely aligns with early stage qualitative activities, that is, Stage I of the process suggested by the SAC [22], and thus with phases/steps 1 and 2 of the review paper [24] and FDA guide [10]. The QIR steps are summarized in Table 3.

Table 3. Activities of the qualitative item review.

Number	Step name	Activities
1	Literature review to identify existing items	Scan literature around established PROMs[a] within target domain/s; it will guide building proposed outcome measure items. Items identified represent the range of domain-relevant experiences.
2	Binning and winnowing	Binning involves categorizing selected items according to meaning and intrinsic structure. Winnowing excludes items that do not fit target domains and characteristics of PROM being developed.
3	Item revision process	Retained items are appropriately revised to ensure they are independent, have similar contexts, concise and simple, and worded to encourage the use of available response options to reduce cognitive burden on respondents.
4	Focus groups and cognitive interviews with target patient cohort	It ensures patient input is elicited in the development of PROM item sets. It enables PROM designers to understand vocabulary and thinking processes of target group and gathers feedback on individual items. It is aimed to bridge relevant gaps between current items and target domain or concepts to be measured. It highlights other measurement areas expressed by patients that are not covered in initial item set.
5	Final item revisions	Items are revised again based on patient input gathered from previous step. Items are tested with the Lexile Analyzer (MetaMetrics, Inc) to assess readability. After revisions are completed, field testing on items may begin, to understand their quantitative characteristics.

[a]PROM: patient-reported outcome measure.

Augmenting the Qualitative Item Review Process for the Socio-Technical Context of Person-Generated Health Data

The development of a PROM-PGHD requires socio-technical consideration of PGHD and the health technologies from which they are produced. Health-related activities of patients are influenced by the social and health context of the patient and their family and community [28]. This contributes to the complexity of what is known as the socio-technical system in health care, referring to the social system that influences and is influenced by implementations of technical systems. Thus, a socio-technical approach to health informatics interventions is crucial [29]. The health tools and technologies that patients use are most effective if they align with the patients' goals for completing health-related activities within the context of their health conditions. Moreover, health information technology interventions need to be responsive to the biomedical realities and personal characteristics of the target patient population [28].

Therefore, in developing a PROM-PGHD, it is important to recognize two domains influencing the outcome to be measured [30,31]: the health condition and the technology category. The evaluation of PGHD's role in self-management and clinical care should draw upon the body of knowledge from both domains [32]. There are different possible effects on health conditions in patients who use data from a web portal, a smart phone app, or a wearable sensor, just as there are different possible health effects of using data from a smartphone app in patients with diabetes, a mental illness, or asthma [1]. This is an important consideration, as the value of a PROM is dependent on its appropriateness based on the needs of the patient population [33].

Our development also factored in a key difference between the objectives of the PROMIS initiative for which the QIR was designed and the objective of PROM-PGHD. The PROMIS initiative's item banks, that is, PROM item sets, were developed to capture patient-reported outcomes from mainstream interventions, in particular health conditions, for example, chronic diseases [16]. Meanwhile, PROM-PGHD items are meant to capture patient-reported outcomes of accessing and utilizing PGHD they themselves have produced with various types of health technology in relation to a particular health condition.

An important consideration of this socio-technical approach is that when it comes to the technology category, outcome measures may extend beyond traditional PROMs of the health condition to include self-reported measures that capture the effects of a patient's interaction with their data, as this interactivity is designed into a type of technology. Thus, we augmented the QIR process of developing PROMs to consider both the health condition and the technology category for which a PROM-PGHD is being developed.

Results

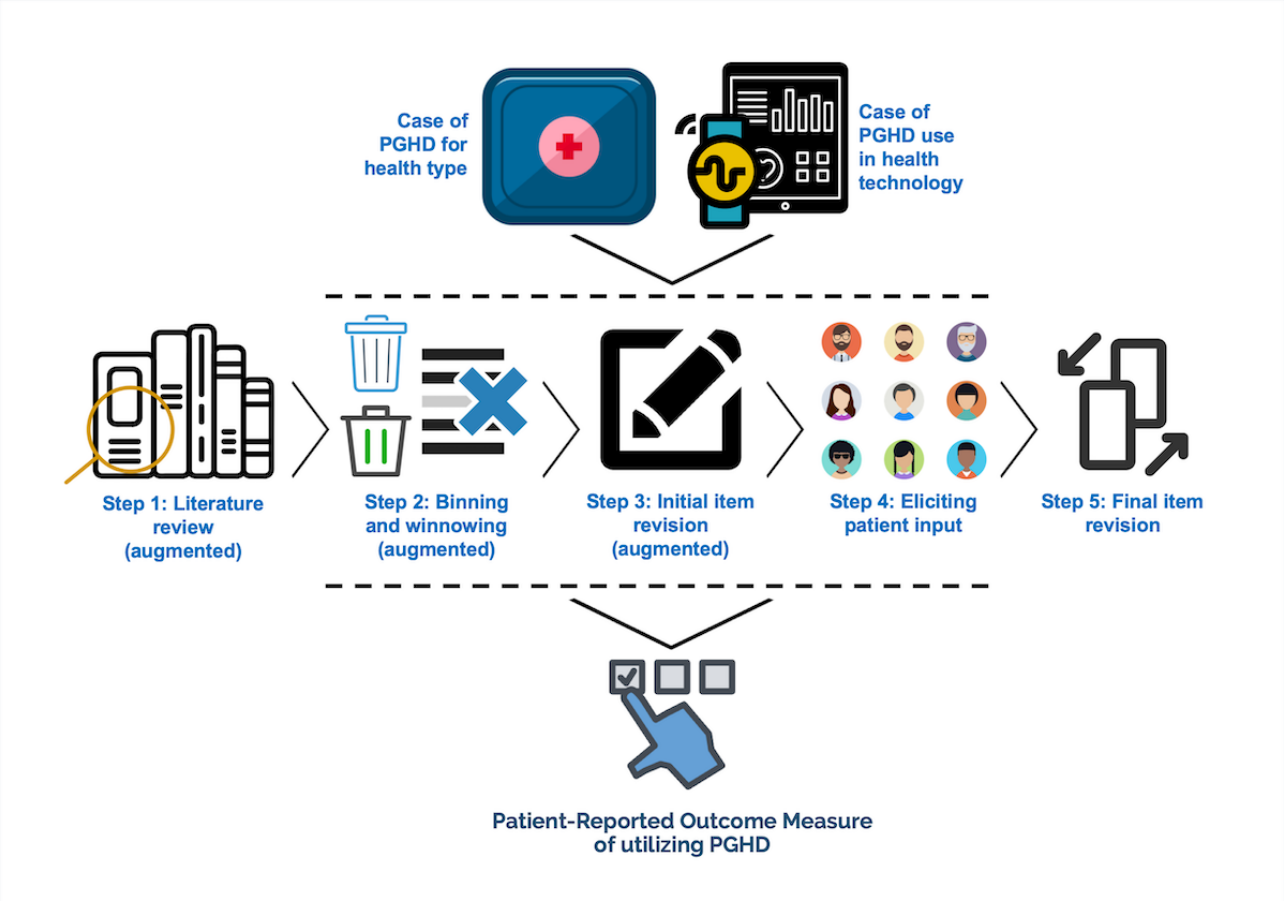
A Worked Example of the Patient-Reported Outcome Measure of Utilizing Person-Generated Health Data Development Method

To illustrate how the PROM-PGHD development method may be used to develop a PROM-PGHD, a worked example is presented based on the steps presented in Table 3. This is further augmented as described above. This example demonstrates how augmenting the first QIR step guides the identification and development of items within the domains of interest and influences the development process. Each of the five steps is outlined, with references to work on each step that we have reported elsewhere. These references to papers published to date are summarized below:

- Step 1, literature review: Dimaguila et al [8].
- Analysis of Step 1 and implementation of Steps 2 and 3: Dimaguila et al [34].
- Step 4, eliciting patient input: Dimaguila et al [7].

Figure 1 outlines the steps of the PROM-PGHD development method and indicates how the socio-technical context influences the process from the beginning.

Figure 1. The steps of the patient-reported outcome measure of utilizing person-generated health data (PGHD) development method, which was augmented from the qualitative item review. Icon sources: Iconfinder and Flaticon.



Case Study

An exemplar PGHD use case is home-based stroke rehabilitation (the health condition) using body-tracking simulated technologies (the technology category) [8]. Stroke is a leading global cause of death and disability [35,36]. Clinical rehabilitation is lengthy and costly; thus, home-based rehabilitation may improve outcomes, and patients may prefer home-based options rather than traveling to clinics [37]. Simulated stroke rehabilitation systems, in particular using the industry-leading Kinect (Microsoft), simulate rehabilitation activities in a clinical environment in real time [38]. These systems use a video gaming console, which may be well suited for home-based rehabilitation. Patients may generate data through different forms of interaction [39-41]. More information on Kinect, for example, how it was designed and types of rehabilitation tasks available, is provided in previously published literature [42-44]. Utilizing PGHD in conjunction with such systems has the potential to generate important new evidence about the efficacy of stroke telerehabilitation. Therefore, a PROM-PGHD of Kinect-based stroke rehabilitation systems is our example of step-by-step item development.

Step 1: Literature Review (Augmented)

The first step, that is, literature review, is key in identifying concepts and items within the domain of interest for the PROM being developed. It identifies items representing the range of domain-relevant experiences [16].

Augmenting it to include the health condition and the technology category recognizes the socio-technical context of PGHD-enabled technologies and ensures that relevant items from both domains are included. This was implemented for the worked example, and as such, influenced the identification of outcome measures from the literature. An extensive literature review was conducted for this example combination of a health condition and a technology type detailed in Dimaguila et al [8]. The review examined the extent of PGHD utilization in studies of Kinect-based simulated rehabilitation systems for stroke and identified outcome measures from which candidate items were drawn for assessment. Outcome measures identified from papers selected in the review include the Game Experience Questionnaire [45] and the Stroke Impact Scale [46].

Step 2: Binning and Winnowing (Augmented)

The second step is *Binning and Winnowing*. The overall objective of the binning (ie, including) activity is to build sets of items that represent an aspect of a particular health condition, for example, walking within a physical function condition [16]. For PROM-PGHD, we endeavored to develop sets of items that instead represented reported effects of PGHD utilization [34]. This is to match the objective of PROM-PGHD. Moreover, an additional exclusion criterion was introduced for winnowing activity. Originally, this step excluded (*winnowed*) items that were too narrow, disease specific, redundant, or confusing [16]. For the purposes of the PROM-PGHD, an additional criterion was added to winnow items whose content would not be able

to measure the effects of utilizing PGHD, as described here [34]. These effects include influencing interest in their care processes [2-4], and changing feelings about health status [3], and were derived from key themes that occurred in a key journal special issue on PGHD [1].

The outcome measure items identified in the previous step with consideration of the socio-technical context of the case study were assessed for appropriateness to PROM-PGHD, that is, their relevance to the reported effects of PGHD [34]. Items were winnowed according to the criteria described earlier. Retained items were binned by aligning existing items selected from Step 1, with reported effects on patients who used PGHD in controlled settings [34].

Step 3: Initial Item Revision (Augmented)

In the third step, that is, item revision, PROM items are revised to ensure consistency of their response options, similarity in wording contexts, conciseness and simplicity of wording, their independence from other questions, and that they encourage the use of available response options [16]. In addition, for PROM-PGHD, it may be necessary to revise some terminology used in the items, so they would better match the target health condition and technology category. Items may be worded quite generally, and revision would make them more specific to the target domains [34]. In the worked example, after Step 2, the preliminary item bank was revised to better match the target domains of Kinect-based stroke rehabilitation systems. Revisions were also conducted to address inconsistent response options and experience-recall time frames for the purpose of maintaining consistency [34]. Suggested uniform response options for the PROMIS rating scales [16] were followed.

Implementing the first step typically results in a number of diverse PROM items (eg, the question) and corresponding response options (eg, range of likelihood from agree to disagree, or a scale of 1-5) [16]. The optimal response options may vary based on the individual items they correspond with, and there is no empirical evidence suggesting that some sets of response options are clearly superior to others, that is, are consistently more accurate at capturing respondent experiences. Thus, it may be necessary to determine the response options through a consensus process with domain experts [16] or with the target patient cohort [34]. Additional response options were added to gather feedback from patients themselves in Step 4, on the appropriateness of the item response types [34]. The revised items were then grouped according to their alignment with a PGHD effect, and according to their response option types, that is, true/false statements, rating scales, and multiple-choice questions [34]. The subsequent step, which elicits patient participation, is expected to improve the suitability of the items [16].

This step resulted in a preliminary PROM-PGHD item bank, which was then presented to patients in the next step [34]. Augmenting the first step of QIR, to consider the socio-technical context of health technologies from which PGHD are produced, ensured that the outcome measures and items considered were drawn from the domains of interest, that is, the health condition and the technology category. Thus, the items that were considered for binning and winnowing, underwent initial item revision and eventually were presented to the patients for comment, covered relevant concepts from both domains [34].

Step 4: Eliciting the Patient Input

In this step, stroke survivors participated in focus groups and semistructured interviews, where they were asked to comment on the concepts and items of the preliminary PROM-PGHD item bank, for example, on the items' clarity and suitability to their experience. Detailed analysis and reporting of the data collected in these studies are presented elsewhere [7]. They were also asked open-ended questions about their experience of accessing and utilizing PGHD for the purpose of gathering concepts that may not have been covered by the current items. Based on the exemplar health and technology case being investigated, the target patient cohort was stroke patients with varying levels of experience with Jintronix (Montreal, Canada), a simulated rehabilitation software system using Kinect version 2 [43] and which is FDA approved [47]. Patient recruitment was conducted at three different sites, with ethics approval granted by the Human Research Ethics Committees of Deakin University (2017-087), Austin Health (HREC/17/Austin/492), and the University of Melbourne (1852259.1).

Some of the PGHD effects previously reported in the literature were reaffirmed by the patients, for example, that PGHD access can increase engagement with the recovery process. However, patient input showed that some effects were dependent on the status of their PGHD, for example, they felt satisfaction only when their PGHD showed an improvement trend [7]. This highlights the importance of eliciting patient input to gather a richer understanding of patient-reported outcomes [12,16].

Step 5: Final Item Revision

This step includes improving the PROM-PGHD items' accuracy in representing the perspectives and experiences of the target patient cohort, and their suitability and clarity. In the worked example, revisions took the form of direct changes to the wording of the items, reduction or addition of response options or scales, and reduction or addition of outcome items. For example, we have learned from our discussions with patients that our preliminary PROM-PGHD lacks an item to measure *levels of frustration*, which patients experience when they see their PGHD fluctuate, that is, indicators of their health status that go up and down over time [7]. The current PROM-PGHD was therefore revised to add *levels of frustration* as an outcome measure.

Finally, the items were run through the MetaMetrics Lexile analyzer (MetaMetrics, Inc) to assess their readability based on sentence length and the commonness of words. This provides an extra layer of assessment to determine if any items could be problematic during implementation, and to conduct revisions as necessary to improve readability [16]. The full revision related to this step in our worked example, to be reported elsewhere, will prepare the PROM-PGHD item set for quantitative field testing [16].

Discussion

Relevance

This paper has argued that a PROM of utilizing PGHD is necessary to provide clearer evidence about the value of implementing related health technologies. PROMs-PGHD would provide a systematic way for patients to gain insights into the health effects they experience from utilizing their PGHD. PROMs-PGHD could also be included routinely as part of the patient record, where PGHD are produced within a patient's care plan. This is similar to how PROMs in general are used together as a set of performance measures to assess the performance of health entities and the services they provide [48,49]. As such, PROMs-PGHD could inform strategies for improving health outcomes.

As highlighted, PROMs-PGHD would fill an evidence gap and promote participatory health by recognizing the value of the patient experience when considering the use and effect of PGHD and the technologies they are produced from. They might generate more evidence about the clinical effectiveness and cost-effectiveness of PGHD-enabled technologies to aid clinicians in choosing appropriate health technologies, and for patients to understand how certain health technologies affect their health management. Moreover, PROMs-PGHD could guide technology designers in developing PGHD-enabled technologies that are more inclusive of patient perspectives, similar to how PROMs could improve the design of clinical registries [15]. Ultimately, PROMs-PGHD could contribute to building evidence-based practice in clinical work with PGHD and facilitate the creation of relevant clinical guidelines.

This paper described, and illustrated via a worked example, a method for developing a PROM-PGHD. The method was guided by an established PROM development process and a participatory health paradigm. As a result, it followed a step-wise approach of involving patients, which iteratively influences the resulting items of the PROM-PGHD as it is developed. Participatory approaches such as this can generate a rich, deep understanding of the effects of a health technology intervention [12] and ensures that the patient perspective is embedded into the resulting PROM-PGHD, which is central to the value of PROMs [14].

The PROM-PGHD development method follows the best practice as it is distilled from the literature, adding to its credibility in producing legitimate measures of patient-reported outcomes. In addition, its consideration of the socio-technical context of health technology interventions increases its sensitivity to personal characteristics and the physiological and health-related factors affecting the target patient cohort [28]. The recognition of the two domains inherent in health informatics [30,31], that is, health condition and technology category, increases the appropriateness of the resulting PROM-PGHD for assessing the effects experienced by the patient cohort.

This worked example has shown that the PROM-PGHD development method is meaningfully applied to a PGHD-enabled technology category used in a specific health condition. It has identified existing PROM items relevant to the chosen domains: stroke and Kinect-based simulated rehabilitation technology. This helps ensure that the resulting PROM-PGHD is reflective of the experiences of patients who are using a technology within the context of their health condition. This allows the PROM-PGHD development method to be used in other cases where health technologies are implemented in health conditions.

It is important for practitioners and developers of health technologies to prioritize the patient's perspective and to be sensitive to how PGHD may affect people differently [8,9]. Future studies should therefore apply the PROM-PGHD development method in other relevant contexts where it may be important to understand how the health condition and technology category have interrelated effects on patients' outcomes from using PGHD [31,32]. Revising and retesting the resulting item banks in clinical samples would also increase the validity of the method [50], and it could be valuable to further explore how other socio-technical factors, such as health literacy, influence responses to the PROM-PGHD.

Limitations

One limitation of the QIR process [16], and thus with the PROM-PGHD development method, is the necessity to change the existing items selected from the literature review. The changes considered to be minor are conducted during the item revision steps. They are necessary to improve the uniformity of the response options that are designed to be read and interpreted by patients [16,34]. However, this process is not believed to substantially alter any existing outcome measure items. Moreover, the subsequent steps that elicit patient participation are expected to improve the suitability of the items [16].

Conclusions

This paper highlights the need for a systematic way of measuring the effects of PGHD on the health of people who utilize them. A method was presented for developing such a measure, called PROM-PGHD, based on best practice within the participatory health paradigm and in consideration of the socio-technical context of PGHD utilization. A new PROM-PGHD development method was illustrated through the example of stroke survivors using Kinect-based poststroke simulated rehabilitation technologies. It was shown that the method can be applied successfully to develop an initial set of items from the domains of the health condition and technology category. This method may be applied to other cases that combine a health condition and a technology category, and thus, this method could have broader relevance for EBP in clinical work with PGHD. Future studies should apply the PROM-PGHD development method within other relevant socio-technical contexts, and revise and retest the resulting item banks.

Acknowledgments

GD would like to acknowledge the Melbourne School of Engineering through which his research scholarship is provided, and his organizational sponsor, Newman College (University of Melbourne).

Icons used to create Figure 1 have been sourced from Iconfinder.com and Flaticon.com.

Conflicts of Interest

None declared.

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Abbreviations

EBP: evidence-based practice
FDA: United States Food and Drug Administration
PGHD: person-generated health data
PROM: patient-reported outcome measure
PROM-PGHD: patient-reported outcome measure of utilizing person-generated health data
PROMIS: Patient-Reported Outcomes Measurement Information System
QIR: qualitative item review
SAC: Scientific Advisory Committee of Medical Outcomes Trust

Edited by G Eysenbach; submitted 29.10.19; peer-reviewed by E Koledova, R Yang, S Iribarren; comments to author 16.12.19; revised version received 12.01.20; accepted 24.01.20; published 07.05.20.

Please cite as:
Dimaguila GL, Gray K, Merolli M
Patient-Reported Outcome Measures of Utilizing Person-Generated Health Data in the Case of Simulated Stroke Rehabilitation: Development Method
JMIR Res Protoc 2020;9(5):e16827
URL: https://www.researchprotocols.org/2020/5/e16827
doi:10.2196/16827
PMID:32379052

Publisher:
JMIR Publications
130 Queens Quay East.
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