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Protocol

Optimizing the Periconception Lifestyle of Women With Overweight Using a Blended Personalized Care Intervention Combining eHealth and Face-to-face Counseling (eFUSE): Protocol for a Randomized Controlled Trial

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Abstract

Background: Maternal overweight has a substantial impact on reproductive, maternal, pregnancy, and neonatal outcomes with long-term and transgenerational health consequences. Interventions that aim to optimize periconception maternal lifestyle can improve maternal and fetal health during pregnancy and throughout the life course. However, it remains difficult to change and adopt adequate lifestyle behaviors. We hypothesize that additional psychological therapy targeting cognitive and affective factors substantially contribute to the effectiveness of these interventions.

Objective: The proposed study aims to examine the feasibility and effectiveness of a blended personalized periconception lifestyle care intervention with additional psychological therapy aimed at women with a BMI≥25 and who are contemplating pregnancy or are already pregnant (≤12 weeks) in reducing inadequate lifestyle behaviors and improving early and late pregnancy outcome.

Methods: The eHealth and Face-to-face Counseling (eFUSE) study follows a single-center two-arm randomized controlled trial design at the Erasmus MC, University Medical Center, with a multicenter regional referral. The female patients with overweight (BMI≥25), together with their male partner, will be stratified by pregnancy status (preconception vs pregnant) and randomized to receive either the blended personalized periconception lifestyle care intervention with additional psychological therapy (n=313) or usual care (n=313). The primary outcome is a change in the lifestyle risk score (between baseline and 24 weeks) between the randomization arms (difference in differences). Secondary outcomes include measurements defined as most relevant by the International Consortium for Health Outcomes Measurement, including behavioral determinants, patient satisfaction, provider feasibility, and maternal pregnancy and neonatal complications.

Results: The study will be open for recruitment from Fall 2021 onward. Data collection is expected to be completed by the beginning of 2023, and the results are expected to be published by Fall 2023.

Conclusions: This study will evaluate the feasibility and effectiveness of a blended periconception lifestyle intervention with additional psychological therapy, aimed at women with a BMI≥25. Positive results of this innovative care approach will be used for implementation in routine medical care of all women with overweight, with the ultimate aim to improve clinical outcomes of these high-risk pregnancies.

Trial Registration: Netherlands Trial Register NL9264; https://www.trialregister.nl/trial/9264

International Registered Report Identifier (IRRID): PRR1-10.2196/28600

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KEYWORDS

eHealth; periconception period; lifestyle intervention; maternal and child health; pregnancy; birth outcomes; healthy lifestyle; psychotherapy; obesity; randomized controlled trial; behavior change

Introduction

Overweight is still a pressing health issue in the general population. During the reproductive period, maternal overweight has a significant impact on fertility, pregnancy, and neonatal outcome with long-term and transgenerational health consequences [1,2]. All these complications have been reported to increase health care use and medical expenditures [3].

Lifestyle interventions that target poor periconception maternal lifestyle behaviors have the potential to improve the chances of pregnancy and uncomplicated outcome. From 2006, we developed and tested the eHealth lifestyle coaching program Smarter Pregnancy in a large survey and randomized controlled trials (RCTs), including a general population cohort and a subfertile cohort of couples receiving either in vitro fertilization or intracytoplasmic sperm injection [4,5]. These studies demonstrated that Smarter Pregnancy is an effective, and cost-effective intervention [6]. At the same time, a periconception lifestyle counseling clinic Healthy Pregnancy and a comparable blended care clinic including the combination of face-to-face counseling and the eHealth coaching program Smarter Pregnancy was developed and evaluated [7,8]. The latter approach showed a high compliance rate; participants increased vegetable, fruit, and folic acid supplement intake; and lowered alcohol and tobacco use [8]. However, the effectiveness in women with overweight is still limited. Over the years, several other lifestyle interventions for pregnant or prepregnant women with overweight have been tested, but most interventions fail to reach clinically meaningful results [9].

Negative cognitive and affective factors, low self-efficacy, and food cravings are strongly associated with poor lifestyle behavior [10]. These factors can effectively be targeted by psychological therapies such as cognitive behavioral therapy, mindfulness, and acceptance and commitment therapy [11]. Psychological therapies provide skills to improve individual women's ability to self-monitor their diet, learn impulse control techniques and behavioral modification strategies such as chewing slowly and taking time to enjoy food [11,12]. Especially for women with overweight and even obesity, psychological therapies are proven to be effective treatment modalities for targeting poor lifestyle behaviors [12-14]. However, to the best of our knowledge, face-to-face counseling and an eHealth program have never been combined with psychological therapies to reach the full potential of a periconception lifestyle intervention for women with overweight and their partner.

Therefore, we are initiating an RCT to study whether a blended personalized periconception lifestyle care intervention with supporting psychological therapy aimed at women with overweight or obesity who are contemplating pregnancy or are already pregnant (≤12 weeks) can significantly change and maintain adequate lifestyle behaviors.

Methods

Overview

The eHealth and Face-to-face Counseling (eFUSE) study follows a two-arm RCT design in a tertiary health care center, with multicenter regional referral, which is embedded in the Rotterdam periconception cohort (Predict study) [15]. The Predict study is an ongoing prospective tertiary hospital-based cohort embedded in the outpatient clinic of the Department of Obstetrics and Gynecology of the Erasmus MC, University Medical Center Rotterdam, the Netherlands. Patients included in the Predict study with overweight (BMI≥25 kg/m^2) are eligible for inclusion in the eFUSE study. Patients included in the eFUSE study will be stratified by pregnancy status (preconception vs pregnant) and randomized to receive either blended personalized periconception lifestyle care with additional psychological therapy or usual care.

Objective

The aim of this trial is to study if a blended personalized periconception lifestyle care approach aimed at women with a BMI≥25 who are contemplating pregnancy or already pregnant (≤12 weeks) can significantly reduce the lifestyle risk score (LRS).

Participants

Patient couples, of whom the woman has a BMI≥25, are invited to participate in this RCT during their first visit to the outpatient antenatal clinic of the Erasmus MC, University Medical Center Rotterdam, Rotterdam, the Netherlands or one of the secondary hospitals, after which they will be referred and counseled for study participation. The first visit can either be a preconception consultation or the first antenatal session (≤12 weeks of gestation). Patient couples will be screened for eligibility by their physician when the woman is in reproductive age (18-45 years), is contemplating pregnancy or is pregnant (≤12 weeks), visits the outpatient antenatal clinic, and has overweight (BMI≥25). Exclusion criteria are multiple pregnancy, history of bariatric surgery, insufficient knowledge of Dutch language, fetal anomalies, or inability to provide informed consent. Women can be included as a single participant if the partner does not participate. When participating, the partner will attend the first face-to-face lifestyle counseling session and will have access to the online lifestyle coaching platform Smarter Pregnancy.

Intervention

Our blended personalized periconception lifestyle care intervention with additional psychological therapy consists of:

- Three face-to-face lifestyle counseling sessions, provided by trained eFUSE counselors, as previously practiced in the proven effective outpatient antenatal clinic Healthy Pregnancy [7]. Both the counseling service and the eHealth platform are based on behavioral change theories [16-18]

and best practices obtained from stakeholders in the field [7,19,20]. Psychological techniques such as motivational interviewing, elements of cognitive behavioral therapy, acceptance and commitment therapy, and mindfulness will be used to support the patient couples toward a significant and sustainable lifestyle change [21,22]. All aspects offered in the blended care intervention are personalized to the individual patient couple, based on the results of the risk assessment and lifestyle questionnaires filled out on the eHealth platform at the first visit.

- The periconception eHealth lifestyle coaching platform Smarter Pregnancy, providing personalized lifestyle risk assessment and coaching via the evidence-based eHealth intervention (www.slimmerzwanger.nl or www.smarterpregnancy.co.uk) [4,5]. Additionally, all participants will be encouraged to download and frequently use the mobile app Headspace, which provides guided meditation resources online [23].

Women allocated to the intervention arm will also be provided with standard care and routine antenatal visits according to local and Dutch guidelines [24].

First Counseling Session

The first counseling session takes place in week 1 of the blended personalized periconception lifestyle care intervention and will be attended by both the woman and male partner. The aim of the first counseling is twofold: first, to raise awareness on the personal lifestyle-associated risk factors for fertility and pregnancy and, second, to facilitate the ongoing provision of tailored lifestyle counseling. In the first session, together with the counselor, participants will be asked to formulate up to three lifestyle behavior goals and develop a plan to reach these goals (identifying thresholds and positive incentives).

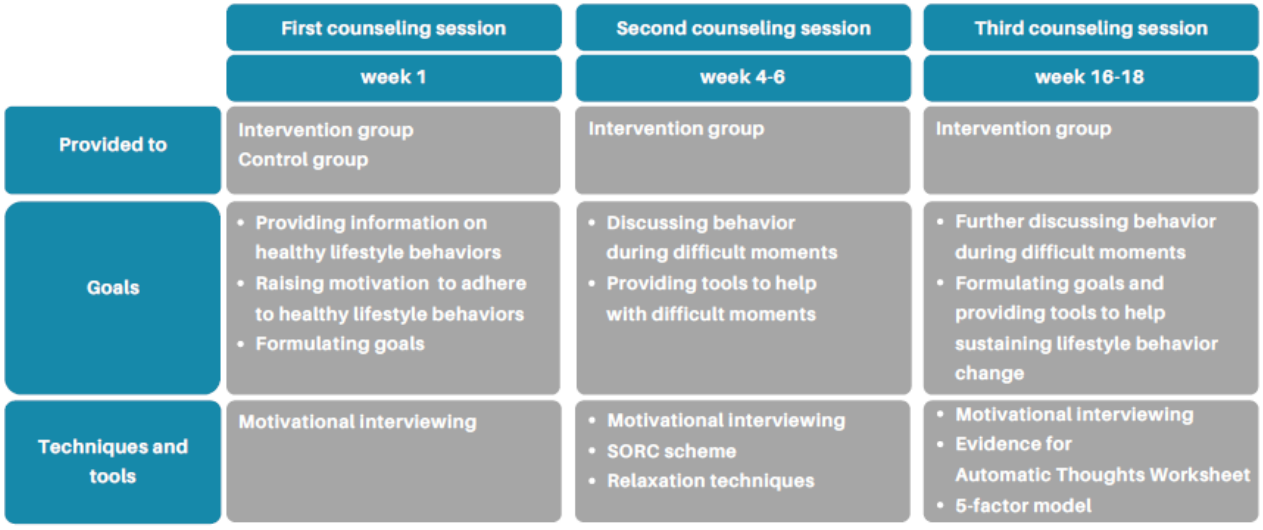
Second and Third Counseling Sessions

As part of the Smarter Pregnancy coaching program, every 6 weeks a digital questionnaire on lifestyle behaviors will be filled out by the participants. During the second (in weeks 4-6 of the blended personalized periconception lifestyle care intervention) and the third counseling sessions (in weeks 16-18 of the blended personalized periconception lifestyle care intervention), results of the questionnaire will be discussed, personal lifestyle goals will be reviewed, progress of lifestyle change will be discussed, and motivational interviewing will be used to support further (sustainment of) behavior change. We expect that the effects of the face-to-face and eHealth components will reinforce each other. The second and third counseling sessions are only mandatory for the woman and her partner is welcome to attend.

During the second and third counseling sessions at the outpatient clinic Healthy Pregnancy, a functional analysis of behavior will be carried out using a situation-organism-reaction-consequences scheme, relaxation techniques will be educated, the automatic thoughts worksheet will be filled out, and the five-factor model will be discussed (Multimedia Appendices 1-3) [25-27]. These components of cognitive behavioral therapy, acceptance and commitment therapy, and mindfulness will teach the women and their partner skills to achieve and maintain long-term lifestyle change.

After the third, which is also the final lifestyle counseling session, participants will be informed that they can continue to use the eHealth platform until week 24 of the blended personalized periconception lifestyle care intervention. Participants are also informed about the possibilities to continue lifestyle counseling and support after the study period ends, which will be their own responsibility. An overview of counseling sessions and the goals and techniques used is depicted in Figure 1.

Figure 1. Overview of counseling sessions. SORC: situation-organism-reaction-consequences.



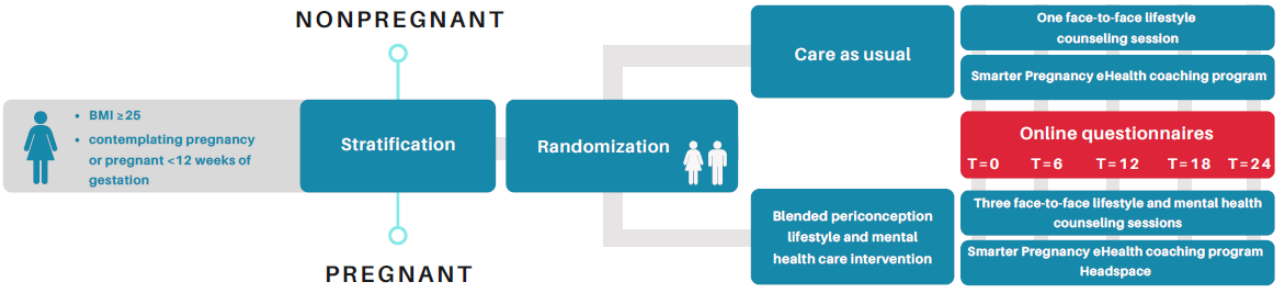
Usual Care

Women with BMI≥25 allocated to the control group will be provided with standard care, which consists of one standard face-to-face lifestyle counseling session at the outpatient clinic Healthy Pregnancy, access to the online coaching program Smarter Pregnancy, and routine antenatal visits according to local and Dutch guidelines (NVOG protocol).

Trial Flow

The trial flow is visualized in Figure 2.

Figure 2. Trial flow of the eHealth and Face-to-face Counseling study.



Outcomes

The main outcome measure is the difference in the change of the LRS (measured in week 0 and week 24 of the blended personalized periconception lifestyle care intervention) between the intervention group and the control group (difference in differences) [28]. The LRS is a locally developed composite score of lifestyle behaviors, including vegetable and fruit intake, folic acid supplement use (only for women), not smoking, and not consuming alcohol. The vegetable and fruit intake will be subdivided into risk scores of 0, 1.5, and 3, where 0 represents an adequate daily intake (≥200 g of vegetables, ≥2 pieces of fruit). A score of 1.5 represents a nearly adequate intake (150-200 g of vegetables, 1.5-2 pieces of fruit). A score of 3 represents an inadequate daily intake (<150 g of vegetables, <1.5 pieces of fruit). Folic acid supplement use is considered to be adequate (score 0) or inadequate (score 3) when the recommended dose of 400 µg per day is either met or not. For male participants, folic acid supplement use will not be taken into account, since there are no widely supported recommendations concerning folic acid supplement use for men. The risk score for smoking will be based on average daily use: no smoking (score 0) and daily smoking of 1 to 5 (score 1), 6 to 14 (score 3), or ≥15 (score 6) cigarettes. Risk scores for alcohol consumption will be based on average weekly use: no alcohol use (score 0) and 1 to 7 (score 1), 8 to 14 (score 2), or ≥15 (score 3) alcoholic beverages (glasses) per week. The LRS ranges from 0 to 18 for women and 0 to 15 for men, and will be monitored via online questionnaires in weeks 0, 6, 12, and 24 of the online coaching program and calculated as the sum of the scores of all lifestyle behaviors.

Secondary outcome measures comprise several questionnaires, in line with the International Consortium for Health Outcomes Measurement recommendations [29]:

- *Determinants of lifestyle behavior* (eg, attitude, action control, self-efficacy, intention, and motivation) using the validated Determinants of Lifestyle Behavior Questionnaire [30], measured at weeks 0, 6, 18, and 24
- *Patient satisfaction* measured using Six Simple Questions [31] at weeks 12 and 24
- *Provider feasibility* using a 5-point Likert scale 6 and 12 months after the start of this study
- *Health status* measured using the validated EQ-5D questionnaire [32] at weeks 12, 18, and 24
- *Health-related costs*: intramural medical costs (hospital registration), iMCQ [33] (extramural medical costs), and iPCQ [34] (productivity loss)
- *Maternal pregnancy complications* (including pregnancy-induced hypertension, pre-eclampsia, HELLP, and gestational diabetes) and *neonatal outcome* (including birth weight, small for gestational age, large for gestational age, and preterm birth) retrieved from medical files

Randomization and Allocation

Eligible consenting participants will be randomly assigned either to the intervention group or control group. The participant assignment protocol will be based on a ratio of 1:1. We will use software where randomization will be done by a predefined scheme for allocation concealment. Stratification will be made by pregnancy status (preconception vs pregnant), followed by random allocation of patients. Because of the automatic nature of the allocation process, direct exposure to the treatment allocation process by any members of the research team is eliminated.

Data Collection

Via a lifestyle questionnaire integrated in the online coaching program Smarter Pregnancy, a baseline screening at week 0 and follow-up screening at weeks 6, 12, 18, and 24 of the program will be performed. The follow-up screening will be used to monitor the change in lifestyle components. The lifestyle questionnaire will comprise of questions regarding vegetable and fruit intake, folic acid supplementation use, tobacco use, and alcohol consumption. Participants will also be asked whether they have downloaded the Headspace app and how frequently they have used it. The additional questionnaires, concerning determinants of lifestyle behavior, patient satisfaction, and health status, will be sent to study participants.

Sample Size Calculation

The primary outcome of this trial is the change in the LRS (between baseline and at 24 weeks) between the randomization arms (difference in differences). Based on an earlier study, we found that the SD of the change score was 1.99 [4]. We aim for a difference in change score between the arms of 0.5. To detect a difference of this size and using a significance level of .05, we can reach a statistical power of 0.80 when we have 500 women. To allow for a 20% drop out, we will include a total of 626 women, 313 in the intervention arm and 313 women in the control arm as calculated by a *t* test. This sample size calculation is based on a *t* test using unadjusted data of a survey. The actual

analysis that will be done in the RCT will be less subjected to confounding factors due to the study design and analysis.

Data Analysis

A CONSORT flowchart will be built to visualize study and participant flow in each group (intervention and control group)[35]. SPSS Statistics for Windows (IBM Corp) and R for Windows (R Foundation for Statistical Computing) will be used. Descriptive statistics for baseline values will be calculated, and comparison between the two groups will be performed by using an independent sample *t* test for continuous variables and a chi-square test for categorical variables. Linear regression analyses adjusted for baseline characteristics will be carried out to see whether the LRS differ significantly between the intervention and the control group. Subgroup analyses will be performed according to pregnancy status. All analyses will be done according to the intention-to-treat principles, and a *P* value<.05 will be considered statistically significant.

Data Management

All researchers involved in the study will be qualified physicians, and they will follow a course in which the organization of clinical studies is taught. According to the original observation records, researchers will complete the case report forms in an accurate and timely manner. All documents will be properly classified, preserved under confidential conditions, and archived. Statistical analysis of the data will be carried out on a pseudonymized data set. Only the data manager will have access to the key file, in which the pseudonymized data is linked to the personal data.

Safety Monitoring and Reporting

This study will have monitoring for quality and regulatory compliance and adheres to the Dutch Data Protection Act. The data being stored will be encrypted. All communication with the participants will take place within the secure online interface that requires an electronic identification.

Ethical Approval and Dissemination

The trial will be conducted in accordance with the principles of the Declaration of Helsinki (2013 version) and will fully comply with the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) reporting guidelines [36]. This study was approved by the Committee of Medical Ethics of the Erasmus Medical Center, Rotterdam (MEC-2020-0113) and registered in the Dutch Trial Registry (NL9264). Written informed consent from each participant will be obtained. The results will be published in peer-reviewed journals to ensure widespread dissemination.

Results

Inclusion will start from Fall 2021 onward at the Erasmus MC, University Medical Center, Rotterdam, the Netherlands, while secondary hospitals can refer patients for inclusion. Data collection is expected to be completed by the beginning of 2023, and the results are expected to be published by Fall 2023.

Discussion

Overview and Expectations

The eFUSE study will evaluate an innovative blended lifestyle care intervention combined with psychological therapy to improve periconception lifestyle behaviors in women with overweight using an RCT. The intervention group will be provided with a blended care approach, including three face-to-face counseling sessions, and access to the periconception eHealth lifestyle care platform Smarter Pregnancy and mobile health app Headspace. In the face-to-face counseling sessions, motivational interviewing will be used and components of cognitive behavioral therapy, acceptance and commitment therapy, and mindfulness will be practiced. The control group will receive standard care, which comprises of one face-to-face counseling session and access to the periconception eHealth lifestyle care platform Smarter Pregnancy. The addition of components of several psychological therapies to a proven effective blended care approach is new and might result in a measure to improve parental lifestyle behaviors before and during pregnancy. We hypothesize that the two additional face-to-face counseling sessions, in which several psychological techniques will be practiced, will support the participating patient couples toward a significant and more sustainable lifestyle change. Moreover, we expect that the effects of the face-to-face sessions and eHealth program reinforce each other. By choosing a proximal primary outcome measure, namely, the LRS, we aim to assess the effects directly influenced by the intervention so that the results can be clearly deduced from the content of our approach.

Strengths and Limitations

This is the first study that will evaluate a blended periconception lifestyle intervention with additional psychological therapy aimed at women with a BMI≥25 in a randomized controlled design. All aspects offered in the blended care approach are personalized to the individual patient couple. Furthermore, both the periconception eHealth lifestyle platform Smarter Pregnancy and the outpatient clinic Healthy Pregnancy have been proven effective before [4,5,7,8]. A possible limitation of this study is that it is hard to unravel which part of this blended periconception lifestyle intervention with mental health components affects lifestyle behaviors and which elements contribute the most.

Conclusion

This study will evaluate a blended periconception lifestyle care intervention with additional psychological therapy aimed at women with a BMI≥25 and their partner. If effective at improving lifestyle behaviors, this approach could be an important measure for all women with overweight or obesity with the potential to improve clinical outcomes for these women who are in the preconception period and are at high risk for pregnancy complications.

Acknowledgments

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Authors' Contributions

RST conceived the study. MvdW, SS, LvR, and RST initiated the study design. SW provided statistical expertise in clinical trial design. MvdW wrote the original draft, and SS, SW, LvR, and RST reviewed and edited the original draft. All authors contributed to refinement of the study protocol and approved the final manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Situation-organism-reaction-consequences scheme.
[DOCX File , 12 KB - resprot_v10i9e28600_app1.docx]

Multimedia Appendix 2
Automatic thought sheet.
[DOCX File , 12 KB - resprot_v10i9e28600_app2.docx]

Multimedia Appendix 3
Five-factor model.
[DOCX File , 30 KB - resprot_v10i9e28600_app3.docx]

References

1. Marchi J, Berg M, Dencker A, Olander EK, Begley C. Risks associated with obesity in pregnancy, for the mother and baby: a systematic review of reviews. Obes Rev 2015 Aug;16(8):621-638. [doi: 10.1111/obr.12288] [Medline: 26016557]
2. Steegers-Theunissen RPM, Twigt J, Pestinger V, Sinclair KD. The periconceptional period, reproduction and long-term health of offspring: the importance of one-carbon metabolism. Hum Reprod Update 2013;19(6):640-655. [doi: 10.1093/humupd/dmt041] [Medline: 23959022]
3. Koning AMH, Kuchenbecker WKH, Groen H, Hoek A, Land JA, Khan KS, et al. Economic consequences of overweight and obesity in infertility: a framework for evaluating the costs and outcomes of fertility care. Hum Reprod Update 2010;16(3):246-254. [doi: 10.1093/humupd/dmp053] [Medline: 20056674]
4. Van Dijk MR, Huijgen NA, Willemsen SP, Laven JS, Steegers EA, Steegers-Theunissen RP. Impact of an mHealth platform for pregnancy on nutrition and lifestyle of the reproductive population: a survey. JMIR Mhealth Uhealth 2016 May 27;4(2):e53 [FREE Full text] [doi: 10.2196/mhealth.5197] [Medline: 27234926]
5. Gootjes DV, van Dijk MR, Koster MP, Willemsen SP, Steegers EA, Steegers-Theunissen RP. Neighborhood deprivation and the effectiveness of mobile health coaching to improve periconceptional nutrition and lifestyle in women: survey in a large urban municipality in the Netherlands. JMIR Mhealth Uhealth 2019 Apr 11;7(4):e11664 [FREE Full text] [doi: 10.2196/11664] [Medline: 30973345]
6. Oostingh EC, Ophuis RH, Koster MP, Polinder S, Lingsma HF, Laven JS, et al. Mobile health coaching on nutrition and lifestyle behaviors for subfertile couples using the Smarter Pregnancy program: model-based cost-effectiveness analysis. JMIR Mhealth Uhealth 2019 Oct 23;7(10):e13935 [FREE Full text] [doi: 10.2196/13935] [Medline: 31647476]
7. Hammiche F, Laven JSE, van Mil N, de Cock M, de Vries JH, Lindemans J, et al. Tailored preconceptional dietary and lifestyle counselling in a tertiary outpatient clinic in The Netherlands. Hum Reprod 2011 Sep;26(9):2432-2441. [doi: 10.1093/humrep/der225] [Medline: 21752799]
8. van der Windt M, van der Kleij RM, Snoek KM, Willemsen SP, Dykgraaf RHM, Laven JSE, et al. Impact of a blended periconception lifestyle care approach on lifestyle behaviors: before-and-after study. J Med Internet Res 2020 Sep 30;22(9):e19378 [FREE Full text] [doi: 10.2196/19378] [Medline: 32996885]
9. Oteng-Ntim E, Varma R, Croker H, Poston L, Doyle P. Lifestyle interventions for overweight and obese pregnant women to improve pregnancy outcome: systematic review and meta-analysis. BMC Med 2012 May 10;10:47 [FREE Full text] [doi: 10.1186/1741-7015-10-47] [Medline: 22574949]
10. Pasold TL, McCracken A, Ward-Begnoche WL. Binge eating in obese adolescents: emotional and behavioral characteristics and impact on health-related quality of life. Clin Child Psychol Psychiatry 2014 Apr;19(2):299-312. [doi: 10.1177/1359104513488605] [Medline: 23749140]
11. Blau LE, Hormes JM. Preventing excess gestational weight gain and obesity in pregnancy: the potential of targeting psychological mechanisms. Curr Obes Rep 2020 Dec;9(4):522-529. [doi: 10.1007/s13679-020-00415-9] [Medline: 33145706]

12. Castelnuovo G, Pietrabissa G, Manzoni GM, Cattivelli R, Rossi A, Novelli M, et al. Cognitive behavioral therapy to aid weight loss in obese patients: current perspectives. Psychol Res Behav Manag 2017;10:165-173. [doi: 10.2147/PRBM.S113278] [Medline: 28652832]
13. Yonkers KA, Forray A, Howell HB, Gotman N, Kershaw T, Rounsaville BJ, et al. Motivational enhancement therapy coupled with cognitive behavioral therapy versus brief advice: a randomized trial for treatment of hazardous substance use in pregnancy and after delivery. Gen Hosp Psychiatry 2012;34(5):439-449 [FREE Full text] [doi: 10.1016/j.genhosppsych.2012.06.002] [Medline: 22795046]
14. Epel E, Laraia B, Coleman-Phox K, Leung C, Vieten C, Mellin L, et al. Effects of a mindfulness-based intervention on distress, weight gain, and glucose control for pregnant low-income women: a quasi-experimental trial using the ORBIT model. Int J Behav Med 2019 Oct;26(5):461-473 [FREE Full text] [doi: 10.1007/s12529-019-09779-2] [Medline: 30993601]
15. Steegers-Theunissen RP, Verheijden-Paulissen JJ, van Uitert EM, Wildhagen MF, Exalto N, Koning AH, et al. Cohort profile: the Rotterdam periconceptional cohort (predict study). Int J Epidemiol 2016 Apr;45(2):374-381. [doi: 10.1093/ije/dyv147] [Medline: 26224071]
16. Prochaska JO, DiClemente CC. Transtheoretical therapy: toward a more integrative model of change. Psychother Theory Res Pract 1982;19(3):276-288. [doi: 10.1037/h0088437]
17. Fogg BJ. A behavior model for persuasive design. In: Proceedings of the 4th International Conference on Persuasive Technology. 2009 Presented at: Persuasive '09; April 26-29, 2009; Claremont, CA. [doi: 10.1145/1541948.1541999]
18. Bolman C, de Vries H. Psycho-social determinants and motivational phases in smoking behavior of cardiac inpatients. Prev Med 1998;27(5):738-747. [doi: 10.1006/pmed.1998.0352] [Medline: 9808806]
19. Bandura A. Health promotion from the perspective of social cognitive theory. Psychol Health 1998 Jul;13(4):623-649. [doi: 10.1080/08870449808407422]
20. Kroeze W, Oenema A, Campbell M, Brug J. The efficacy of Web-based and print-delivered computer-tailored interventions to reduce fat intake: results of a randomized, controlled trial. J Nutr Educ Behav 2008;40(4):226-236. [doi: 10.1016/j.jneb.2007.09.008] [Medline: 18565463]
21. Armstrong M, Mottershead T, Ronksley P, Sigal R, Campbell T, Hemmelgarn B. Motivational interviewing to improve weight loss in overweight and/or obese patients: a systematic review and meta-analysis of randomized controlled trials. Obes Rev 2011 Sep;12(9):709-723. [doi: 10.1111/j.1467-789X.2011.00892.x] [Medline: 21692966]
22. Hayes SC, Luoma JB, Bond FW, Masuda A, Lillis J. Acceptance and commitment therapy: model, processes and outcomes. Behav Res Ther 2006 Jan;44(1):1-25. [doi: 10.1016/j.brat.2005.06.006] [Medline: 16300724]
23. Economides M, Martman J, Bell MJ, Sanderson B. Improvements in stress, affect, and irritability following brief use of a mindfulness-based smartphone app: a randomized controlled trial. Mindfulness (N Y) 2018;9(5):1584-1593 [FREE Full text] [doi: 10.1007/s12671-018-0905-4] [Medline: 30294390]
24. NVOG. Richtlijn Basis Prenatale zorg: opsporing van de belangrijkste zwangerschapscomplicaties bij laag-risico zwangeren (in de 2de en 3de lijn). Utrecht: Nederlandse Vereniging voor Obstetrie en Gynaecologie; 2015.
25. Hanley GP, Iwata BA, McCord BE. Functional analysis of problem behavior: a review. J Appl Behav Anal 2003;36(2):147-185. [doi: 10.1901/jaba.2003.36-147] [Medline: 12858983]
26. Hope D, Heimberg R, Juster H. Managing Social Anxiety: A Cognitive-Behavioral Therapy Approach Client Workbook. New York: Psychological Corp; 2004.
27. Williams C, Garland A. A cognitive–behavioural therapy assessment model for use in everyday clinical practice. Adv Psychiatr Treatment 2018 Jan 02;8(3):172-179 [FREE Full text] [doi: 10.1192/apt.8.3.172]
28. Hoek J, Schoenmakers S, Baart EB, Koster MPH, Willemsen SP, van Marion ES, et al. Preconceptional maternal vegetable intake and paternal smoking are associated with pre-implantation embryo quality. Reprod Sci 2020 Nov;27(11):2018-2028 [FREE Full text] [doi: 10.1007/s43032-020-00220-8] [Medline: 32542536]
29. Nijagal MA, Wissig S, Stowell C, Olson E, Amer-Wahlin I, Bonsel G, et al. Standardized outcome measures for pregnancy and childbirth, an ICHOM proposal. BMC Health Serv Res 2018 Dec 11;18(1):953 [FREE Full text] [doi: 10.1186/s12913-018-3732-3] [Medline: 30537958]
30. Lakerveld J, Bot SD, Chinapaw MJ, Knol DL, de Vet HC, Nijpels G. Measuring pathways towards a healthier lifestyle in the Hoorn Prevention Study: the Determinants of Lifestyle Behavior Questionnaire (DLBQ). Patient Educ Couns 2011 Nov;85(2):e53-e58 [FREE Full text] [doi: 10.1016/j.pec.2011.01.014] [Medline: 21296535]
31. Harvey S, Rach D, Stainton MC, Jarrell J, Brant R. Evaluation of satisfaction with midwifery care. Midwifery 2002 Dec;18(4):260-267. [doi: 10.1054/midw.2002.0317] [Medline: 12473441]
32. Petrou S, Morrell J, Spiby H. Assessing the empirical validity of alternative multi-attribute utility measures in the maternity context. Health Qual Life Outcomes 2009 May 06;7:40 [FREE Full text] [doi: 10.1186/1477-7525-7-40] [Medline: 19419553]
33. Bouwmans C, Hakkaart-van Roijen L, Koopmanschap M, Krol M, Severens H, Brouwer W. iMTA Medical Cost Questionnaire (iMCQ). Rotterdam: Institute for Medical Technology Assessment, Erasmus Universit; Feb 2013:1-41.
34. Bouwmans C, Krol M, Severens H, Koopmanschap M, Brouwer W, Hakkaart-van Roijen L. The iMTA productivity cost questionnaire: a standardized instrument for measuring and valuing health-related productivity losses. Value Health 2015 Sep;18(6):753-758 [FREE Full text] [doi: 10.1016/j.jval.2015.05.009] [Medline: 26409601]

35. Begg C, Cho M, Eastwood S, Horton R, Moher D, Olkin I, et al. Improving the quality of reporting of randomized controlled trials. The CONSORT statement. JAMA 1996;276(8):637-639. [Medline: 8773637]
36. Chan A, Tetzlaff J, Gøtzsche PC, Altman D, Mann H, Berlin J, et al. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. BMJ 2013 Jan 08;346:e7586 [FREE Full text] [doi: 10.1136/bmj.e7586] [Medline: 23303884]

Abbreviations

eFUSE: eHealth and Face-to-face Counseling
LRS: lifestyle risk score
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCT: randomized controlled trial
SPIRIT: Standard Protocol Items: Recommendations for Interventional Trials

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Protocol

Adapting to the Pandemic: Protocol of a Web-Based Perinatal Health Study to Improve Maternal and Infant Outcomes

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Abstract

Background: The identification of interconnected health risks during the perinatal period offers an opportunity to prevent negative maternal and infant health outcomes. Marijuana, opioid, and other substance use during pregnancy is a rapidly growing public health concern with significant and costly health consequences for the woman and the developing fetus. Pregnant persons who misuse substances are disproportionately more likely to engage in risky sexual behaviors resulting in sexually transmitted infections (STIs), which are on the rise in this population and can lead to adverse effects on maternal health and on fetal development.

Objective: Our goal is to continue testing an innovative and low-cost technology-delivered intervention, the Health Check-Up for Expectant Moms (HCEM), which simultaneously targets alcohol and drug use and STI risk during pregnancy, both of which are on the rise during the COVID-19 pandemic.

Methods: We describe the ways in which we have adapted the web-based HCEM intervention to continue recruitment and study enrollment during the pandemic.

Results: Study recruitment, visits, and participant safety assessments were all successfully modified during the initial year of the COVID-19 pandemic. Compared to in-person recruitment that occurred prepandemic, remote recruitment yielded a greater proportion of women enrolled in the study (83/136, 61.0% vs 43/52, 83%) in a shorter period (12 months vs 7 months).

Conclusions: Despite study challenges related to the pandemic, including time and effort adapting to a remote protocol, remote recruitment and visits for this study were found to constitute a successful approach.

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KEYWORDS

COVID-19; pregnancy; COVID-19 pandemic; alcohol use; drug use; sexually transmitted infections; technology-delivered interventions

Introduction

Overview

Alcohol, marijuana, opioid, and other substance use during pregnancy is a rapidly growing public health concern with significant and costly health consequences for the woman and developing fetus [1]. Women who misuse substances are disproportionately more likely to engage in risky sexual behaviors that can result in sexually transmitted infections (STIs). Pregnant persons are a scientifically complex group as national STI prevalence rates are on the rise among this population, leading to adverse effects on maternal health and on fetal development [2].

COVID-19 and Women's Health

The impact of the COVID-19 pandemic on women's health has been significant. Women have reported experiencing more severe stress than men resulting in greater health impact, and pregnant women have reported more health-related worry and high levels of anxiety directly related to the COVID-19 pandemic [3,4]. Pregnant women are particularly impacted by the pandemic as they are at increased risk for severe illness compared to nonpregnant women, and they may be at higher risk for preterm birth [5]. Since the onset of the COVID-19 pandemic, there are numerous reports that women's alcohol and other drug use has been rising in the United States. The US Centers for Disease Control and Prevention reported that approximately 12% of adult women reported either beginning or increasing their substance use to cope with pandemic-related stress [6]. Frequency of binge drinking—for women, defined as four or more drinks on one occasion—has increased substantially (over 40%) during this time, and cases of alcohol-related liver diseases have increased, especially among young women [7]. Moreover, marijuana use continues to escalate among pregnant women, with the most commonly cited reasons for use cited as relief of stress or anxiety, nausea or vomiting, and pain [8]. Pregnant women with opioid use disorders have faced unique challenges to care during the pandemic due to their complex health care needs (eg, clinic travel to receive medication and stigma) [9].

The co-occurrence of alcohol and substance use and sexual risk-taking contribute significantly to STI acquisition. With respect to the impact of the COVID-19 pandemic on sexual health, STIs were already at record highs before the pandemic and climbing, especially for childbearing women. Recent reports (2019) reveal increases from the previous year in the prevalence of gonorrhea, chlamydia, and syphilis of 5%, 3%, and 14%, respectively; among women of childbearing age, there was a 36% increase in syphilis cases [2]. Furthermore, there was a 40% increase in congenital syphilis cases, and an alarming 22% increase in newborn deaths related to congenital syphilis during the same time period [2]. Access to STI screening and treatment has been limited during the pandemic due to restrictions [10], likely leading to continued health consequences among this group.

The perinatal period has been identified as an urgent time to address and prevent these co-occurring risks [11], and technology-delivered interventions are ideally suited given their low cost and potential reach [12]. We are currently testing an innovative and low-cost technology-delivered intervention, the Health Check-Up for Expectant Moms (HCEM) (see study protocol in Tzilos Wernette et al [13]), which is theoretically grounded, consistent with motivational interviewing, and informed by the Information-Motivation-Behavior model, simultaneously targeting alcohol and drug use risk and risky sexual behavior during pregnancy. The HCEM is a 60-minute intervention that is guided by a narrator; provides information, including short video testimonials, highlighting the bidirectional relationships among these risk factors; and provides motivational strategies to enhance behavioral skills, including male and female condom use. In this paper, we highlight the ways in which our study team has adapted our research protocol and study procedures so that we can continue recruitment, assessment, and intervention remotely during the COVID-19 pandemic. Remote study participation may have potential advantages for participants, including lessening the burden of travel time, costs, and inconvenience associated with in-person visits [14].

Methods

Our study uses a two-group, randomized controlled design with a baseline session (prior to 22 weeks pregnant), plus two brief booster sessions within 1 month of study enrollment. We conduct three follow-up assessments at 2 and 6 months from baseline, and a postpartum assessment at 6 weeks postpartum. All sessions are asynchronously delivered via technology using the Computerized Intervention Authoring Software [15]. Additionally, each session includes the assessment of risk behaviors (eg, risky sexual behavior and alcohol and drug use) using the "timeline follow-back" interview method, a calendar-assisted structured interview [16]. Study recruitment prior to the pandemic was conducted exclusively in person at obstetric and primary care clinics. During the pandemic, recruitment efforts shifted to remote (eg, phone, text messaging, and online). Study participants include 250 pregnant women, aged 18 years or older; participants endorse the following risk factors in order to be eligible for the study: (1) unprotected sex in the past 30 days in addition to having more than one male partner in the last 6 months and/or having uncertainty about current sexual partner's monogamy and (2) current alcohol and drug use risk [17,18]. The study protocol was approved by the University of Michigan Medical Institutional Review Board (HUM00143896) and registered at ClinicalTrials.gov (NCT03826342).

Results

Overview

All in-person behavioral research studies university-wide were paused in March 2020 due to the COVID-19 pandemic. This impacted our study in three important ways. Primarily, we could no longer recruit new participants or conduct any study visits, including assessments and viewing of the intervention or control conditions. Next, STI testing and biological (eg, hair and urine) sample collection for the assessment of drug use was suspended since this was no longer done in person during a perinatal study

visit. Furthermore, because we were no longer seeing women in person, we had to modify our guidelines around assessing for participant safety, including the remote assessment of suicidality. Finally, the following modifications to our technology-based intervention and protocol were made in order to continue during the pandemic. The changes we implemented are detailed below in Table 1 [19], by category; for each point, we describe the original protocol followed by modifications (ie, "current protocol").

Table 1. Modifications to the Health Check-Up for Expectant Moms protocol in response to the COVID-19 pandemic.

Study aspects and protocols	Details
Study visits	
Baseline visits	
Original protocol	Baseline visits were conducted in person with research staff via interviews and accessing the CIAS[a] platform using a study iPad.
Current protocol	Baseline visits were adapted to be completed over the telephone and online through an individualized weblink to the CIAS platform.
Delivery of follow-up assessments	
Original protocol	Delivery of follow-up assessments (2 and 6 months from baseline and 6 weeks postpartum) was conducted in person with research staff via interviews and accessing the CIAS platform using a study iPad.
Current protocol	Delivery of all follow-up assessments was modified to be completed over the phone and through an individualized weblink to the CIAS platform.
Collection of biological samples	
Original protocol	Collection of biological samples (urine and hair) for drug use assessment was conducted in person at clinic by research staff.
Current protocol	Collection of biological samples is temporarily suspended.
Incentive payments	
Original protocol	Incentive payments (US $200 in cash) were made in person at study visits.
Current protocol	Incentive payments (US $200) are made via electronic gift card (emailed) or check (mailed).
Modified COVID-19 assessment[b]	
Current protocol	A modified COVID-19 assessment was added to every study visit: the COVID-19 Family Stress Screener [19] was adapted for our study.
Intervention arm content	
Original protocol	Intervention arm content included references to booklet given in person and to the male and female condom demonstrators, which was part of the in-person intervention.
Current protocol	Intervention arm content was updated to reflect remote nature of visits (eg, no longer refers to booklet given in person or to male and female condom demonstrators).
Informed consent	
Original protocol	Signed informed consent was obtained by research staff in person at the clinic.
Current protocol	Informed consent process is conducted over the phone (copy of consent emailed to participants) and the research staff obtains consent verbally.
Safe sex kits	
Original protocol	Safe sex kits (eg, male and female condoms and dental dams) and study booklets were offered to the participants in person during the intervention study visit.
Current protocol	Safe sex kits and study booklets are mailed to interested intervention participants with their permission.
Informational handouts	
Original protocol	All informational handouts (intervention and control) and local resources were provided to the participants in person at study visits.
Current protocol	All informational handouts and list of local resources are emailed, including the study booklet for participants in the intervention arm.
Provider-ordered sexually transmitted infection (STI) tests	
Original protocol	STI test results (urine samples) were collected at our clinic labs at each study visit.
Current protocol	New data are collected of all provider-ordered STI tests during participant's pregnancy and postpartum period (not part of original protocol, in which we only collected study STI test results).
Recruitment	
Potential participants	
Original protocol	Potential participants were identified from clinic schedules and approached by research staff in person at clinics.

Study aspects and protocols	Details
Current protocol	Potential participants are still identified from clinic schedules, but recruitment resumes remotely via telephone calls, text messages, and email messages.
Call patients[b]	
Current protocol	Patients are not called until after their second obstetrics visit to help ensure active pregnancy (modified during COVID-19 pandemic, given remote procedures).
Interested patients	
Original protocol	Interested patients met with research staff to complete the screening survey in person at the clinic using the study iPad.
Current protocol	Interested patients are emailed a weblink to complete the screening survey online.
Screening consent form	
Original protocol	The screening consent form was offered to the patient in person prior to completing the survey questions.
Current protocol	The screening consent form appears on the webpage before any survey questions can be viewed.
Compensation	
Original protocol	All prospective study participants (eligible and ineligible) were physically given a US $5 gift card for their time by the research staff upon completing the screening survey at the clinic.
Current protocol	All prospective study participants are emailed US $5 electronic gift card for their time upon completing the screening survey.
Eligible patients	
Original protocol	Eligible patients were scheduled for the baseline visit and consented in person at the clinic.
Current protocol	Eligible patients are contacted by the research assistant via telephone, where more detailed study information is given; a copy of the consent form is emailed; and a baseline visit is scheduled for interested patients.
Participant safety, suicide risk assessment, and child abuse and neglect	
Modified procedures	
Original protocol	We did not include questions explicitly asking about suicide risk or child abuse and neglect. Participants that spontaneously indicated any distress from the study were given a list of referral options that included information on how to contact a social worker within our health system and/or were assessed by clinic social worker in person during the study visit.
Current protocol	We modified our procedures for suicide risk assessment to reflect remote nature of visits (ie, research staff can no longer go to clinic social worker with participant to assess severity in person, as was done in the original protocol). We also modified our protocol for steps to take if our study team becomes aware of child abuse and neglect remotely, including procedures for how to report.
List of local resources	
Original protocol	A list of local resources was provided to all participants at the baseline study visit.
Current protocol	An updated list of local resources is emailed and includes online resources (eg, Alcoholics Anonymous and Narcotics Anonymous remote meetings) during COVID-19 and changes to hours and/or procedures for all other local resources (eg, food pantries, counseling, and STI testing).

[a]CIAS: Computerized Intervention Authoring Software.

[b]This study aspect only came about as a result of the COVID-19 pandemic and only includes a current protocol.

Participant Recruitment

While the pandemic caused significant initial delays to our study recruitment, since adapting to remote recruitment, we have exceeded the total number of patients screened compared to prepandemic recruitment. Remote recruitment over a 7-month period, from August 2020 to March 2021, has yielded 1122 contacts, with 305 women being screened. In the previous 12 months, from April 2019 to March 2020, we approached 892 women in the clinics and screened 232 women. Furthermore, of all women who were screened and were eligible prior to the pandemic, only 61.0% (83/136) went on to enroll in the study, whereas during remote recruitment, a greater proportion (43/52, 83%) of women enrolled in the study.

Discussion

Principal Findings

In this paper, we provide an overview of the HCEM intervention and study methodology. The COVID-19 pandemic has been disruptive to most facets of life globally, including research efforts. We highlight the ways in which we successfully adapted our study protocol to continue recruitment and intervention efforts with pregnant women during the pandemic. Study recruitment, visits, and participant safety assessments were all modified during the initial year of the COVID-19 pandemic.

Despite the challenges of the pandemic on women's health and intervention efforts, there have been silver linings. Clinically, reduced health care visits and more telehealth visits have had some positive impacts on pregnant women [20-22]. Across the country, clinical treatment programs for substance use have ramped up telehealth utilization, offering care through a mix of telephone and/or video visits, with limited in-person visits to reduce COVID-19 exposure risk. This has been particularly beneficial to perinatal women seeking care for substance use disorder, including opioid use disorder, with relaxed regulations around travel to crowded clinics to receive treatment medications (eg, methadone) and psychotherapy, which help to overcome known treatment barriers (ie, stigma, health care access, transportation, and childcare) in this population [9,20-22]. Our own research has also seen positive impacts as a result of the COVID-19 pandemic, particularly in terms of study recruitment. The ability to offer "contact-free" visits alleviates anxiety surrounding the risks of in-person visits, and the convenience of being able to take the study screener and assessments from home seems to have increased interest in study participation.

Remote recruitment yielded a larger percentage of women screened in a shorter time frame compared to in-person recruitment. Furthermore, a large percentage of eligible women went on to enroll in the study. Study procedures and intervention content had to be adapted to reflect the remote delivery, but because the groundwork for the study was primarily technology based, it was a feasible and successful transition that took place over the course of 3 months. Our study team had to carefully consider potential issues related to participant safety, given that we no longer had in-person access to clinical care providers in the event of an emergency. This resulted in revisions to our procedures for how to respond to the disclosure of suicide risk and child abuse and neglect reporting. Our study assessments—both the original and modified versions—do not include questions explicitly asking about suicide risk. Rather, if a participant spontaneously shares a desire or plan to hurt themselves and/or suicide or self-harm is explicitly mentioned, we have in place an adapted protocol of action steps to remotely assess suicidality risk (ie, low, moderate, or high). For example, if a participant reports any suicidal intent, but indicates that she has no likelihood of acting on these thoughts in the near future, our staff provides her with resources (eg, National Suicide Prevention Lifeline and local resources, including social work) and offers to notify their primary care physician or mental health provider. If the participant discloses that they are somewhat or very likely to harm themselves, our research staff expresses concern and recommends that they speak to a professional as soon as possible. They also contact the principal investigator (PI) or clinical backup of the study who would plan to follow up with them by phone immediately. The research staff would provide numbers for local crisis and emergency mental health services within our health system that are offered. The PI would take appropriate action depending on the level of risk (eg, high risk would require a referral to the emergency department closest to the study participant). To date, we have not had a participant disclose suicidality.

Conclusions

Despite study challenges related to the pandemic, including time and effort adapting to a remote protocol, remote recruitment and remote visits for this study were found to constitute a successful approach. We also recognize the potential advantages to participants in accessing our study remotely, including lessening the burden of time, costs, and inconvenience associated with traveling for in-person visits at the clinic [14]. It is important to note, however, that there are limitations to remote delivery of study visits, which may pose challenges for generalizing to other research studies or clinical settings that may not offer remote care. First, because study participation requires access to a telephone and a device with a reliable internet connection, it is possible that we could exclude low-income and marginalized women who might not have access to the required technology, and who are also the most vulnerable to negative health outcomes. Second, in our remote protocol, we are no longer able to collect biological (ie, hair and urine) samples as a secondary measure for drug use. Third, as this study is ongoing, our outcomes are pending. Notwithstanding these unknowns, just as COVID-19 has likely permanently changed the way we seek and utilize health care, it has also altered the way we conduct clinical behavioral research. In both instances, there are many benefits to embrace and maintain as we move forward.

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Authors' Contributions

GTW, KC, OM, QMN, and CZ all contributed to the design of the study adaptations. KC contributed to participant recruitment and data entry. GTW, KC, OM, QMN, and CZ all contributed to the analysis, interpretation, and writing. All authors contributed to the editing, review, and approval of the manuscript.

Conflicts of Interest

None declared.

References

1. Substance Abuse and Mental Health Services Administration. Key Substance Use and Mental Health Indicators in the United States: Results From the 2019 National Survey on Drug Use and Health (HHS Publication No. PEP20-07-01-001, NSDUH Series H-55). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration; 2020. URL: https://www.samhsa.gov/data/sites/default/files/reports/rpt29393/2019NSDUHFFRPDFWHTML/2019NSDUHFFR090120.htm [accessed 2021-08-03]
2. New CDC report: STDs continue to rise in the US. Centers for Disease Control and Prevention. 2019 Oct 08. URL: https://www.cdc.gov/nchhstp/newsroom/2019/2018-STD-surveillance-report-press-release.html [accessed 2021-08-03]
3. Connor J, Madhavan S, Mokashi M, Amanuel H, Johnson NR, Pace LE, et al. Health risks and outcomes that disproportionately affect women during the COVID-19 pandemic: A review. Soc Sci Med 2020 Dec;266:113364 [FREE Full text] [doi: 10.1016/j.socscimed.2020.113364] [Medline: 32950924]
4. Naurin E, Markstedt E, Stolle D, Enström D, Wallin A, Andreasson I, et al. Pregnant under the pressure of a pandemic: A large-scale longitudinal survey before and during the COVID-19 outbreak. Eur J Public Health 2021 Feb 01;31(1):7-13 [FREE Full text] [doi: 10.1093/eurpub/ckaa223] [Medline: 33231625]
5. Pregnant and recently pregnant people: At increased risk for severe illness from COVID-19. Centers for Disease Control and Prevention. 2021 Mar 05. URL: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/pregnant-people.html#anchor_1614966846976 [accessed 2021-08-03]
6. Czeisler M, Lane RI, Petrosky E, Wiley JF, Christensen A, Njai R, et al. Mental health, substance use, and suicidal ideation during the COVID-19 pandemic - United States, June 24-30, 2020. MMWR Morb Mortal Wkly Rep 2020 Aug 14;69(32):1049-1057 [FREE Full text] [doi: 10.15585/mmwr.mm6932a1] [Medline: 32790653]
7. Pollard MS, Tucker JS, Green HD. Changes in adult alcohol use and consequences during the COVID-19 pandemic in the US. JAMA Netw Open 2020 Sep 01;3(9):e2022942 [FREE Full text] [doi: 10.1001/jamanetworkopen.2020.22942] [Medline: 32990735]
8. Ko JY, Coy KC, Haight SC, Haegerich TM, Williams L, Cox S, et al. Characteristics of marijuana use during pregnancy - Eight states, Pregnancy Risk Assessment Monitoring System, 2017. MMWR Morb Mortal Wkly Rep 2020 Aug 14;69(32):1058-1063 [FREE Full text] [doi: 10.15585/mmwr.mm6932a2] [Medline: 32790656]
9. McCarthy JJ, Jones HE, Terplan M, Rudolf VP, von Klimo MC. Changing outdated methadone regulations that harm pregnant patients. J Addict Med 2021 Apr 01;15(2):93-95. [doi: 10.1097/ADM.0000000000000720] [Medline: 32826620]
10. Mmeje OO, Coleman JS, Chang T. Unintended consequences of the COVID-19 pandemic on the sexual and reproductive health of youth. J Adolesc Health 2020 Sep;67(3):326-327 [FREE Full text] [doi: 10.1016/j.jadohealth.2020.06.019] [Medline: 32690467]
11. ACOG Practice Bulletin No. 117: Gynecologic care for women with human immunodeficiency virus. Obstet Gynecol 2010;116(6):1492-1509. [doi: 10.1097/AOG.0b013e3182054cae] [Medline: 21099636]
12. Ondersma SJ, Svikis DS, Thacker LR, Beatty JR, Lockhart N. Computer-delivered screening and brief intervention (e-SBI) for postpartum drug use: A randomized trial. J Subst Abuse Treat 2014 Jan;46(1):52-59 [FREE Full text] [doi: 10.1016/j.jsat.2013.07.013] [Medline: 24051077]
13. Tzilos Wernette G, Plegue M, Mmeje O, Sen A, Countryman K, Ngo Q, et al. Reducing sexual health risks and substance use in the prenatal setting: A study protocol for a randomized controlled trial. Contemp Clin Trials 2019 Sep;84:105827 [FREE Full text] [doi: 10.1016/j.cct.2019.105827] [Medline: 31419607]
14. McDermott MM, Newman AB. Remote research and clinical trial integrity during and after the coronavirus pandemic. JAMA 2021 May 18;325(19):1935-1936. [doi: 10.1001/jama.2021.4609] [Medline: 33885728]
15. Ondersma SJ, Chase SK, Svikis DS, Schuster CR. Computer-based brief motivational intervention for perinatal drug use. J Subst Abuse Treat 2005 Jul;28(4):305-312 [FREE Full text] [doi: 10.1016/j.jsat.2005.02.004] [Medline: 15925264]
16. Sobell LC, Sobell MB. Timeline follow-back. In: Litten RZ, Allen JP, editors. Measuring Alcohol Consumption. Totowa, NJ: Humana Press; 1992:41-72.
17. Sokol RJ, Martier SS, Ager JW. The T-ACE questions: Practical prenatal detection of risk-drinking. Am J Obstet Gynecol 1989 May;160(4):863-868; discussion 868. [doi: 10.1016/0002-9378(89)90302-5] [Medline: 2712118]
18. Yonkers K, Gotman N, Kershaw T, Forray A, Howell H, Rounsaveille B. Screening for prenatal substance use: Development of the Substance Use Risk Profile-Pregnancy scale. Obstet Gynecol 2010;116(4):827-833. [doi: 10.1097/aog.0b013e3181ed8290]
19. Huth-Bocks A. COVID-19 Family Stress Screener. 2020. URL: https://commons.srcd.org/HigherLogic/System/DownloadDocumentFile.ashx?DocumentFileKey=4d647e65-0459-4c72-a051-c671d42eb9ab [accessed 2021-08-31]
20. Moreland A, Guille C, McCauley JL. Increased availability of telehealth mental health and substance abuse treatment for peripartum and postpartum women: A unique opportunity to increase telehealth treatment. J Subst Abuse Treat 2021 Apr;123:108268. [doi: 10.1016/j.jsat.2020.108268] [Medline: 33612199]
21. Patton EW, Saia K, Stein MD. Integrated substance use and prenatal care delivery in the era of COVID-19. J Subst Abuse Treat 2021 May;124:108273 [FREE Full text] [doi: 10.1016/j.jsat.2020.108273] [Medline: 33771277]
22. Sadicario JS, Parlier-Ahmad AB, Brechbiel JK, Islam LZ, Martin CE. Caring for women with substance use disorders through pregnancy and postpartum during the COVID-19 pandemic: Lessons learned from psychology trainees in an

integrated OBGYN/substance use disorder outpatient treatment program. J Subst Abuse Treat 2021 Mar;122:108200 [FREE Full text] [doi: 10.1016/j.jsat.2020.108200] [Medline: 33250270]

Abbreviations

HCEM: Health Check-Up for Expectant Moms
PI: principal investigator
STI: sexually transmitted infection

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Protocol

The Effects of 3D Immersion Technology (3Scape) on Mental Health in Outpatients From a Short-Term Assessment, Rehabilitation, and Treatment Program: Feasibility Protocol for a Randomized Controlled Trial

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Abstract

Background: Mental health conditions are prevalent among Canadians and are a leading cause of disability. Each year, 1 in 5 Canadians experiences a mental health issue. A total of 5% of people aged ≥65 years perceive their mental health as fair or poor, and 6.3% of them have mood disorders. Regarding older adults with cognitive impairments such as dementia, up to 40%-50% of them experience depression at some point. We believe that older adults can benefit significantly from information and telecommunication technologies as a strategy for improving mental health conditions such as depression and anxiety, while simultaneously improving their quality of life. 3Scape Systems Inc is an Alberta-based private company that has produced a series of specialized 3D videos designed to simulate real-life events and engage individuals living with mental health disorders and cognitive impairments such as dementia.

Objective: This study aims to explore the trial design and effects of 3Scape videos on older adults' symptoms of depression and anxiety and the efficacy of this technology in improving the quality of life of patients attending the Short-Term Assessment, Rehabilitation, and Treatment Psychiatry Day Hospital program at Glenrose Rehabilitation Hospital and to provide data to estimate the parameters required to design a definitive randomized controlled trial.

Methods: The trial will use a randomized controlled design comprising 15 intervention participants and 15 control group participants. The participants will be adults aged ≥65 years who are cognitively intact or have minimal cognitive impairment (ie, Montreal Cognitive Assessment score ≥18), and are clients of the Short-Term Assessment, Rehabilitation, and Treatment Psychiatry Day Hospital program at Glenrose Rehabilitation Hospital. This study's primary outcome variables are related to clients' depressive and anxiety symptoms and their quality of life. The control group will receive the standard of care (ie, the Short-Term Assessment, Rehabilitation, and Treatment Psychiatry Day Hospital program at Glenrose Rehabilitation Hospital). The intervention group will receive the same standard of care as the control group and will use 3Scape Systems videos for therapeutic activities.

Results: Our study is currently on hold because of the COVID-19 pandemic. The recruitment process is expected to resume by November 2021, and the primary impact analysis is expected to be conducted by February 2022.

Conclusions: This study will provide valuable information such as the measurement of comparative intervention effects, perception of older adults and mental health therapists about the 3Scape Systems, the associated costs of treatment, and product costs. This will contribute to the evidence planning process, which will be crucial for the future adoption of 3Scape Systems.

Trial Registration: International Standard Randomized Controlled Trial Number (ISRCTN): 93685907; https://www.isrctn.com/ISRCTN93685907.

International Registered Report Identifier (IRRID): PRR1-10.2196/25017

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KEYWORDS

technology assessment; mental health; technology for rehabilitation; clinical engineering; biomedical engineering

Introduction

Background and Rationale

Mental health disorders disrupt a person's thinking, feeling, mood, and ability to relate to others, affecting their daily functioning. Mental health conditions are prevalent among Canadians. Mental health conditions are the leading causes of disability, with 1 in 5 Canadians experiencing a mental health concern each year. In Canada, mental health conditions are associated with high health care resource use [1,2]. In older adults, mental conditions may be aggravated by concomitant medical health issues (eg, stroke), as many of them can no longer lead active lives because of cognitive and physical decline and psychosocial factors such as isolation and poverty. According to Statistics Canada, 5% of people aged ≥65 years perceive their mental health as fair or poor [3] and 6.3% of them have mood disorders [4]. Mental health disorders contribute significantly to morbidity and mortality in older adults and reduced quality of life. Regarding older adults with cognitive impairments such as dementia, up to 40%-50% of them experience depression at some point [5]. The high prevalence of mental health conditions in Canada places a substantial burden on individuals with mental illness, caregivers, and the health care system in general. For example, by 2015, the estimated public and private mental health expenditure was Can $15.8 (US $12.7) billion, representing 7% of the total health care expenditure, and by 2022 this expenditure is expected to increase by up to 9% [2]. Reminiscence therapy is a widely used nonpharmacological psychosocial intervention in people with mental health conditions and cognitive impairments such as dementia. Reminiscence therapy involves a discussion of past events and experiences, using tangible prompts to evoke memories or stimulate conversations [6]. The literature suggests that reminiscence therapy can significantly reduce social isolation, depression, and anxiety, while simultaneously improving quality of life in older people within urban aged care settings [6-8].

We believe that older adults can benefit significantly from information and telecommunication technologies as a strategy for improving mental health conditions such as depression and anxiety, while simultaneously improving their quality of life. Information and telecommunication technologies have the potential to improve the delivery of reminiscence therapy, as these technologies facilitate access to and the selection of biographical information and related contents, or by providing novel multimodal interaction forms (eg, virtual reality) to trigger memories [9,10]. Previous investigations have studied the impact of information and telecommunication technologies on reminiscence therapy on the quality of caregiver and patient relationships, subjective patients' well-being [11], alleviating depressive symptoms in older adults [12], and supporting social interactions in residential care [13]. 3D immersive technologies (or immersive technologies) such as virtual reality and 3D display have also been shown to have a variety of positive effects on the mental, emotional, and social health of older adults [14]. In addition, there is an opportunity to indirectly reduce caregiver and health care professional burden by delivering stimulating viewing content to older adults affected by mental health conditions, thereby enhancing their daily experience. Although these immersive technologies are slowly becoming more accessible (ie, in terms of cost), there is a lack of literature on the benefits of 3D immersion technology for the mental health well-being of seniors. As a result, whether 3D immersion technology has a positive effect on older adults' mental health conditions and the burden of self-care remains an open question.

3Scape Systems Inc is an Alberta-based private company that has produced a series of specialized 3D videos designed to simulate real-life events and engage individuals living with mental health disorders and cognitive impairments such as dementia [15]. These videos are based on the principles of reminiscence therapy, with each video highlighting a specific topic that is present in society, including animals, music, and nature. The goals of these videos are to trigger positive memories, engage individuals, and invite comfort and familiarity. Through a series of clinical evaluations, with the aim of determining the efficacy of the 3Scape system, qualitative and quantitative data were collected to ascertain whether the use of these immersive video productions has an impact on self-care or caregiver burden, the use of antipsychotic medications, mood, agitation, emotion, engagement, tolerability of 3D intervention, satisfaction with life, and the quality of life of older adults with and without cognitive impairment [16]. However, there were important threats to the internal validity of these studies, as there were no control conditions or groups; thus, the quality of evidence provided was very low.

Evaluation Objectives and Research Questions

This study aims to explore the trial design and effect of 3Scape videos on older adults' depressive and anxiety symptoms and quality of life and the efficacy in terms of caregiver burden of the Short-Term Assessment, Rehabilitation, and Treatment Psychiatry Day Hospital program at Glenrose Rehabilitation Hospital and to provide data to estimate the required parameters to design a definitive randomized controlled trial (RCT). Thus, this study has the following five research questions:

1. Is the designed protocol feasible for conducting a future definitive RCT?
2. Do the 3Scape videos affect older adults' depressive and anxiety symptoms, mood, and overall quality of life compared with clients who receive the standard of care?
3. What are the overall experiences, beliefs, and attitudes of older adults while watching 3Scape videos?

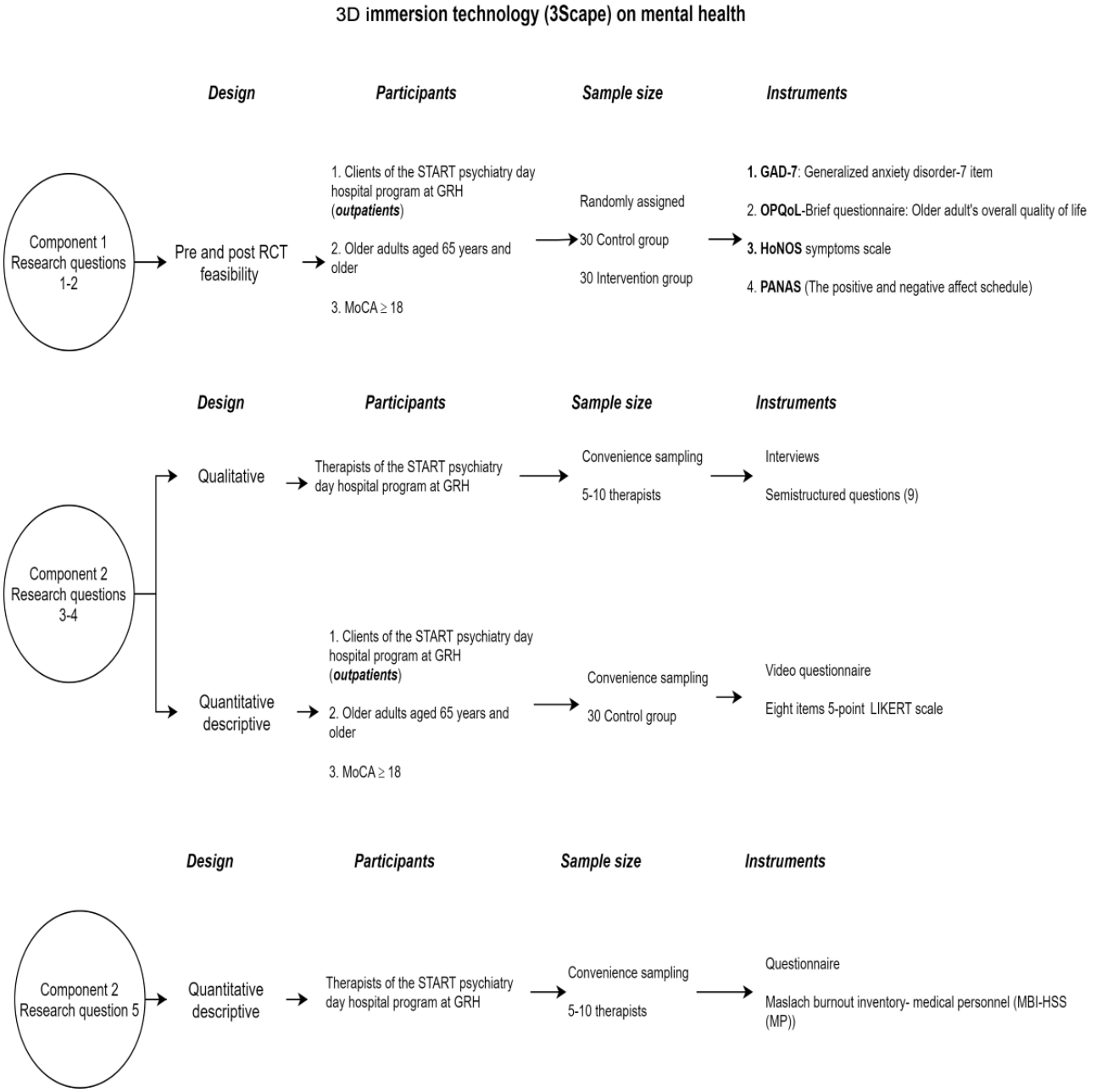
4. What are the overall experiences, beliefs, and attitudes of therapists while watching 3Scape videos?
5. Do 3Scape videos affect caregivers' burden compared with the same caregivers who provide the standard of care?

Methods

Study Design

This study will use a multimethod research design. The *Methods* section is presented in accordance with the study's research questions. Additional details have been provided in Figure 1.

Figure 1. Study components. GRH: Glenrose Rehabilitation Hospital; HoNOS: Health of the Nation Outcome Scale; MoCA: Montreal Cognitive Assessment; OPQoL-Brief: Older People's Quality of Life-Brief; RCT: randomized controlled trial.



- Research questions 1-3, feasibility parallel-group RCT: The experimental group will receive the intervention, which consists of sessions with the 3Scape videos, whereas the control group will receive the standard of care used at the Short-Term Assessment, Rehabilitation, and Treatment Psychiatry Day Hospital program at Glenrose Rehabilitation Hospital (see the *Outcome Variables* section for more details). For this pilot study, we will follow the CONSORT (Consolidated Standards of Reporting Trials) guidelines for randomized feasibility studies [17]. The *Methods* section is presented with regard to the objectives of the study.
- Research question 4, study design: qualitative description design [18].
- Research question 5, study design: quantitative descriptive [19].

Study Setting

This study will be conducted at the Short-Term Assessment, Rehabilitation, and Treatment Psychiatry Day Hospital at Glenrose Rehabilitation Hospital located in Edmonton, Alberta, Canada.

Eligibility Criteria

Inclusion Criteria

The study participants will include adults aged ≥65 years attending the Short-Term Assessment, Rehabilitation, and Treatment Psychiatry Day Hospital program at Glenrose Rehabilitation Hospital who are cognitively intact or with minimal cognitive impairment; that is, Montreal Cognitive Assessment score ≥18 [20].

Exclusion Criteria

Potential participants who are unable to provide informed consent, are unable to communicate in the English language, have a significant sensory impairment (which would prevent adequate viewing of the 3D videos), have a mental health diagnosis with behavioral disturbances such as the potential for aggression or severe agitation, with aphasia, or other diagnoses that would prevent the participant from completing surveys, or have posttraumatic stress disorder or zoophobia will be excluded.

Interventions

The eligible participants will be randomly assigned 1:1 to either the experimental group or the control group.

Control Group

This group will receive standard care consisting of (1) standard psychiatric nursing care (including some individual counseling), (2) medication trials or titration (antidepressants, antianxiety medicines, sleep medicines), and (3) group therapies (psychoeducation, cognitive behavioral therapy, stress management groups, dialectical behavior therapy, exercise groups, community engagement and wellness groups, leisure groups, and grief and loss groups). Every group runs twice a week for 6 weeks (1.5 months). The patients simultaneously attend 3 therapy groups for 6 weeks. That is, the patients attend 3 therapy sessions per day, twice a week. Each patient attends every group at some point during their 20-week stay in the program. Each group session is 1 hour long. Therefore, the patients receive 36 hours of standard care every 6 weeks for a total of 108 hours on the Short-Term Assessment, Rehabilitation, and Treatment program.

Experimental (Intervention) Group

In the experimental arm, the psychoeducation (Leisure Choices) group therapy (on the Short-Term Assessment, Rehabilitation, and Treatment program) will be replaced by five 3D video screenings (the intervention); in addition, they will receive the same standard care. The five 3D video screening sessions will be delivered as one session per week within a 6-week time frame. Each session will take approximately 1 hour, consisting of one 20-minute video screening and a postvideo screening discussion and questionnaire. A therapist and a member of the research team will be present during the video screening sessions. The therapist will lead the video screening sessions and the postvideo screening discussion (20 minutes of video and 20 minutes of discussion). The research team will observe alertness during video screenings sessions. After the discussion, the research team will administer two questionnaires (Positive and Negative Affect Schedule [PANAS] and postscreening survey), which will take approximately 20 minutes. Each session will take 1 hour overall. The videos will be screened in any order. The goal of these videos is to trigger positive memories, engage individuals, and bring comfort and familiarity. The topics of the videos are as follows: (1) *The Path*, (2) *Remembering*, (3) *The Dance*, (4) *The Memory Box*, and (5) *Baby Animals*. A sample of the videos can be found on the company's website [15]. The sessions will take place at the Courage Center at Glenrose Rehabilitation Hospital. No more than 5 participants will be present during each video screening session.

Outcome Variables

Research Questions 1-2 (Primary Outcome Variables)

Older adults' depressive and anxiety symptoms, mood, overall quality of life, and engagement are the primary outcome variables for these research questions. Older adults' depressive and anxiety symptoms will be assessed using the Generalized Anxiety Disorder-7 item (GAD-7) scale patient self-report tool [21] and the Health of the Nation Outcome Scale (HoNOS; a clinician rating tool) symptoms [22], older adults' mood will be measured using PANAS (20-item self-report questionnaire) [23], and older adults' overall quality of life will be measured using Older People's Quality of Life-Brief (OPQoL-Brief) questionnaire scale-13 items self-reported tool [24].

Research Questions 1-2 (Secondary Outcome Variables)

Engagement while watching the 3Scape videos will be measured using an engagement scale developed by team members in a previous study [25]. This is an 8-point Likert scale that has been shown to be understood by older adults, even those with mild cognitive impairments.

Research Question 3 (Participants: Older Adults)

Participants will be asked to participate in a postsurvey to provide feedback on their experiences while watching the 3Scape videos. The overall experience, beliefs, and attitudes of older adults while watching the 3Scape videos will be measured using an instrument (height items 5-point Likert scale and 4 open-ended questions) developed by the University of Calgary in a previous study on this technology.

Research Question 4 (Participants: Therapists)

Participants will be asked to participate in a poststudy interview to provide feedback on their experiences, with their patients using the 3Scape videos.

Research Question 5 (Participants: Therapists)

The caregiver burden will be assessed by using the burnout and workload perception among health care providers, measured by the Maslach Burnout Inventory-Human Services Survey for Medical Personnel (MBI-HSS MP) [26].

All of the measures have good to excellent metric properties [27,28].

Independent Variable

The independent variable in this study is the type of intervention used. This variable has two levels (ie, control and intervention); the *Interventions* section provides more details.

Confounding Variables

Age, gender, mental health condition, and groups in which the patients are involved during the intervention will be applied, and whether the patients are taking any medication will be analyzed as confounding variables.

Participant Timeline

Overview

This feasibility trial consisted of a 6-week intervention treatment phase; this study does not have a follow-up phase. The total trial data collection period will be 8 months. As shown in Table 1, Figure 2, and Figure 3, the measurements will be taken as follows.

Table 1. Key variables and measurements.

Variables	Participants	Measurement	T_0	T_1	T_2	T_3	T_5	T_6	T_7	T_8
Primary outcome										
GAD-7[a]	Older adults	GAD-7 scale	✓[b,c,d]	✓[c,d]	✓[d]	✓[d]	✓[d]	✓[d]	✓[d]	✓[c,d]
HoNOS[e]	Older adults	HoNOS, a clinician rating tool	✓[c,d]	✓[c,d]	✓[d]	✓[d]	✓[d]	✓[d]	✓[d]	✓[c,d]
OPQoL-Brief[f]	Older adults	OPQoL-Brief scale	✓[c,d]	✓[c,d]	✓[d]	✓[d]	✓[d]	✓[d]	✓[d]	✓[c,d]
PANAS[g]	Older adults	PANAS	✓[c,d]	✓[c,d]	✓[d]	✓[d]	✓[d]	✓[d]	✓[d]	✓[c,d]
Secondary outcomes										
Engagement	Older adults	Engagement scale	✓[d]	✓[d]	✓[d]	✓[d]	✓[d]	✓[d]	✓[d]	✓[d]
Experiences while watching the 3Scape videos	Older adults and therapists	Semistructured interview								✓
MBI-HSS MP[h]	Therapists	MBI-HSS MP								✓
Covariates										
Demographics	Older adults and therapists	Self-report assessment questionnaire	✓[c,d]							

[a]GAD-7: Generalized Anxiety Disorder-7.

[b]Outcome present.

[c]Control groups.

[d]Intervention groups.

[e]HoNOS: Health of the Nation Outcome Scale.

[f]OPQoL-Brief: Older People's Quality of Life-Brief.

[g]PANAS: Positive and Negative Affect Schedule.

[h]MBI-HSS MP: Maslach Burnout Inventory-Human Services Survey for Medical Personnel.

Figure 2. Flow of participants. GAD-7: Generalized Anxiety Disorder-7 item; HoNOS: Health of the Nation Outcome Scale; MoCA: Montreal Cognitive Assessment; OPQoL-Brief: Older People's Quality of Life-Brief; PTSD: posttraumatic stress disorder.

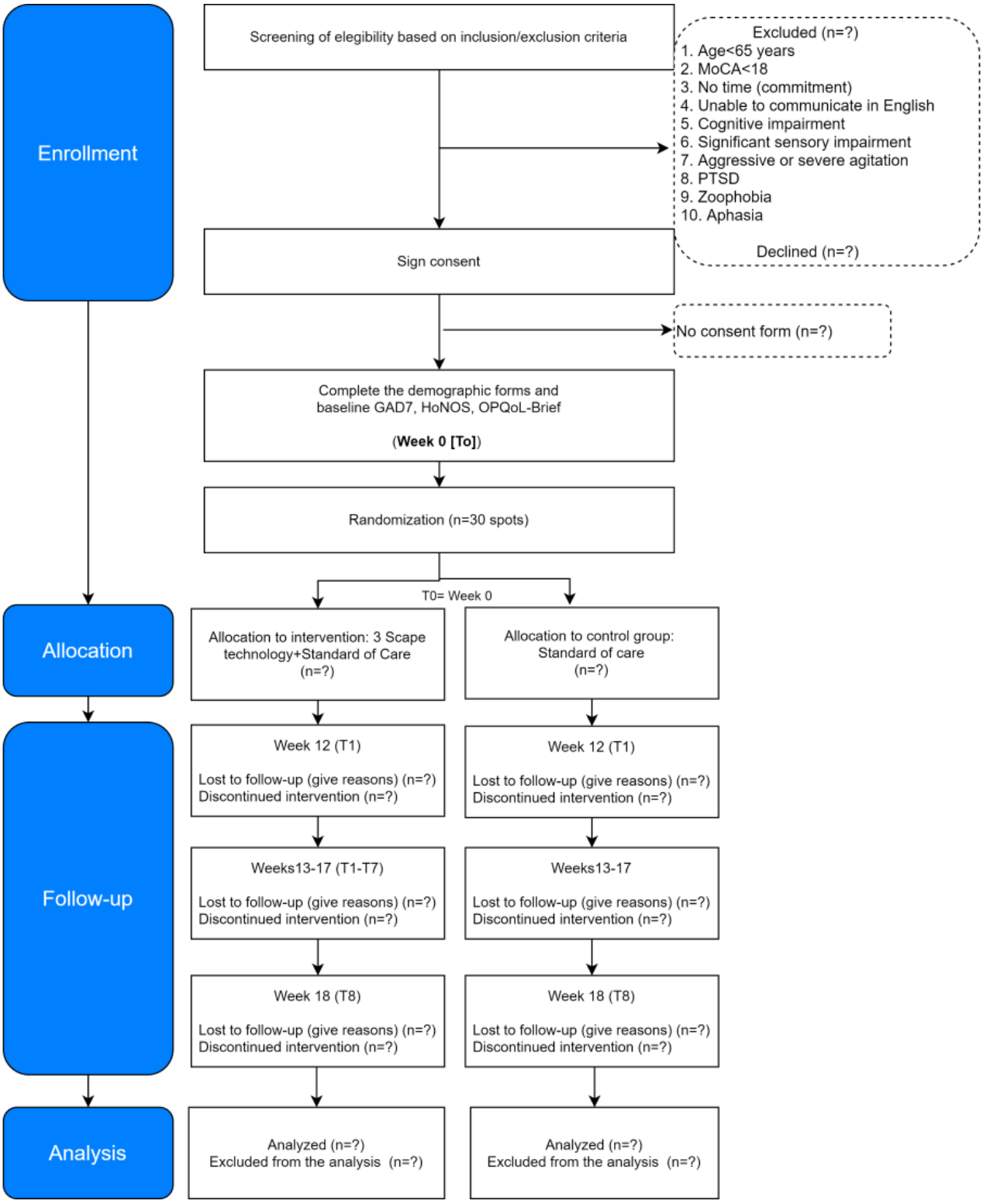
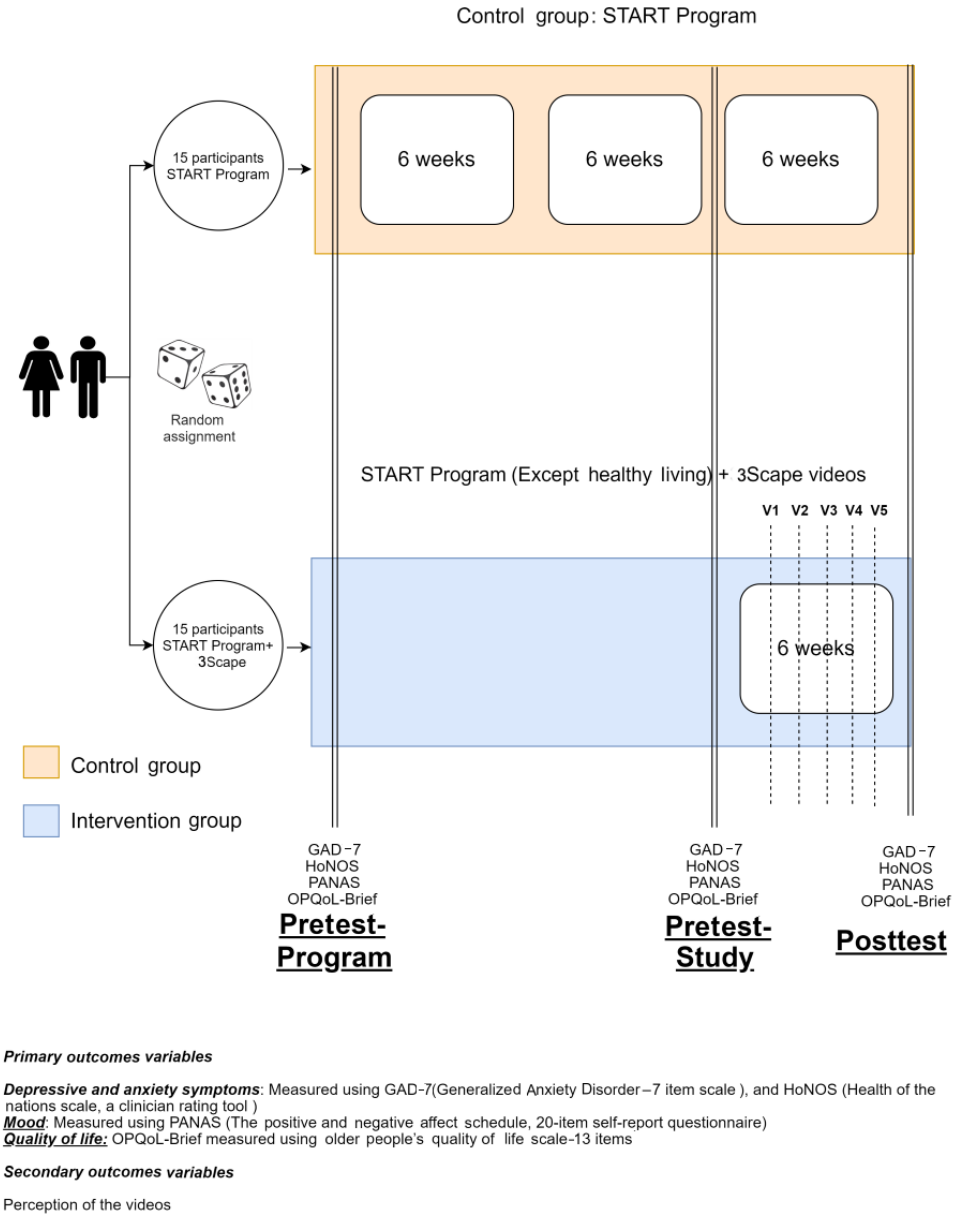


Figure 3. Study design schema.



Intervention Group (Participants: Older Adults)

Research questions 1-2 (primary outcome variables): at the enrollment of the program (week 0 [T_0], called the pretest program enrollment), the pretest before starting showing the videos (week 12 [T_1]), and at the posttest when the participants finish the program and watch the videos (week 18 [T_8]).

- Research questions 1-2 (secondary outcome variables): after watching each video, that is, weeks 13-17 (T_{1-7}).
- Research question 3 (participants, older adults): after watching every video (week 18 [T_8]).

Control Group (Participants: Older Adults)

- Research question 1-2 (Primary outcome variables): at the enrollment of the program (week 0 [T_0], called the pretest program enrollment), week 12 (T_1), and at the posttest when the participants finish the program and watch the videos (week 18 [T_8]).

For the therapists involved in the intervention group, the measurements will be taken as follows: research questions 4 and 5 (participants, therapists): week 12 [T_1].

Sample Size

Research Questions 1-3 (Participants: Older Adults)

As this is a feasibility study, a sample size calculation is not required [17]. However, we can estimate the number of participants we will be able to recruit during the data collection period. In this feasibility study with a statistical power of 0.8, an α of .05, and an effect size of 1.20, the minimum required sample size will be 24 participants in total (12 in each group [19]). We aim to recruit 15 participants for each group, for a total sample size of 30, to compensate for a 20% dropout rate. Sample size calculations are estimated using G*Power (version 3.1.9.4, Universitat Kiel) [29].

Research Questions 4-5 (Participants: Therapists)

We aim to recruit 5-10 therapists participating in the Short-Term Assessment, Rehabilitation, and Treatment Psychiatry Day Hospital program who provided the intervention.

Recruitment

Participants (Older Adults)

An invitation to participate will be posted in the Short-Term Assessment, Rehabilitation, and Treatment Psychiatry Day Hospital program at Glenrose Rehabilitation Hospital. Therapists will support recruitment strategies, including the provision of information sessions and one-on-one conversations with potential participants. The first contact with a potential participant will be made through one of the therapists not involved in the research team. Therapists who are already involved in the clinical care of the patients will then determine the individuals' willingness to be approached by the therapist researcher regarding participation and then obtain their consent for the study, as the case may be.

Allocation

Sequence Generation

Probability sampling will be used. Random sequence generation will be prepared in advance by a research team member (AMC) on an Excel file spreadsheet (RAND function) using permuted block randomization with a block size of 4 and a ratio of 1:1.

Concealment Mechanism

Allocation concealment will be ensured, as we will not release the randomization code until the patients have been recruited to the trial and all of the baseline measurements have been completed.

Implementation

If a potential participant meets the inclusion criteria, the therapist researcher (MKW) will ask the study coordinator to check whether a place is available in the study for that participant in a given group. If a place is available, then the therapist researcher (MKW), or another therapist involved in the recruitment process, will invite the participant to participate in the study, explain the study to him or her, and ask him or her to sign the consent form. If a potential participant is assigned to a particular therapist researcher (MKW), the therapist would not invite the participant to participate in the study. Instead, a secondary therapist researcher will do so. As a result, the freedom to decline will not be compromised. Once the participants or their substitute decision makers have signed the consent form and given their assent, the therapist researcher (MKW) will inform the study coordinator. The study coordinator will allocate each participant to 1 arm of the trial according to the allocation protocol and will assign a code. This code will be given to the therapist researcher (MKW) and research assistants (RAs) who will conduct the assessments.

Blinding (Masking)

The assessments of outcome variables will be conducted by RAs who are blinded to the treatment allocation. Owing to the nature of the intervention, neither the participants nor the therapist can be blinded to the treatment allocation, but they are strongly encouraged not to disclose the participants' allocation status during the assessments. An RA will enter the data into a computer on separate datasheets, and a senior RA will conduct the data analysis under the supervision of the principal investigator (PI; AMC).

Data Collection Methods

Research Questions 1-2 (Participants: Older Adults)

A therapist on the Short-Term Assessment, Rehabilitation, and Treatment Psychiatry Day Hospital program at Glenrose Rehabilitation Hospital with an RA, that is, RA 1, will administer the intervention (5 video screenings). The control group will receive standard care at the Short-Term Assessment, Rehabilitation, and Treatment Psychiatry Day Hospital program Glenrose Rehabilitation Hospital. The PANAS scale will be administered after each session along with the 3Scape videos to the intervention group participants (10 minutes). The GAD-7, HoNOS, and OPQoL-Brief will be administered to all participants at the beginning and end of the Short-Term Assessment, Rehabilitation, and Treatment program, as this is part of the standard care. In addition, we will administer the same measures (ie, GAD-7, HoNOS, and OPQoL-Brief) to the participants on both arms before and after each group therapy is conducted (ie, 6 weeks apart). The administration of these measures will take approximately 30 minutes. RA 2, who will be blinded to the group allocation, will administer these measures. The participants will be asked not to inform the evaluators about the kind of intervention they had received. The sessions will be conducted in a quiet room at the Courage Center.

Research Question 3 (Participants: Older Adults)

The overall experience, beliefs, and attitudes of older adults while watching the 3Scape videos will be measured using an instrument (8 items on a 5-point Likert scale and 4 open-ended questions) developed by the University of Calgary in a previous study on this technology.

Research Question 4

Interviews will be conducted for the therapists. Semistructured questions (topic guided) will examine the usefulness of 3Scape videos for the treatment of the mental health condition of older adults. Interviews will be audiotaped for later analysis by team members. To ensure anonymity, the older adults' and therapists' responses will not be connected to their identities. RA 2 will conduct the surveys. The administration of these measures will take approximately 15 minutes.

Research Question 5

The MBI-HSS MP will be administered to every therapist who provides the intervention to study the participants at the pretest and posttest. The administration of these measures will take approximately 20-30 minutes. RA 2 will administer these measures.

Data Analyses

Research Questions 1, 2, and 3

The analyses will be conducted in SPSS using intention-to-treat principles. Descriptive statistics will be used to characterize the

groups during the pretest. Owing to the small sample size, comparisons of the GAD-7, HoNOS, OPQoL-Brief, and PANAS scores within the groups will be performed using a Wilcoxon signed-rank test ($P \leq .05$), and comparisons between the groups will be calculated using the Mann–Whitney U test ($P \leq .05$). The GAD-7, HoNOS, OPQoL-Brief, and PANAS scores will be used to analyze the clinical significance, established as a change of 2 or more units [30]. Participants' engagement will be analyzed using descriptive statistics.

Research Question 4

The audiotapes will be transcribed and content analysis will be performed. The content analysis will be data driven. Data codes will be inductively generated using the data collected. Through the coding, a small number of themes or categories will be generated. The analyses will be performed by an RA, and a consensus in the interpretations will be achieved through a discussion among the research team members. The validity of the interpretations will be discussed with and agreed upon by every member of the research team. NVivo 10 software will be used to conduct data analysis.

Research Question 5

Descriptive statistics will be used to characterize the groups at pretest and posttest. Owing to the small sample size, comparisons of the MBI-HSS MP scores within the groups will be performed using a Wilcoxon signed-rank test ($P \leq .05$), and comparisons between the groups will be calculated using a Mann–Whitney U test ($P \leq .05$).

Ethics and Dissemination

Research Ethics Approval

All procedures were approved by the ethics committee of Alberta University and the Northern Alberta Clinical Trials Research Centre, Canada.

Incentives

The participants will not receive any incentive for participating in this study.

Withdrawal From the Study

The participants and substitute decision makers can request to withdraw from the study at any time either orally or in writing. The participants will be able to withdraw from the study at any time before the group analysis is calculated. If a participant withdraws, his or her information will not be taken into account in the analysis. In the event that a participant requests to have his or her data destroyed, the research team will honor this request by shredding and recycling the paper records and erasing any records stored on a computer hard drive using commercial software applications designed to remove all data from storage devices. However, once all of the participants' data have been analyzed, the participant cannot withdraw. The participants will be informed of this in a consent letter. The deadline for withdrawal will be once all of the participants' data have been collected and data analysis is underway. This will occur during the 8 months of the study.

Consent or Assent

Signed consent will be obtained from all participants in the study. For those who are unable to provide their informed consent, one of the therapist researcher (MKW), or another therapist involved in the recruitment process, will approach each potential participant and his or her substitute decision maker to provide information on the study. If these potential participants and their substitute decision makers provide their consent, the substitute decision makers will sign the consent form, and we will seek the potential participants' assent.

Confidentiality

We will assign numerical codes to the participants instead of using their names or other identifiers. Only the study coordinator will have access to the master list, where these codes are linked to the participants' first names. With the exception of direct conversations with each participant, their names will not be used, only their numbers. Hard copies of the consent forms, questionnaires, and study notes will be stored in a locked filing cabinet in a laboratory (Corbett Hall 1-45, Faculty of Rehabilitation Medicine, University of Alberta). All of the de-identified electronic study documents will be encrypted and stored on a password-protected computer located in a laboratory (Corbett Hall 1-45, Faculty of Rehabilitation Medicine, University of Alberta).

Access to Data

All PIs will be given access to the cleaned data sets. The master list will be stored on a password-protected computer, located in the PI's laboratory (Corbett Hall 1-45, Faculty of Rehabilitation Medicine, University of Alberta). Only the study coordinator will have access to the master list. The data will be retained for 5 years. There are no plans for future use of data other than publishing them in peer-reviewed journals and at conferences. The data will not become part of a data repository and will not be involved in the creation of a research database or registry for future research use. After 5 years, the data will be destroyed. This will be done by shredding the paper records. Records stored on a computer hard drive will be erased using commercial software applications designed to remove all data from storage devices.

Quality Assurance and Safety

We will follow the CONSORT guidelines for clinical trial feasibility [17]. In addition, we will assess the quality of our study using the Physiotherapy Evidence Database scale [19].

Results

The 3Scape study was launched in April 2020. As of August 2021, our study is on hold due to the COVID-19 pandemic. The recruitment process is expected to resume by November 2021, and the primary impact analysis is expected to be conducted by February 2022. This project is an excellent example of how industry and the health care system can support each other to grow and diversify Alberta's economy, and promote the entry of this valuable technology into the global rehabilitation market.

Discussion

Principal Findings

The primary objective of this proposed study is to assess the feasibility of conducting a definitive trial on the effectiveness of 3Scape technologies. The results of this project will inform the development of best practices for older adults with mental health conditions such as depression and anxiety, which affect as much as 6.3% of the population of older adults. Currently, our study is on hold because of the COVID-19 pandemic. The recruitment process is expected to resume by November 2020, and the primary impact analysis is expected to be conducted by February 2021.

The level of evidence that immersive technologies have an impact on older adults' mental health conditions and the burden of care is low. The 3Scape Systems Inc videos have the potential to become a sound alternative at the midpoint between these 2 extremes. 3Scape Systems has a technological readiness level of 9 [31], thus having a sufficient level of readiness that can be tested in a real-world clinical setting. This feasibility study is the first RCT to evaluate the potential benefits of 3Scape Systems. Conducting this RCT will provide valuable information. First, the estimates can be used for sample size calculations in future RCTs. Second, as we will measure the patients' outcome variables on 4 different occasions during the intervention, the results of this study will guide therapists on the expected percentage of a patient's improvement and how progress was achieved over a period of 10 weeks. The results of this project will provide them with information on the feasibility of adopting 3Scape Systems.

Conclusions

In conclusion, this study will provide valuable information such as the measurement of comparative intervention effects, perception of older adults and therapists about the 3Scape Systems, the associated costs of treatment, and product costings. This will contribute to the evidence planning process, which will be crucial for the future adoption of 3Scape Systems.

Acknowledgments

This study was supported by Glenrose Rehabilitation Hospital.

Authors' Contributions

AMC led the overall design of the evaluation; DR and MKW also contributed to the design. AMC drafted the manuscript, and DR, MKW, and AML edited and reviewed the manuscript. AMC is the PI of this evaluation.

Conflicts of Interest

None declared.

References

1. Mental Health and Chronic Diseases - Issue Brief No 2. Centers for Disease Control and Prevention. 2012. URL: https://www.cdc.gov/workplacehealthpromotion/tools-resources/pdfs/issue-brief-no-2-mental-health-and-chronic-disease.pdf [accessed 2021-08-16]
2. Canadian Institute for Health Information. Health System Resources for Mental Health and Addictions Care in Canada. Ottawa: Canadian Institute for Health Information; 2019.
3. Perceived mental health, by age group. Statistics Canada. 2020. URL: https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1310009603 [accessed 2021-08-16]
4. Mood disorders, by age group. Statistics Canada. 2020. URL: https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1310009618 [accessed 2021-08-16]
5. Changes in mood and behaviour. Alzheimer Society, Canada. URL: https://alzheimer.ca/en/Home/Living-with-dementia/Understanding-behaviour/Depression [accessed 2021-07-29]
6. O' Philbin L, Woods B, Farrell EM, Spector AE, Orrell M. Reminiscence therapy for dementia: an abridged Cochrane systematic review of the evidence from randomized controlled trials. Expert Rev Neurother 2018 Sep;18(9):715-727. [doi: 10.1080/14737175.2018.1509709] [Medline: 30092689]
7. Korte J, Bohlmeijer ET, Smit F. Prevention of depression and anxiety in later life: design of a randomized controlled trial for the clinical and economic evaluation of a life-review intervention. BMC Public Health 2009 Jul 20;9(1):250 [FREE Full text] [doi: 10.1186/1471-2458-9-250] [Medline: 19619284]
8. Franck L, Molyneux N, Parkinson L. Systematic review of interventions addressing social isolation and depression in aged care clients. Qual Life Res 2016 Jun;25(6):1395-1407. [doi: 10.1007/s11136-015-1197-y] [Medline: 26646806]
9. Lazar A, Thompson H, Demiris G. A systematic review of the use of technology for reminiscence therapy. Health Educ Behav 2014 Oct 01;41(1 Suppl):51-61 [FREE Full text] [doi: 10.1177/1090198114537067] [Medline: 25274711]
10. Bejan A, Gündogdu R, Butz K, Müller N, Kunze C, König P. Using multimedia information and communication technology (ICT) to provide added value to reminiscence therapy for people with dementia : lessons learned from three field studies. Z Gerontol Geriatr 2018 Jan;51(1):9-15. [doi: 10.1007/s00391-017-1347-7] [Medline: 29218401]

11. Laird EA, Ryan A, McCauley C, Bond RB, Mulvenna MD, Curran KJ, et al. Using mobile technology to provide personalized reminiscence for people living with dementia and their carers: appraisal of outcomes from a quasi-experimental study. JMIR Ment Health 2018 Sep 11;5(3):e57 [FREE Full text] [doi: 10.2196/mental.9684] [Medline: 30206053]
12. Westerhof GJ, Lamers SM, Postel MG, Bohlmeijer ET. Online therapy for depressive symptoms: an evaluation of counselor-led and peer-supported life review therapy. Gerontologist 2019 Jan 09;59(1):135-146. [doi: 10.1093/geront/gnx140] [Medline: 28961958]
13. Ibarra F, Baez M, Fiore F, Casati F. Designing for co-located and virtual social interactions in residential care. In: Proceedings of the 2018 ACM Conference Companion Publication on Designing Interactive Systems. 2018 Presented at: DIS '18: Designing Interactive Systems Conference 2018; June 9 - 13, 2018; Hong Kong China p. 129-134. [doi: 10.1145/3197391]
14. Lin CX, Lee C, Lally D, Coughlin J. Impact of virtual reality (VR) experience on older adults' well being. In: Zhou J, Salvendy G, editors. Human Aspects of IT for the Aged Population. Applications in Health, Assistance, and Entertainment. Cham: Springer; 2018:89-100.
15. 3Scape Systems. URL: https://www.3scapesystems.com/ [accessed 2021-07-29]
16. Clinical Studies. 3Scape Systems. 2021 Jul 28. URL: https://3scapesystems.com/clinical-studies [accessed 2021-07-28]
17. Eldridge SM, Chan CL, Campbell MJ, Bond CM, Hopewell S, Thabane L, PAFS consensus group. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. Br Med J 2016 Oct 24;355:i5239 [FREE Full text] [doi: 10.1136/bmj.i5239] [Medline: 27777223]
18. Bradshaw C, Atkinson S, Doody O. Employing a qualitative description approach in health care research. Glob Qual Nurs Res 2017;4:2333393617742282 [FREE Full text] [doi: 10.1177/2333393617742282] [Medline: 29204457]
19. Portney LG, Watkins MP. Foundations of Clinical Research: Applications to Practice. Third Edition. New Jersey: Prentice-Hall Inc; 2007:1-912.
20. Nasreddine Z, Phillips N, Chertkow H. MoCA Version 3. 2011. URL: http://thehub.utoronto.ca/family/wp-content/uploads/2016/12/MoCA-Instructions-English.pdf [accessed 2016-11-08]
21. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med 2006 May 22;166(10):1092-1097. [doi: 10.1001/archinte.166.10.1092] [Medline: 16717171]
22. Wing JK, Beevor AS, Curtis RH, Park SG, Hadden J, Burns A. Health of the Nation Outcome Scales (HoNOS). Research and development. Br J Psychiatry 1998 Jan 03;172(1):11-18. [doi: 10.1192/bjp.172.1.11] [Medline: 9534825]
23. Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect: the PANAS scales. J Pers Soc Psychol 1988 Jun;54(6):1063-1070. [Medline: 3397865]
24. Bowling A, Hankins M, Windle G, Bilotta C, Grant R. A short measure of quality of life in older age: the performance of the brief Older People's Quality of Life questionnaire (OPQOL-brief). Arch Gerontol Geriatr 2013;56(1):181-187. [doi: 10.1016/j.archger.2012.08.012] [Medline: 22999305]
25. Rincón RA, Miguel-Cruz A, Liu L, Stroulia E. Engagement during computer serious games: a rapid literature review. In: Proceedings of the 46th Annual Scientific and Educational Meeting of the CAG. Engagement During Computer Serious Games: A rapid literature review. Inth Annual ScientificEducational Meeting of the CAG; 2017 Presented at: 46th Annual Scientific and Educational Meeting of the CAG; October 19-21, 2017; Winnipeg, Manitoba. Canada.
26. Schaufeli W, Leiter M, Maslach C, Jackson S. The MBI-General Survey. In: Maslach C, Jackson S, Leiter M, editors. Maslach Burnout Inventory Manual. Palo Alto, CA: Consulting Psychologists Press; 1996.
27. Bowling A. The psychometric properties of the older people's quality of life questionnaire, compared with the and the WHOQOL-OLD. Curr Gerontol Geriatr Res 2009;2009:298950 [FREE Full text] [doi: 10.1155/2009/298950] [Medline: 20168974]
28. James M, Painter J, Buckingham B, Stewart MW. A review and update of the Health of the Nation Outcome Scales (HoNOS). BJPsych Bull 2018 Apr;42(2):63-68 [FREE Full text] [doi: 10.1192/bjb.2017.17] [Medline: 29502543]
29. Erdfelder E, Faul F, Buchner A. GPOWER: A general power analysis program. Behav Res Method Instrum Comput 1996 Mar;28(1):1-11. [doi: 10.3758/bf03203630]
30. Law M, Baptiste S, Carswell A, McColl M, Polatajko H, Pollock N. The Canadian Occupational Performance Measure. 3rd Edition. Ottawa: CAOT Publications ACE; 2000.
31. Technology Readiness Assessment Guide. U.S. Department of Energy, Washington, D.C. 2009. URL: https://www.directives.doe.gov/directives-documents/400-series/0413.3-EGuide-04/@@images/file [accessed 2021-08-16]

Abbreviations

CONSORT: Consolidated Standards of Reporting Trials
GAD-7: Generalized Anxiety Disorder-7 item
MBI-HSS MP: Maslach Burnout Inventory-Human Services Survey for Medical Personnel
OPQoL-Brief: Older People's Quality of Life-Brief
PANAS: Positive and Negative Affect Schedule
PI: principal investigator
RA: research assistant

RCT: randomized controlled trial

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Protocol

An Activity Tracker–Guided Physical Activity Program for Patients Undergoing Radiotherapy: Protocol for a Prospective Phase III Trial (OnkoFit I and II Trials)

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Abstract

Background: The positive impact that physical activity has on patients with cancer has been shown in several studies over recent years. However, supervised physical activity programs have several limitations, including costs and availability. Therefore, our study proposes a novel approach for the implementation of a patient-executed, activity tracker–guided exercise program to bridge this gap.

Objective: Our trial aims to investigate the impact that an activity tracker–guided, patient-executed exercise program for patients undergoing radiotherapy has on cancer-related fatigue, health-related quality of life, and preoperative health status.

Methods: Patients receiving postoperative radiotherapy for breast cancer (OnkoFit I trial) or neoadjuvant, definitive, or postoperative treatment for other types of solid tumors (OnkoFit II trial) will be randomized (1:1:1) into 3-arm studies. Target accrual is 201 patients in each trial (50 patients per year). After providing informed consent, patients will be randomized into a standard care arm (arm A) or 1 of 2 interventional arms (arms B and C). Patients in arms B and C will wear an activity tracker and record their daily step count in a diary. Patients in arm C will receive personalized weekly targets for their physical activity. No further instructions will be given to patients in arm B. The target daily step goals for patients in arm C will be adjusted weekly and will be increased by 10% of the average daily step count of the past week until they reach a maximum of 6000 steps per day. Patients in arm A will not be provided with an activity tracker. The primary end point of the OnkoFit I trial is cancer-related fatigue at 3 months after the completion of radiotherapy. This will be measured by the Functional Assessment of Chronic Illness

Therapy-Fatigue questionnaire. For the OnkoFit II trial, the primary end point is the overall quality of life, which will be assessed with the Functional Assessment of Cancer Therapy-General sum score at 6 months after treatment to allow for recovery after possible surgery. In parallel, blood samples from before, during, and after treatment will be collected in order to assess inflammatory markers.

Results: Recruitment for both trials started on August 1, 2020, and to date, 49 and 12 patients have been included in the OnkoFit I and OnkoFit II trials, respectively. Both trials were approved by the institutional review board prior to their initiation.

Conclusions: The OnkoFit trials test an innovative, personalized approach for the implementation of an activity tracker–guided training program for patients with cancer during radiotherapy. The program requires only a limited amount of resources.

Trial Registration: ClinicalTrials.gov NCT04506476; https://clinicaltrials.gov/ct2/show/NCT04506476. ClinicalTrials.gov NCT04517019; https://clinicaltrials.gov/ct2/show/NCT04517019.

International Registered Report Identifier (IRRID): DERR1-10.2196/28524

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KEYWORDS

cancer; fatigue; physical activity; quality of life; activity tracker; exercise program; radiotherapy; digital health

Introduction

Radiotherapy is a key treatment modality for the curative treatment of various tumor entities. Despite continuous technical improvements in facilitating increasingly precise dose delivery, side effects are inevitable in many cases [1]. Among patients with breast cancer, cancer-related fatigue (CRF) is the most frequent side effect reported during and after postoperative radiotherapy [2]. Among patients with other tumor sites that were treated with preoperative or definitive radiochemotherapy, CRF has also been frequently reported. However, local acute and late side effects of treatment can cause further impairments in health-related quality of life (HRQoL) [1]. In addition, sedentary behavior during preoperative radiotherapy can have a negative impact on the postoperative course of a patient (eg, in terms of recovery and wound complications). The beneficial effect that physical activity has on patients with cancer has been clearly established over recent years and is supported by many clinical studies [3-5]. Moreover, many international organizations have updated their recommendations to include exercise as an important part of cancer therapy (ie, exercise before, during, and after cancer therapy) [6-8]. Guidelines for the inclusion of exercise in oncologic treatments for patients with cancer have been published recently [9]. In this context, physical activity training can be implemented at different time points during treatment. The goal of prerehabilitation is to improve the fitness of patients prior to undergoing a major medical intervention, such as cancer surgery [10]. Faster recovery, fewer wound complications, and improved HRQoL have been exhibited by patients who have participated in a prerehabilitation program [11-13]. In patients with breast cancer, low levels of physical activity are associated with a 22% higher risk of breast cancer mortality [14]. Furthermore, a recent meta-analysis has shown that physical activity during oncological treatments is a highly effective measure for reducing CRF [15]. Additionally, in patients that survive cancer after oncological treatment, a higher level of physical activity is associated with improved HRQoL and, in some studies, even improved cancer-specific survival [14,16]. Although the pathomechanisms leading to CRF remain unclear to date, previous studies have suggested a close relationship between CRF and proinflammatory pathways, including pathways that lead to increases in levels of interleukins [17,18].

Activity trackers, which are also called *wearables*, have been used by a growing population to record physical activity and biodata, such as pulse and sleep patterns. Although fitness wristbands were initially considered purely as lifestyle products, in recent years, the scientific benefits of these products have increasingly come to the fore [17-19]. However, no prospective trials that include activity trackers as part of patients' radiotherapy have been conducted to assess these trackers' efficacy in reducing CRF and improving HRQoL.

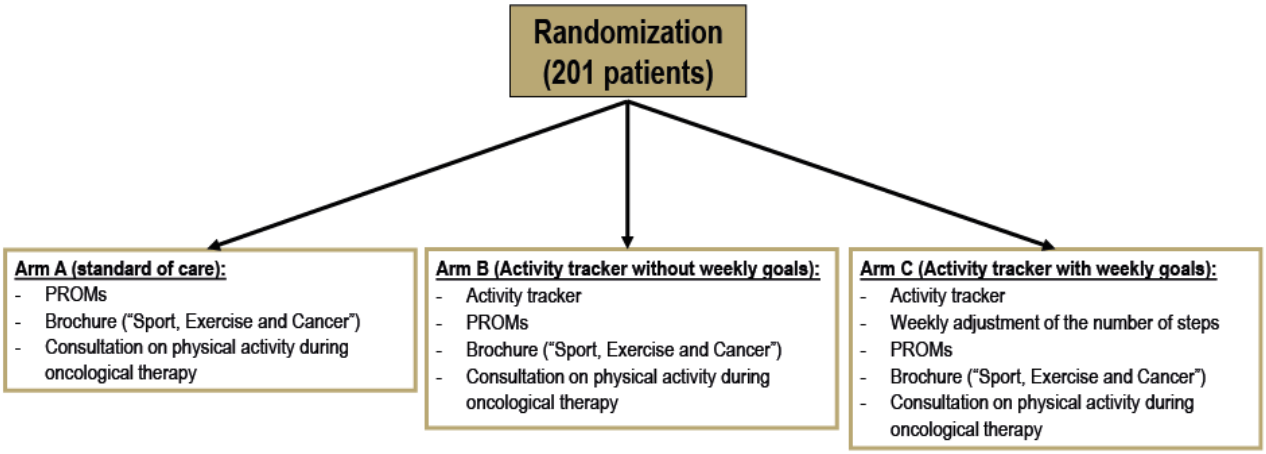
In the presented OnkoFit studies, we aim to investigate whether an activity tracker–based fitness program can reduce CRF and improve the quality of life and preoperative health status of patients undergoing radiotherapy.

Methods

Study Setting and Participants

The OnkoFit trials are two independent, single-center, randomized prospective phase III trials that have been certified by the working group radiological oncology of the German Cancer Society. After providing informed consent, patients will be randomized to a standard arm (arm A) or 1 of 2 interventional arms (arm B and C) in a 1:1:1 ratio (Figure 1). All patients will be recruited by the Department of Radiation Oncology at the University Hospital Tuebingen.

Figure 1. Overview of study arms of the OnkoFit I and OnkoFit II trials. In each study, patients will be randomized (1:1:1; 67 patients per arm) into the 3 arms after providing informed consent. PROM: patient-reported outcome measures.



The OnkoFit I trial is exclusively designed for patients with breast cancer, while the OnkoFit II trial is open to patients undergoing preoperative, definitive, or postoperative radiotherapy for various tumor sites. The separation of the tumor entities in two different trials allows for two different end points. Although the end point of the OnkoFit I trial—fatigue at 3 months after radiotherapy—has been evaluated in a pilot trial that was conducted in our department [2], it was determined that for patients undergoing neoadjuvant radiochemotherapy, this end point might be too early, especially for patients who undergo surgery after neoadjuvant radiochemotherapy.

A summary of key inclusion and exclusion criteria is provided in Textbox 1. We anticipate the recruitment of 50 patients per year in each trial. The course of the study is displayed in Figure 2.

Textbox 1. Inclusion and exclusion criteria of the OnkoFit trials.

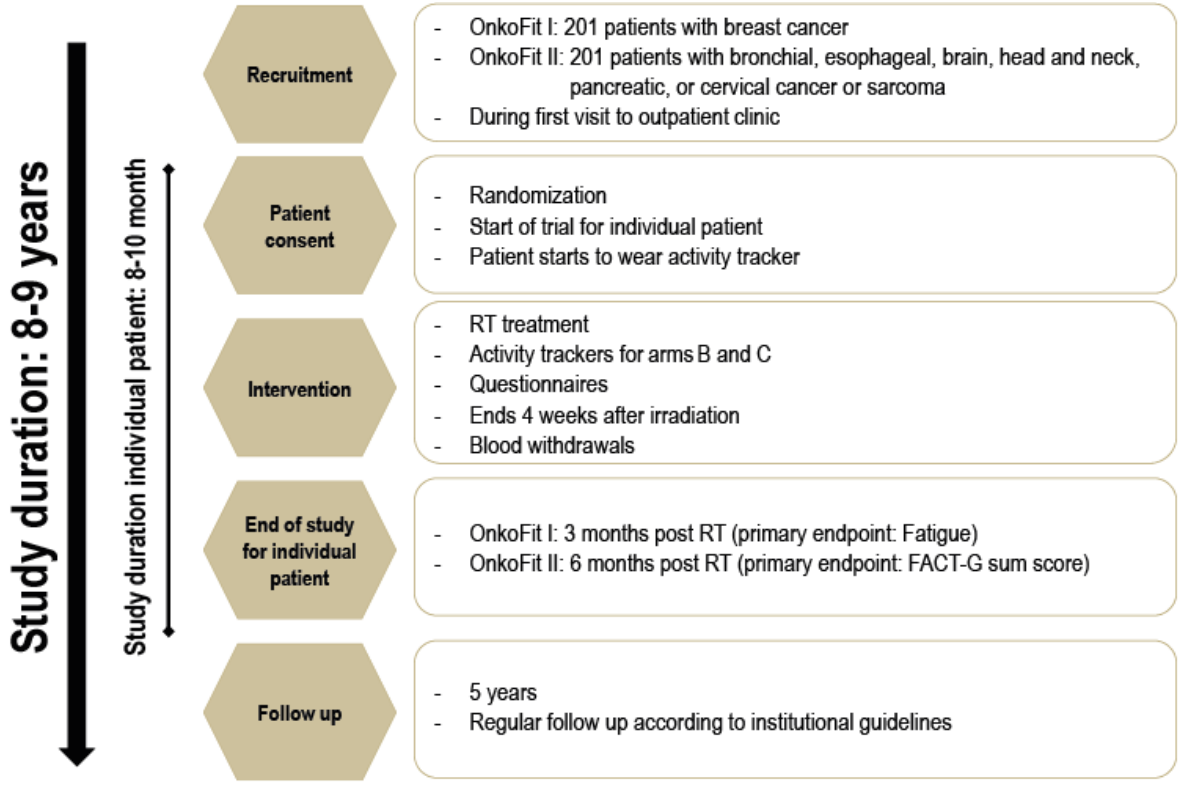
Inclusion criteria

- OnkoFit I trial
  - Informed consent
  - Age>18 years
  - Histologically confirmed breast cancer
  - Easter Cooperative Oncology Group score of 0-2
  - Indication for postoperative radiotherapy after breast-conserving surgery or mastectomy
- OnkoFit II trial
  - Informed consent
  - Age>18 years
  - Diagnosis of lung cancer, esophageal cancer, brain tumors, head and neck tumors, pancreatic cancer, rectal cancer, sarcoma, and uterus cervix cancer
  - Easter Cooperative Oncology Group score of 0-2
  - Indication for preoperative, definitive, or postoperative radiochemotherapy
  - Planned duration of treatment of at least 4 weeks

Exclusion criteria

- OnkoFit I trial
  - Participation in other interventional trials
  - History of using an activity tracker
  - Pregnancy
  - Recent cardiovascular events (stroke, myocardial infarction within the last 6 months, and a cardiac insufficiency New York Heart Association grade of >I)
  - Easter Cooperative Oncology Group score of 3-4
  - Comorbidities with impairments of mobility, such as paraplegia
- OnkoFit II trial
  - Participation in other interventional trials
  - History of using an activity tracker
  - Pregnancy
  - Recent cardiovascular events (stroke, myocardial infarction within the last 6 months, and a cardiac insufficiency New York Heart Association grade of >I)
  - Easter Cooperative Oncology Group score of 3-4
  - Comorbidities with impairments of mobility, such as paraplegia

Figure 2. Overview of the study design and expected duration. FACT-G: Functional Assessment of Cancer Therapy-General; RT: radiotherapy.



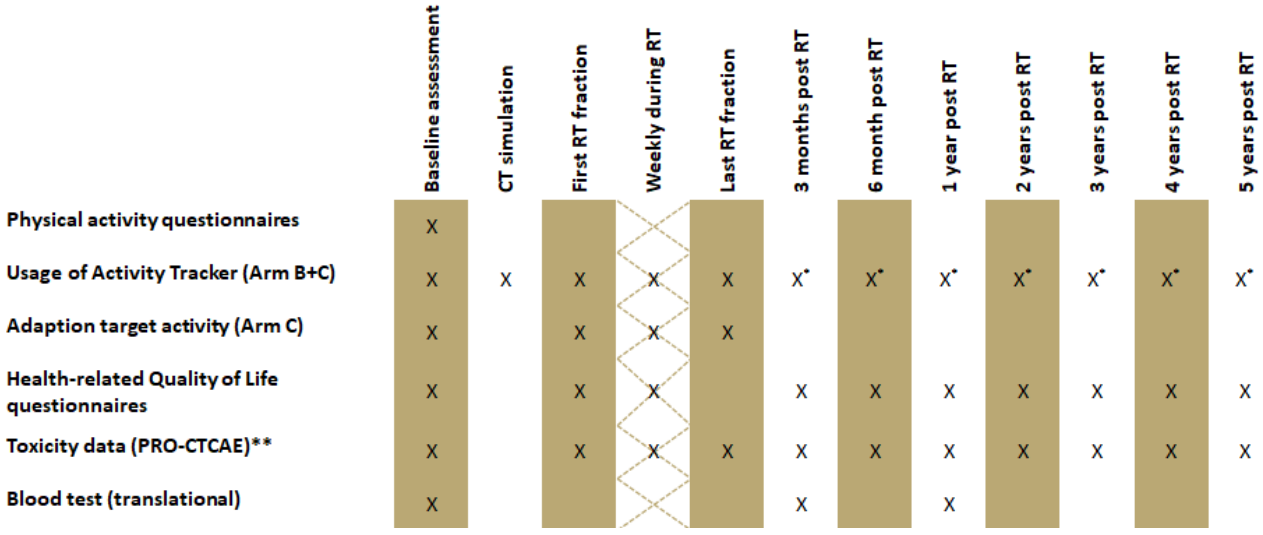
Treatment Groups and Interventions

After providing informed consent, patients will be included into either the OnkoFit I trial or OnkoFit II trial and randomized into 1 of the 3 arms of the studies (Figure 1). Both studies aim to include 201 subjects each.

Arm A: Standard of Care

In this arm, patients will be advised to conduct at least 1.5 hours of moderate physical activity or 75 minutes of strenuous physical activity per week. Patients will receive an educational patient brochure (written in the German language) about the rational and potential benefits of physical activity during cancer treatment. Activity trackers will not be provided to the patients (Figure 3).

Figure 3. Overview of the procedure plan and follow-ups for after radiotherapy. The quality-of-life questionnaires include the Patient Health Questionnaire-8, Functional Assessment of Cancer Therapy-Breast, Functional Assessment of Chronic Illness Therapy-Fatigue, and European Organisation for Research and Treatment of Cancer Quality of Life-Cancer 30 questionnaire. *The use of the activity tracker after intervention completion is based on patients' preferences. **PRO-CTCAE items were selected based on the anatomical region treated. PRO-CTCAE: Patient-Reported Outcomes Common Terminology Criteria for Adverse Events; RT: radiation therapy.



Arm B: Activity Tracker Without Weekly Goals

As in arm A, patients in arm B will be advised to conduct 1.5 hours of moderate physical activity or 75 minutes of strenuous physical activity per week and will receive the previously mentioned patient brochure. In addition, patients will be given an activity tracker. They will be instructed to wear it throughout the day and document the daily step count in a patient activity diary, which will be provided to each patient. No instructions will be provided with regard to daily or weekly goals for step counts (Figure 3).

Arm C: Activity Tracker With Weekly Goals

As in the other arms, patients will be counseled about conducting 1.5 hours of moderate physical activity or 75 minutes of strenuous exercise and will receive the patient brochure. The same activity tracker as that in arm B will be given to patients. However, in arm C, patients will receive weekly goals for their average step counts during treatment. The baseline step count will be assessed from the time of informed consent provision until the time of computed tomography simulation (computed tomography scans of patients will be taken prior to treatment to allow for radiation treatment planning). This period usually amounts to approximately 7 days. The patients will document daily step counts in a patient activity diary. At the time of computed tomography simulation, the mean daily step count will be calculated; this will constitute the basis for the upcoming week's goal for step counts. If the average step count is 6000 or higher, the new goal will be to not fall under this value. If the average step count is less than 6000, the new goal will be calculated by increasing the past week's step count average by 10%. If, for instance, the average step count is 3000 steps, the new target will be 3300 steps. The last change to the target step count will take place during the last week of radiotherapy. The highest possible target step count is 6000. This means that an average of 5800 steps in 1 week will result in a new goal of 6000 steps. We chose this 6000-step threshold based on a literature search we conducted, which suggested that a sedentary lifestyle is defined by threshold [16] (Figure 3).

In all arms, blood samples will be taken at baseline, at the end of radiotherapy, and at 6 months after the end of treatment. The activity trackers that will be used in this trial are commercially available accelerometers.

Clinical End Points and Instruments Used

OnkoFit I Trial

For the OnkoFit I trial, the primary end point will be fatigue, which will be scored according to the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) subscale. The end point will be assessed 3 months after the completion of radiotherapy. The FACIT-F questionnaire, which consists of 40 questions, was validated to assess fatigue in patients with cancer among our own patient cohort in a pilot project, which was conducted prior to the OnkoFit trials [2], as well as in many other studies [20,21]. The secondary end points will include treatment compliance, patient-reported acute and late toxicity, disease-free survival, and overall survival.

OnkoFit II Trial

For the OnkoFit II trial, the primary end point will be the overall HRQoL, which will be assessed by the Functional Assessment of Cancer Therapy-General sum score. This end point will be measured 6 months after the end of treatment in order to account for possible surgical interventions and possible recovery thereafter. In addition to the secondary end points listed for the OnkoFit I trial, we will assess the frequency of unplanned inpatient treatments for patients planned for ambulatory treatments and the frequency of postoperative complications (which will be assessed by using the Clavien-Dindo classification system) [22] in patients receiving preoperative radiotherapy.

Treatment-related toxicities will be scored by using the German translation of the Patient-Reported Outcomes Common Terminology Criteria for Adverse Events (PRO-CTCAE), which were developed by the National Cancer Institute. Briefly, the assessment of the severity and frequency of symptoms will be based on a 5-tier scale that ranges from "none" to "very severe" or from "never" to "almost always." Depending on the treated site (breast cancer: 8 questions; head and neck: 27 questions; thoracic and abdominal lesions: 21/24 questions; brain cancer: 20 questions; sarcoma: 14 questions), specific sets of questions were created. The patient-reported outcome measurement questionnaires for patients with head and neck cancer as well as patients with thoracic and abdominal tumor lesions have been used in our department [1]. The selection of PRO-CTCAE items was based on our long-term experience with the most frequent side effects that occur during and after radiotherapy for treated regions. Depression will be assessed with the Patient Health Questionnaire-8 [23,24]. In order to assess baseline fitness and sports activities, a questionnaire was developed in cooperation with the Department of Sports Medicine at the University Tuebingen. The questionnaire contains questions concerning the individual fitness histories and baseline activity levels of individual patients in the form of patient-reported outcome measurement–related questions. The questionnaire includes 18 questions and is based on the previous work of the Department of Sports Medicine at the University Tuebingen and other groups [25,26].

Translational Subproject

To further expand our knowledge on the possible pathomechanisms behind CRF and the potential effects that exercise has on the course and severity of CRF, blood samples will be taken from patients before radiotherapy, at the end of radiotherapy, and at 6 months after radiotherapy for the evaluation of inflammatory markers, such as neutrophil counts and interleukin-6 and C-reactive protein levels.

Follow-up

Based on patients' preferences, patients can keep the activity tracker after the completion of treatment. Independent of this decision, patients will be seen for follow-up at 3, 6, and 12 months after the completion of radiotherapy. Thereafter, follow-ups will take place yearly for up to 5 years.

Sample Size and Statistical Considerations

Previous studies were able to demonstrate a medium to high effect size with regard to the influence that physical activity has on the fatigue and HRQoL of patients with cancer. Based on a medium effect size (Cohen *f*=0.25) with an α error of 5% and a power of 80%, a one-way independent sample analysis of variance was conducted. Per the results of this analysis, 201 patients (67 patients per arm) will be recruited for each trial [27]. A dropout rate of 20% was assumed for the calculation of the number of patients. Randomization will be carried out via block randomization with variable block lengths.

Data Safety and Confidentiality

It will not be possible to record the position of patients in terms of their geographical location via the activity tracker. The clinical and personal data of patients will not be stored on the device. The assignment of the fitness trackers to the patients will be pseudonymized. The storage of fitness data and the linking of patient-related data will only be carried out within the hospital's information technology system. Therefore, these data will be subject to the hospital's data protection and data security regulations. For the purpose of publication, all data will be presented anonymously.

Results

Both studies have been approved by the Institutional Review Board of University Clinic Tuebingen (OnkoFit I trial reference number: 201/2020BO2; OnkoFit II trial reference number: 202/2020B02) and are registered on ClinicalTrials.gov (OnkoFit I trial number: NCT04506476; OnkoFit II trial number: NCT04517019). The recruitment of patients started on August 1, 2020. The results will be published in a peer-reviewed journal upon the completion of the trial. As of June 2021, we have recruited 49 patients in the OnkoFit I trial and 12 patients in the OnkoFit II trial. Per our recruitment plan, 50 patients are expected to be recruited in both OnkoFit I and OnkoFit II trials per year. The reasons for the more rapid recruitment in the OnkoFit I trial than in the OnkoFit II trial are manifold. One reason is the prioritization of the OnkoFit I trial over the OnkoFit II trial during the COVID-19 pandemic. Another reason is the decline of the number of patients who are eligible for the OnkoFit II trial during the pandemic. However, we expect that the recruitment rate in the OnkoFit II will accelerate soon.

Discussion

Trial Implications

The benefit of physical activity both during and after various kinds of cancer treatments has been shown in several randomized trials. Physical activity not only improves HRQoL but also has the capability to reduce the severity of negative treatment effects. With regard to patients undergoing radiotherapy, the feasibility and positive impact of combining radiotherapy with physical activity has been observed, and further clinical studies are currently being conducted (Exercise Therapy in Radiation Therapy [EXERT] trial; NCT03905356) [28]. However, measured variables as well as definitions of end points greatly vary between different studies on using activity trackers in cancer care, and there is a great need for randomized trials that clarify optimal time points as well as strategies [24]. The rationale behind the OnkoFit trials is to test a physical activity program that requires only few resources and is easy to implement even in the workflow of departments that treat a very large numbers of patients (≥1000 patients per year). Even though there is no doubt that a one-to-one supervised physical activity program that is conducted over several weeks would be desirable, this is often not feasible due to costs, limitations in geographical reach, and a lack of qualified personal [29]. Moreover, in a qualitative interview study conducted by Hardcastle et al [30], survivors of breast cancer expressed that they would favor home-based programs for exercise. The high acceptance of activity trackers among patients with cancer has been reported previously [31-33]. In our pilot study, which investigated the feasibility of continuous activity monitoring, 19 of 23 patients regularly used a commercially available activity tracker during radiotherapy. In the same study, we observed very plausible results regarding changes in physical activity during the course of treatment [33]. These results are also supported by a study conducted by Ohri et al [34], who showed a correlation between decreasing step counts and a forthcoming need for the inpatient treatment of patients with lung cancer during radiotherapy.

We see several advantages in an activity tracker–based training program. First, most activity tracker devices are easy to use and can be intuitively used by most older patients without any previous experience with such devices. Second, these devices provide real-time feedback to patients, which results in self-awareness and motivation. Third, the quantitative measures of physical activity levels can be remotely shared with caregivers, thereby providing an objective view on a patient's constitution and whether activity goals have been met [17]. The OnkoFit I and II trials have been designed as 3-arm trials. By introducing an arm in which patients receive an activity tracker but no predefined goals, we hope to study whether patients in the interventional arm, which provides weekly targets, actually have a higher level of physical activity and whether any potential effects that are observed at the end of the study are associated with the intervention.

Since acute and long-term side effects vary widely between patients with breast cancer undergoing radiotherapy and patients receiving preoperative or definitive radiotherapy, different end points were defined for the OnkoFit I and OnkoFit II trials. Additionally, the time points for assessment vary. In the OnkoFit II trial, the end point will be assessed 6 months after the end of radiotherapy and therefore later than in the OnkoFit I trial (the assessment will be conducted at 3 months), since patients receiving preoperative radiotherapy may still be in reconvalescence from surgery 3 months after the end of radiotherapy.

Patients undergoing radiochemotherapy in a neoadjuvant setting are at risk of increased side effects during and after concomitant surgery if they experience (severe) toxicity after the completion of radiation treatment. The concept of prehabilitation, which is defined as a rehabilitation program that is initiated before treatment, has gained more and more recognition in the field of oncology in recent years [35]. In two studies on colorectal

patients, a prehabilitation program markedly improved functional recovery after resection, thereby underscoring the program's potentially large benefit for patients [36,37]. In the context of neoadjuvant treatment, a study is currently underway for evaluating the effect that a concomitant prehabilitation program (conducted during chemotherapy) has on treatment outcomes and morbidity in patients with ovary cancer [38]. Similarly, another group has evaluated the effect that a prehabilitation program has on functional outcomes, particularly swallowing and the quality of life among patients undergoing radiochemotherapy for head and neck cancer [39]. Available data have been recently summarized by Squires and colleagues [40], with an emphasis on cardiovascular health after cancer therapy. In the context of the OnkoFit II trial, we aim to investigate whether the proposed fitness tracker–based exercise program can function as a prehabilitation program for patients undergoing neoadjuvant radiotherapy and thus decrease the number of postoperative complications.

One of the limitations of the proposed study is the lack of a supervised preintervention and postintervention fitness test (eg, ergometry), which would provide a more objective perspective on the fitness levels of patients than the fitness questionnaire—the one that will be used in our trials—alone. Furthermore, the trials were designed as monocenter trials that will be conducted at a single institution, which might limit the generalizability of the data.

Conclusion

The randomized OnkoFit I and II trials will investigate a unique approach to conducting a patient-executed fitness program during and after radiation therapy. In these trials, activity trackers will be used to improve HRQoL; reduce the severity of treatment side effects, including CRF; and improve the preoperative health status of patients. The findings of these trials will help to further our knowledge on combining exercise therapy with radiation treatment that focuses on the patient point of view.

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Conflicts of Interest

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References

1. Hauth F, Bizu V, App R, Lautenbacher H, Tenev A, Bitzer M, et al. Electronic patient-reported outcome measures in radiation oncology: Initial experience after workflow implementation. JMIR Mhealth Uhealth 2019 Jul 24;7(7):e12345 [FREE Full text] [doi: 10.2196/12345] [Medline: 31342906]
2. Hauth F, De-Colle C, Weidner N, Heinrich V, Zips D, Gani C. Quality of life and fatigue before and after radiotherapy in breast cancer patients. Strahlenther Onkol 2020 Nov 19:281-287. [doi: 10.1007/s00066-020-01700-1] [Medline: 33211138]
3. Janni W, Rack B, Friedl T, Müller V, Lorenz R, Rezai M. Abstract GS5-03: Lifestyle intervention and effect on disease-free survival in early breast cancer pts: Interim analysis from the randomized SUCCESS C study. In: Cancer Res. 2019 Presented at: 2018 San Antonio Breast Cancer Symposium; December 4-8, 2018; San Antonio, Texas. [doi: 10.1158/1538-7445.sabcs18-gs5-03]
4. Cannioto RA, Hutson A, Dighe S, McCann W, McCann SE, Zirpoli GR, et al. Physical activity before, during, and after chemotherapy for high-risk breast cancer: Relationships with survival. J Natl Cancer Inst 2021 Jan 04;113(1):54-63. [doi: 10.1093/jnci/djaa046] [Medline: 32239145]
5. McTiernan A, Friedenreich CM, Katzmarzyk PT, Powell KE, Macko R, Buchner D, 2018 Physical Activity Guidelines Advisory Committee. Physical activity in cancer prevention and survival: A systematic review. Med Sci Sports Exerc 2019 Jun;51(6):1252-1261 [FREE Full text] [doi: 10.1249/MSS.0000000000001937] [Medline: 31095082]
6. Campbell KL, Winters-Stone KM, Wiskemann J, May AM, Schwartz AL, Courneya KS, et al. Exercise guidelines for cancer survivors: Consensus statement from international multidisciplinary roundtable. Med Sci Sports Exerc 2019 Nov;51(11):2375-2390. [doi: 10.1249/MSS.0000000000002116] [Medline: 31626055]
7. Hayes SC, Newton RU, Spence RR, Galvão DA. The exercise and sports science Australia position statement: Exercise medicine in cancer management. J Sci Med Sport 2019 Nov;22(11):1175-1199 [FREE Full text] [doi: 10.1016/j.jsams.2019.05.003] [Medline: 31277921]
8. Schmitz KH, Courneya KS, Matthews C, Demark-Wahnefried W, Galvão DA, Pinto BM, et al. American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. Med Sci Sports Exerc 2010 Jul;42(7):1409-1426. [doi: 10.1249/MSS.0b013e3181e0c112] [Medline: 20559064]

9. Schmitz KH, Campbell AM, Stuiver MM, Pinto BM, Schwartz AL, Morris GS, et al. Exercise is medicine in oncology: Engaging clinicians to help patients move through cancer. CA Cancer J Clin 2019 Nov;69(6):468-484 [FREE Full text] [doi: 10.3322/caac.21579] [Medline: 31617590]
10. Carli F, Gillis C, Scheede-Bergdahl C. Promoting a culture of prehabilitation for the surgical cancer patient. Acta Oncol 2017 Feb;56(2):128-133. [doi: 10.1080/0284186X.2016.1266081] [Medline: 28067101]
11. Jianjun W, Xing W, Guozhong Y, Chuming Z, Jiang Y. Application of exercised-based pre-rehabilitation in perioperative period of patients with gastric cancer. Open Med (Wars) 2019;14:875-882 [FREE Full text] [doi: 10.1515/med-2019-0103] [Medline: 31844678]
12. Goh J, Ladiges WC. Exercise enhances wound healing and prevents cancer progression during aging by targeting macrophage polarity. Mech Ageing Dev 2014 Jul;139:41-48. [doi: 10.1016/j.mad.2014.06.004] [Medline: 24932991]
13. Dunne DFJ, Jack S, Jones RP, Jones L, Lythgoe DT, Malik HZ, et al. Randomized clinical trial of prehabilitation before planned liver resection. Br J Surg 2016 Apr;103(5):504-512. [doi: 10.1002/bjs.10096] [Medline: 26864728]
14. Nelson SH, Marinac CR, Patterson RE, Nechuta SJ, Flatt SW, Caan BJ, et al. Impact of very low physical activity, BMI, and comorbidities on mortality among breast cancer survivors. Breast Cancer Res Treat 2016 Feb;155(3):551-557 [FREE Full text] [doi: 10.1007/s10549-016-3694-2] [Medline: 26861056]
15. Mustian KM, Alfano CM, Heckler C, Kleckner AS, Kleckner IR, Leach CR, et al. Comparison of pharmaceutical, psychological, and exercise treatments for cancer-related fatigue: A meta-analysis. JAMA Oncol 2017 Jul 01;3(7):961-968 [FREE Full text] [doi: 10.1001/jamaoncol.2016.6914] [Medline: 28253393]
16. Balhareth A, Aldossary MY, McNamara D. Impact of physical activity and diet on colorectal cancer survivors' quality of life: a systematic review. World J Surg Oncol 2019 Aug 31;17(1):153 [FREE Full text] [doi: 10.1186/s12957-019-1697-2] [Medline: 31472677]
17. Brickwood K, Watson G, O'Brien J, Williams AD. Consumer-based wearable activity trackers increase physical activity participation: Systematic review and meta-analysis. JMIR Mhealth Uhealth 2019 Apr 12;7(4):e11819 [FREE Full text] [doi: 10.2196/11819] [Medline: 30977740]
18. Shin G, Jarrahi MH, Fei Y, Karami A, Gafinowitz N, Byun A, et al. Wearable activity trackers, accuracy, adoption, acceptance and health impact: A systematic literature review. J Biomed Inform 2019 May;93:103153. [doi: 10.1016/j.jbi.2019.103153] [Medline: 30910623]
19. Cheatham SW, Stull KR, Fantigrassi M, Motel I. The efficacy of wearable activity tracking technology as part of a weight loss program: a systematic review. J Sports Med Phys Fitness 2018 Apr;58(4):534-548. [doi: 10.23736/S0022-4707.17.07437-0] [Medline: 28488834]
20. Montgomery GH, David D, Kangas M, Green S, Sucala M, Bovbjerg DH, et al. Randomized controlled trial of a cognitive-behavioral therapy plus hypnosis intervention to control fatigue in patients undergoing radiotherapy for breast cancer. J Clin Oncol 2014 Feb 20;32(6):557-563 [FREE Full text] [doi: 10.1200/JCO.2013.49.3437] [Medline: 24419112]
21. Van Belle S, Paridaens R, Evers G, Kerger J, Bron D, Foubert J, et al. Comparison of proposed diagnostic criteria with FACT-F and VAS for cancer-related fatigue: proposal for use as a screening tool. Support Care Cancer 2005 Apr;13(4):246-254. [doi: 10.1007/s00520-004-0734-y] [Medline: 15549424]
22. Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, et al. The Clavien-Dindo classification of surgical complications: five-year experience. Ann Surg 2009 Aug;250(2):187-196. [doi: 10.1097/SLA.0b013e3181b13ca2] [Medline: 19638912]
23. Sweegers MG, Altenburg TM, Chinapaw MJ, Kalter J, Verdonck-de Leeuw IM, Courneya KS, et al. Which exercise prescriptions improve quality of life and physical function in patients with cancer during and following treatment? A systematic review and meta-analysis of randomised controlled trials. Br J Sports Med 2018 Apr;52(8):505-513. [doi: 10.1136/bjsports-2017-097891] [Medline: 28954800]
24. Beauchamp UL, Pappot H, Holländer-Mieritz C. The use of wearables in clinical trials during cancer treatment: Systematic review. JMIR Mhealth Uhealth 2020 Nov 11;8(11):e22006 [FREE Full text] [doi: 10.2196/22006] [Medline: 33174852]
25. Weis J, Bartsch HH. Die Erfassung tumorbedingter Fatigue: Übersicht über Messinstrumente und methodische Probleme. In: Weis J, Bartsch HH, editors. Fatigue bei Tumorpatienten: Prävalenz und Rehabilitationsbedarf. Basel: S. Karger AG; 2006.
26. Brehm W, Duan Y, Mair T, Strobl H, Tittlbach S. Körperlich-sportliche Aktivität als Gesundheitsverhalten: Methodenband; Forschungsprojekt in Kooperation zwischen dem Institut für Sportwissenschaft der Universität Bayreuth. Bayreuth: Universität Bayreuth/Institut für Sportwissenschaft; 2010.
27. Kessels E, Husson O, van der Feltz-Cornelis CM. The effect of exercise on cancer-related fatigue in cancer survivors: a systematic review and meta-analysis. Neuropsychiatr Dis Treat 2018;14:479-494 [FREE Full text] [doi: 10.2147/NDT.S150464] [Medline: 29445285]
28. Zaorsky N. Exercise therapy in radiation therapy (EXERT). ClinicalTrials.gov. URL: https://clinicaltrials.gov/ct2/show/NCT03905356?term=NCT03905356&draw=2&rank=1 [accessed 2021-08-05]
29. Hardcastle SJ, Maxwell-Smith C, Kamarova S, Lamb S, Millar L, Cohen PA. Factors influencing non-participation in an exercise program and attitudes towards physical activity amongst cancer survivors. Support Care Cancer 2018 Apr;26(4):1289-1295. [doi: 10.1007/s00520-017-3952-9] [Medline: 29090387]

30. Hardcastle SJ, Kane R, Chivers P, Hince D, Dean A, Higgs D, et al. Knowledge, attitudes, and practice of oncologists and oncology health care providers in promoting physical activity to cancer survivors: an international survey. Support Care Cancer 2018 Nov;26(11):3711-3719. [doi: 10.1007/s00520-018-4230-1] [Medline: 29740694]
31. Nguyen NH, Hadgraft NT, Moore MM, Rosenberg DE, Lynch C, Reeves MM, et al. A qualitative evaluation of breast cancer survivors' acceptance of and preferences for consumer wearable technology activity trackers. Support Care Cancer 2017 Nov;25(11):3375-3384. [doi: 10.1007/s00520-017-3756-y] [Medline: 28540402]
32. Champ CE, Ohri N, Klement RJ, Cantor M, Beriwal S, Glaser SM, et al. Assessing Changes in the Activity Levels of Breast Cancer Patients During Radiation Therapy. Clin Breast Cancer 2018 Feb;18(1):e1-e6. [doi: 10.1016/j.clbc.2017.08.009] [Medline: 28916400]
33. Gani C, Hauth F, Bizu V, Boeke S, Lautenbacher H, Zips D. Fitnesstracker in Radioonkologie – Ein nützliches Tool zur Identifikation von Patienten mit supportivmedizinischem Bedarf? Ergebnisse der GiRO-Fit Studie. 2019 Mar 8 Presented at: AGSMO Jahreskongress 2019 Supportive Therapie bei Krebs; March 15–16., 2019; Berlin p. 1-16. [doi: 10.1159/000497740]
34. Ohri N, Halmos B, Bodner WR, Cheng H, Guha C, Kalnicki S, et al. Daily step counts: A new prognostic factor in locally advanced non-small cell lung cancer? Int J Radiat Oncol Biol Phys 2019 Nov 15;105(4):745-751. [doi: 10.1016/j.ijrobp.2019.07.055] [Medline: 31398385]
35. Minnella EM, Carli F. Prehabilitation and functional recovery for colorectal cancer patients. Eur J Surg Oncol 2018 Jul;44(7):919-926. [doi: 10.1016/j.ejso.2018.04.016] [Medline: 29754828]
36. Li C, Carli F, Lee L, Charlebois P, Stein B, Liberman AS, et al. Impact of a trimodal prehabilitation program on functional recovery after colorectal cancer surgery: a pilot study. Surg Endosc 2013 Apr;27(4):1072-1082. [doi: 10.1007/s00464-012-2560-5] [Medline: 23052535]
37. Minnella EM, Bousquet-Dion G, Awasthi R, Scheede-Bergdahl C, Carli F. Multimodal prehabilitation improves functional capacity before and after colorectal surgery for cancer: a five-year research experience. Acta Oncol 2017 Feb;56(2):295-300. [doi: 10.1080/0284186X.2016.1268268] [Medline: 28079430]
38. Lambaudie E, Bannier/Braticevic C, Villaron/Goetgheluck C, Zemmour C, Boher J, Ben Soussan P, et al. TRAINING-Ovary 01 (connecTed pRehabiliAtIoN pelvIc caNcer surGery): multicenter randomized study comparing neoadjuvant chemotherapy for patients managed for ovarian cancer with or without a connected pre-habilitation program. Int J Gynecol Cancer 2020 Dec 01:920-924. [doi: 10.1136/ijgc-2020-002128] [Medline: 33262113]
39. Guillen-Sola A, Soler NB, Marco E, Pera-Cegarra O, Foro P. Effects of prophylactic swallowing exercises on dysphagia and quality of life in patients with head and neck cancer receiving (chemo) radiotherapy: the Redyor study, a protocol for a randomized clinical trial. Trials 2019 Aug 14;20(1):503 [FREE Full text] [doi: 10.1186/s13063-019-3587-x] [Medline: 31412947]
40. Squires RW, Shultz AM, Herrmann J. Exercise training and cardiovascular health in cancer patients. Curr Oncol Rep 2018 Mar 10;20(3):27. [doi: 10.1007/s11912-018-0681-2] [Medline: 29525828]

Abbreviations

CRF: cancer-related fatigue
EXERT: Exercise Therapy in Radiation Therapy
FACIT-F: Functional Assessment of Chronic Illness Therapy-Fatigue
HRQoL: health-related quality of life
PRO-CTCAE: Patient-Reported Outcomes Common Terminology Criteria for Adverse Events

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Protocol

Effectiveness of an Internet-Based Machine-Guided Stress Management Program Based on Cognitive Behavioral Therapy for Improving Depression Among Workers: Protocol for a Randomized Controlled Trial

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Abstract

Background: The effect of an unguided internet-based cognitive behavioral therapy (iCBT) stress management program on depression may be enhanced by applying artificial intelligence (AI) technologies to guide participants adopting the program.

Objective: The aim of this study is to describe a research protocol to investigate the effect of a newly developed iCBT stress management program adopting AI technologies on improving depression among healthy workers during the COVID-19 pandemic.

Methods: This study is a two-arm, parallel, randomized controlled trial. Participants (N=1400) will be recruited, and those who meet the inclusion criteria will be randomly allocated to the intervention or control (treatment as usual) group. A 6-week, six-module, internet-based stress management program, SMART-CBT, has been developed that includes machine-guided exercises to help participants acquire CBT skills, and it applies machine learning and deep learning technologies. The intervention group will participate in the program for 10 weeks. The primary outcome, depression, will be measured using the Beck Depression Inventory II at baseline and 3- and 6-month follow-ups. A mixed model repeated measures analysis will be used to test the intervention effect (group × time interactions) in the total sample (universal prevention) on an intention-to-treat basis.

Results: The study was at the stage of recruitment of participants at the time of submission. The data analysis related to the primary outcome will start in January 2022, and the results might be published in 2022 or 2023.

Conclusions: This is the first study to investigate the effectiveness of a fully automated machine-guided iCBT program for improving subthreshold depression among workers using a randomized controlled trial design. The study will explore the potential of a machine-guided stress management program that can be disseminated online to a large number of workers with minimal cost in the post–COVID-19 era.

Trial Registration: UMIN Clinical Trials Registry（UMIN-CTR) UMIN000043897; https://upload.umin.ac.jp/cgi-open-bin/ctr_e/ctr_view.cgi?recptno=R000050125

International Registered Report Identifier (IRRID): PRR1-10.2196/30305

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KEYWORDS

deep learning; unguided intervention; universal prevention; workplace; depression; machine learning

Introduction

Background

Both depressive disorders and subthreshold symptoms of depression are major public health problems because of the high prevalence of depression and its substantial impacts in terms of distress, disability, and impaired quality of life [1,2]. Depression is also a leading cause of productivity loss, such as impaired work performance and missed days at work, in the workplace [3]. The primary prevention of depression is important to improve quality of life and the human capital of companies or organizations and the whole society [4].

Internet-based (or web-based) online stress management programs that incorporate cognitive behavioral therapy (CBT) have been shown to be effective in reducing symptoms of depression and the risk of major depressive disorder among symptomatic groups [5,6], and in the general [7] and working population [8]. Such internet-based CBT (iCBT) programs are easy for people to access and can be delivered to a large number of people at a relatively low cost compared to face-to-face or group-based CBT programs. In particular, during a pandemic, such as COVID-19, a stress management program, which does not require face-to-face contact, is highly desirable.

However, previous reviews reported a clear difference in the effects of iCBT programs with and without therapist support [9,10]. The effect sizes for improving stress, depression, and anxiety of adults were moderate (Cohen *d*=0.61-0.64) for iCBT programs guided by therapists, in which mental health specialists, such as psychologists, help participants to learn CBT skills, for instance, by responding to their questions or providing feedback on their homework in the program. On the other hand, the effect sizes were smaller (Cohen *d*=0.25-0.33) for fully automated self-guided iCBT programs without therapist support [9,10]. Moreover, in the workplace, guided interventions showed better intervention effects on the symptoms of stress and depression than unguided interventions (Hedges *g*=0.39 and 0.34, respectively) [8]. In addition, unguided iCBT interventions may be effective in reducing depression in the short term (eg, 3 months), but they sometimes fail to show intermediate-term (eg, 6 months or longer) effects [11,12]. However, a guided iCBT program requires trained therapists and thus needs more financial and human resources than an unguided program. This might limit the dissemination and implementation of CBT programs in a low-resource setting, such as small enterprises and middle- and low-income countries [13].

Concerning the target population of interventions, interventions that focus on high-risk or symptomatic populations (selective and indicated interventions) often yielded greater effects than a universal intervention [14]. For instance, among web-based psychological interventions in the workplace, the effect sizes of web-based psychological interventions were larger for indicated interventions than for universal prevention interventions (Hedges *g*=0.52 and 0.25, respectively) [8]. However, the reduction in symptoms may last for a shorter duration for selective and indicated interventions compared to universal interventions [15]. Universal interventions also have an advantage in possessing a less stigmatizing nature than other interventions in the field of mental health [16]. Thus, universal preventive interventions are recognized as a potentially desirable approach [17]. If we successfully enhance the effectiveness of this approach, a universal prevention intervention would be a more promising approach for the prevention of depression in the community or workplace.

A possible strategy to improve the effect of a fully automated unguided iCBT program is to incorporate an automated function to support users' learning in an unguided program that is equivalent to therapist-guided ones by applying programmed interactions between a user and the system, for instance, individualized feedback regarding the assessment of stress and mental health status to the user, a step-by-step guide to develop the CBT skills of the user, suggestions regarding options available to the user, and advice on homework done by the user to improve his/her skills. Automated machine algorithms for these functions could be developed applying a machine-learning prediction based on a large data set, a scenario-based chatbot guide, and a deep learning technology to evaluate the appropriateness of a user's responses in his/her homework exercises. To date, no such "machine-guided" iCBT program has been tested for its effectiveness in alleviating depression among workers.

Objectives

To address these unresolved issues, our randomized controlled trial (RCT) aims at investigating the effectiveness of a fully automated machine-guided iCBT program supported by artificial intelligence (AI) technologies, called "SMART-CBT," for subthreshold symptoms of depression (the primary outcome) at 3- and 6-month follow-ups and for secondary outcomes (psychological distress, fear of COVID-19, and sick leave days at 3- and 6-month follow-ups, and major depressive episodes [MDEs] over a 12-month period) compared to treatment as usual (TAU). Participants will be healthy workers selected from the general working population (universal prevention). We hypothesize that this fully automated machine-guided program will improve the symptoms of depression compared with the control group, with an equal or greater effect size as in previous guided web-based psychological interventions at the 6-month follow-up (0.16-0.25) [8,18] in the total sample (universal prevention). We will also investigate the effect on depression among participants with subthreshold depression (indicated intervention).

Methods

Trial Design

The study will be a nonblinded, parallel, two-arm RCT with a single intervention group that will receive the SMART-CBT intervention and a control group that will receive TAU. The allocation ratio of the intervention group to the control group

is 1 to 1. Participants will be randomly allocated to either the intervention group or the control group after they have completed a baseline online questionnaire. Follow-up surveys will be conducted at 3, 6, and 12 months after the baseline measurement, using online questionnaires. The study protocol has been registered at the UMIN Clinical Trials Registry (UMIN-CTR; ID UMIN000043897). This protocol manuscript has been reported according to the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) guideline checklist [19].

Participants

The target population of this RCT will be healthy full-time workers from the general working population, because our intention is to develop a "generic" internet-based stress management program that is effective and can be disseminated to workers across industries and occupations. Full-time employees currently working in companies/organizations in Japan will be invited to participate in the study through an internet survey company (Macromill Inc). The inclusion criteria are as follows: (1) adult (age 20-60 years), (2) full-time employee, and (3) access to the internet via a PC, smartphone, or tablet. The exclusion criteria are as follows: (1) not on long-term sick leave or maternity/childcare leave or not temporally laid off at the time of recruitment, (2) no sick leave of 15 days or more in the past 3 months, (3) not receiving treatment from mental health professionals, (4) no MDE in the past month (based on the self-report Mini-International Neuropsychiatric Interview [MINI]), and (5) not a business owner, self-employed individual, freelancer, or part-time worker.

Procedure

Participants will be recruited from a pool of 300,000 people living in all 47 prefectures of Japan who registered with an online survey company. A clinical research coordinator (CRC) from the survey company will send an invitation to this population, with a description of the study's aim and procedure, and obtain online informed consent to participate in the study. We will recruit 1600 participants in total, including 200 males and 200 females in each of four age groups (20-29, 30-39, 40-49, and 50-60 years old). The CRC will ask those who agree to participate in the study to complete an online questionnaire for the baseline survey. We expect that at least 1400 individuals will be eligible based on the inclusion and exclusion criteria. These participants will be randomly allocated to either the intervention group (n=700) or the control group (n=700). Participants in the intervention group will be asked to use the intervention program for 6 weeks after the baseline survey, and they will be encouraged to revisit and review the program for an additional 4 weeks. Participants in the control group will be given a chance to receive the intervention program upon completion of the study. The participants in the intervention group will be given a token equivalent to JPY 1000 (USD 9.1) if they complete all modules of the program. The participants in the control group will be given a token equivalent to JPY 100 (USD 0.91). Participants in both groups will be given a token equivalent to JPY 30 (USD 0.27) for completing each of the surveys (baseline, and 3-, 6-, and 12-month follow-up surveys).

Intervention

The SMART-CBT program is a 6-week web-based training course to provide CBT stress management skills, accessed by using a URL through a PC or smartphone via the internet (Multimedia Appendix 1). We did not develop a special app for this program. The program is structured as six modules, with one module given per week. Each module consists of a lecture of about 10 minutes, followed by a module-specific exercise (Table 1). In addition, a seventh module (a lecture only) was developed to address coping with psychological stress due to the COVID-19 pandemic, considering that the study will be conducted while the pandemic is still ongoing. Unlike the other modules, participants may access this COVID-19–specific module any time after they start the program. Participants in the control group, as well as the intervention group, will be able to access in-house occupational health services or mental health services from an outside-company employee assistance program, through arrangements made by their companies (TAU condition).

Table 1. The structure and content of the machine-guided internet-based stress management program applying artificial intelligence technology based on cognitive behavioral therapy (SMART-CBT).

Module number	Module theme	Lecture (number of webpages)	Exercise (applied computational technologies)
Module 1	The stress model and its components	Concepts of stressors and stress reactions; specific examples of stressors and stress reactions (six pages)	Self-assessment of the levels of job stressors and psychological stress reactions (machine-learning predictions using linear and logistic regressions)
Module 2	The case formulation with the five-part model of CBT[a]	Five-part model of CBT; explanation of each component using a fictitious sample case (five pages)	To list components of the five-part CBT model based on own experience or a fictitious case (button-based bot and deep learning)
Module 3	Behavior activation and relaxation	Theory of behavior activation; practical tips to plan active behaviors; and breathing techniques for relaxation (five pages)	(1) To list candidate behaviors related to feeling better; (2) to select behaviors based on the effect and feasibility; and (3) to make a plan for behavior activation (button-based bot with a prefixed scenario)
Module 4	Cognitive restructuring: (1) awareness of the association between thoughts and mood	Theory of cognitive restructuring; understanding of the theory with two fictitious cases; schemas; and how to identify thoughts behind moods (five pages)	(1) To describe events, thoughts, and moods; and (2) to associate thoughts and moods (button-based bot and deep learning)
Module 5	Cognitive restructuring: (2) changing mood by balanced thinking	Finding evidence that supports the thought and that does not support the thought; creating balanced thinking; and monitoring changing mood (six pages)	(1) To describe events, thoughts, and moods; (2) to associate thoughts and moods; (3) to find evidence that supports the thought and that does not support the thought; (4) to create balanced thinking; and (5) to confirm improved mood (button-based bot and deep learning)
Module 6	Problem solving skills	Psychological theory of problem solving; problems finding and problems shaping; listing possible solutions; and review of the outcome of an implemented solution and improve the solution (eight pages)	N/A[b]
Module COVID-19 (accessible anytime)	Coping with stress due to COVID-19	Stress due to COVID-19 outbreaks; introduction of stress management techniques (behavioral activation and cognitive restructuring); keeping a healthy lifestyle; and seeking help if needed (four pages)	N/A

[a]CBT: cognitive behavioral therapy.

[b]N/A: not applicable; no exercise is available for the module.

Modules

Each of the six modules was developed for a specific learning goal as follows: the stress model and its components in Module 1; case formulation with the five-part model of CBT in Module 2 [20]; behavior activation in Module 3 [21,22], with a brief introduction to relaxation [23]; cognitive restructuring involving awareness of the association between thoughts and moods in Module 4; cognitive restructuring involving changing mood through balanced thinking in Module 5 [24,25]; and problem solving skills in Module 6 [26,27]. These topics are adopted from our previous iCBT stress management program [18]. A seventh module is included concerning stress and coping with stress due to COVID-19.

Lectures

Each lecture is text-based, consisting of six to seven pages including basic information about a topic, guided by a dialogue among a psychology counselor, a healthy employee as a client, and an AI avatar, Mr Smart, representing the system. No audio or video lecture is used. These lectures were developed based on our previous iCBT stress management program [18]. The lecture in the COVID-19 module consists of four pages providing information about stress profiles and lifestyle changes during the COVID-19 pandemic, and introduces basic skills for improving mental health and coping with stress due to the COVID-19 pandemic, including the possible usefulness of CBT-based approaches included in other modules of the program [28], a healthy lifestyle, and help seeking [29,30].

Exercises

A unique feature of the program is that it includes fully automated interactive exercises on the topic of each module, following the lecture, in order to facilitate participants' motivation to study, understand, and acquire skills relevant to the topic. Each exercise starts with a brief summary of the corresponding lecture, followed by automated interactive learning sequences guided by a predetermined scenario, linear regression prediction algorithm, or machine learning algorithm set up in the system. No exercise was prepared for Module 6 or the COVID-19 module.

Module 1 Exercise

For Module 1, after the lecture talks about the concepts and specific examples of job stressors, stress reactions, and long-term health outcomes, participants are asked to do a self-assessment of the levels of job stressors and psychological stress reactions. An 18-item questionnaire was developed that

includes six three-item scales measuring job demands, job control, supervisor support, coworker support, and positive (vigor) and negative (depression) emotions, adopting scales and items from an already established job stress questionnaire (the Brief Job Stress Questionnaire) [31]. Five of the scales are the same as the original scales; for the sixth, a depression scale was constructed by selecting three of the six original items that showed the highest factor loadings in a factor analysis of the original scale. First, criteria were created to roughly classify participants into five groups according to each scale score using the national norm data as follows: low (<5%), low-average (5%-24%), average (25%-74%), high-average (75%-95%), and high (>95%). These criteria will be used to inform a participant of his/her relative position in terms of each scale.

Job stressors and emotional reactions have been associated with poor levels of health [32] and work performance [33]. Job stressors may also have a spillover effect on family relationships [34] and a crossover effect on the well-being of a family member [35]. Informing participants of predictions regarding these possible outcomes of one's work and life based on the self-assessment may motivate participants to engage in the program or even reduce depression [36]. Data from a large 1-year follow-up online survey (n=2800, with a response rate of 68%) of full-time employees conducted between 2018 and 2019 was used to develop a prediction model based on the above six scales at baseline for achievement at work and personal life-related outcomes. The former was measured on a presenteeism item from the WHO Health and Work Performance Questionnaire (range 0-10) [37,38], an item simply asking about any successful event in the job (yes=1 or no=0), and an item asking whether there had been any troublesome events at work (yes=1 or no=0). Personal life–related outcome measures included items regarding subjective health status (excellent/good=1 or fair/poor=0), trouble in family relationships (yes=1 or no=0), poor relationship with family (yes=1 or no=0), and any undesirable event for a family member (yes=1 or no=0). The model was developed using linear or logistic regression to predict these outcomes at follow-up on the six scale scores, adjusting for sex and age at baseline. A sum of regression coefficients for the six scales that were statistically significant was used as an index to indicate work performance or the probability of each event 1 year later and was expressed on a 10-point scale. A personalized message will be displayed on the screen with these predictions to inform the participant what could happen in his/her work and personal life in the next year, based on the current levels of job stressors and emotional reactions.

Module 2 Exercise

For Module 2, which talks about the CBT case formulation, two sequential exercises have been prepared to inform participants about how to list each of the components of the five-part CBT model (event, thought, mood, behavior, and physical symptoms) [20]. In the first exercise, a case of an employee experiencing a stressful event at work is introduced. A participant is asked to classify 10 predetermined words related to the condition of this person into the most appropriate group for the four remaining components. The answer will be automatically scored (0-10 points), and he/she will be presented with another word, also with the correct answers. The participant will be encouraged to repeat this exercise until he/she scores 8 points or higher. In the second exercise, participants will be asked to fill in their own words for five boxes corresponding to the five components. Participants may do this based on their past experience or based on the case presented in the previous exercise. Once a participant completes the task, his/her responses will be automatically scored by an algorithm developed in terms of the accuracy of his/her responses.

For this module, the algorithm was developed by applying the long short-term memory (LSTM) model, one of the recurrent neural network (RNN) models that has feedback connections to deal with a series of pieces of information [39], such as a sentence including a set of words, to existing data. A large anonymous sample of 23,502 words or sentences reported for the five components by users of an online depression self-care program based on CBT was used (U2Plus, Cotree Co) [40]. The five LSTM algorithms for each component of CBT (event, thought, mood, behavior, and physical symptoms) judge whether the sentences in each box were correctly filled in. For creating supervised data, a total of 16 clinical psychologists rated each word or sentence if it included the five components according to the five-part CBT model [20]. The overall interrater reliability among the 16 clinical psychologists for the initial 1200 words/sentences was 87.3% (range 83.3%-91.3% among the pairs), and kappa was 0.714 (range 0.639-0.799 among the pairs).

For the development, validation, and evaluation of the deep learning algorithms, the supervised data were randomly divided into training data (80% of the data, N=18,801) and test data (20% of the data, N=4701), using the train_test_split from Scikit-learn. Next, the words/sentences in the training data were morphologically analyzed and counted by a Python program package, Janome [41], and the top 7500 words were coded into unique numbers. Other words were treated as out of vocabulary. The coded words were embedded into the LSTM algorithms. The sentence length was set to 20, and longer sentences were cut into multiple sentences with fewer than 20 words. Embedding size, hidden layer size, batch size, and the number of an epoch of learning were set to 32, 32, 512, and 50, respectively. A total of 20% of the training data was randomly selected and used for the validation process. Adam was adopted as an optimizer of the algorithms [42]. The learning rate was set to 0.0001. To avoid overfitting, 20% of the neural network was dropped out. Early stopping was implemented if the loss value for a given learning epoch was greater than the loss values for two previous consecutive epochs. After the validation process, the classification performance of the LSTM algorithms was tested for accuracy, sensitivity, and specificity, using the test data. The performance of the five LSTM algorithms ranged from 0.794 to 0.839 for accuracy, from 0.771 to 0.822 for sensitivity, and from 0.847 to 0.902 for specificity. All of the processes were implemented by Keras version 2.2.4 and TensorFlow version 1.14.0 in Python. An input by a participant to this exercise will be evaluated by the LSTM algorithm to be scored 0% to 100% and categorized into four groups using the sample data as a norm as follows: excellent (top 25%), good (the second 25%), moderate (25% below the average), or fair

(bottom 25%). A word or phrase is highlighted for attention if it is judged by the algorithm to not be in an appropriate place. In addition, tips for categorizing the four components in the appropriate group will be shown on the screen. A participant will be encouraged to redo the exercise if his/her score is not in the top 25% and strongly encouraged to do so if the score is in the bottom 25%.

Module 3 Exercise

In Module 3, which talks about behavior activation, there is an exercise in which a participant can practice planning behaviors that make him/her feel better, following the basic principle of the behavioral activation treatment . First, he/she is asked to type in a box on the screen behaviors that might make him/her feel better. A total of 128 popular behaviors that might make people feel better (eg, walking and listening to music) were collected from 12 clinical psychologists, with ratings of the degree of being easily executed and the possible effect on mood for each behavior. A total of 33 behaviors not recommended for behavioral activation (eg, drinking alcohol to excess, gambling, etc) were also collected. The aforementioned large online survey asked the 2800 respondents to rate whether each of the 128 behaviors would make them feel better. A total of 40 behaviors that were endorsed by 1% or more of the respondents for men or women were selected to be part of the recommended list, because of the high diversity of the responses. These behaviors were sorted by a sum of the ratings of the degree of being easily executed and the possible effect on mood by clinical psychologists.

The list is used to help a participant to list behaviors that might make him/her feel better in the first part of the exercise, taking into account the sex of the participant. Participants will be asked to select up to three behaviors that they would like to try. Each of these behaviors will be evaluated by using an algorithm to be recommended or discouraged. This algorithm compares an input word or phrase with words or phrases in the list of recommended behaviors or that of nonrecommended behaviors. If it matches, the algorithm will show a label of being "recommended" or "avoided" for that behavior [43]. In the latter case, a message will appear to suggest reconsidering engaging in that behavior. In the next step, participants will be asked to rate each behavior on the degree of ease of execution and its expected effect on their mood using a scale from 0 to 10, and then, the system will recommend the behavior with the highest sum scores the most. Based on their preferences and the recommendation from the system, participants will select one behavior to set up a behavior activation plan, such as the date and place to execute the behavior. They will be able to save the plan to the system, and come back to review it later. An additional option function will follow-up the adherence of participants to the plan. Following the date set up to carry out the plan, the system will ask participants if they have finished the plan and how their moods have been changed by it. Based on their responses, the system will provide the participants with automatically generated comments and advise them to continue the plan or change to another one.

Module 4 Exercise

In Module 4, which discusses cognitive restructuring (part 1) and awareness of the association between thoughts and moods, an exercise will help participants become aware of how their thoughts and moods are associated. This exercise starts with 10 questions on schemas that may underlie maladaptive ways of thinking (such as black or white thinking, overgeneralization, etc) [22]. Participants will be asked whether these schemas apply to their own thinking. The data will be stored in the system for later use. Like the second exercise of Module 2, in this exercise, participants will be asked to enter a stressful event or situation, thoughts, and moods (three of the five components of the CBT model) into corresponding boxes on the screen; they will be permitted to do this exercise either based on their own experience or by selecting one of five fictitious cases provided by the system, or using previous saved data that they created in the second exercise of Module 2. They will also be asked to rate the extent to which they feel each presented mood on a scale from 0 to 100. The responses in the three boxes will be automatically scored by an algorithm developed by the authors to assess its accuracy, with each one being scored 0% to 100%, and categorized into four quartile groups using the sample data as a norm. Participants will be encouraged to redo the input if their score is not in the top 25%. In the next step, they will be asked to select the most relevant thought and mood if there are multiple ones. In the final step, they will be asked to think about whether the selected thought and mood are associated, in other words, if the mood would change if the thought changes. If the participants confirm the association, the exercise ends. If not, the participants will be asked to go back to the selection of thoughts and moods and redo the exercise.

Module 5 Exercise

In Module 5, which discusses cognitive restructuring (part 2), that is, changing mood through balanced thinking, an exercise to cover all the steps of cognitive restructuring will be presented. Participants will be asked to (1) fill in events, thoughts, and moods; (2) select one thought that is most relevant to the mood; (3) review the association between the thought and mood; (4) describe evidence that supports the thought; (5) search for evidence that does not support the thought; and (6) engage in balanced thinking and monitor changes in mood. Steps 1 to 3 use the same components of the Module 4 exercise. In step 4, participants will be asked to enter reasons that they think the thought is true (ie, evidence that supports the thought), and indicate their degree of confidence for the reason. Then, they will be asked to enter evidence that does not support the thought, which is sometimes a hard step for people.

A system was developed to help participants be aware of evidence that does not support their thoughts in three ways. First, refer to a list of 12 patterns of evidence that does not support the thought, which was developed through extensive discussion by a group consisting of clinical psychologists, mental health researchers, and master's and doctoral students specializing in mental health, to classify patterns of 289 sets of evidence that does not support the thought extracted from data already collected from the five-part CBT case formulation reported by participants in a previous iCBT program [18]. Second, considering that the use of old sayings may help in

communicating therapeutic techniques with patients and bringing about cognitive reframing in CBT [44,45], refer to a selection of 50 well-known sayings rank-ordered by the frequency of endorsement for possible effects on improving mood or reducing stress calculated from data collected via an internet survey of full-time employees (N=4120), expecting that participants may find a new way of thinking beyond their schemas by studying the philosophy underlying the saying. Third, for schemes reported by participants in the Module 4 exercise, common tips to find evidence that does not support the thought are suggested by the system, which were developed through a discussion among clinical psychologists and mental health researchers. Once words or phrases of evidence that does not support the thought are entered, the participant is asked to rate the degree of confidence for each word or phrase, using a scale from 0 to 100.

The next screen shows all the information entered about the event, the thought, the list of moods, the evidence that supports the thought, and the evidence that does not support the thought. Then, the participants will be asked to create statements that reflect balanced thinking. Tips to help participants to create balanced thinking will be provided if they request them. They will also be able to ask the system to show a sample statement of balanced thinking, which will be created by automatically connecting a word/phrase of evidence that supports the thought and a word/phrase for evidence that does not support the thought, with the highest confidence rating.

In the final step of the exercise, after participants have created the statement of balanced thinking, they will be asked to rate their mood using a scale from 0 to 100. The system automatically detects changes in mood from those entered in the mood box before, and shows an “improvement” message when mood improves. Finally, participants will be asked to rate their overall mood change using a 4-point scale (a lot, to some extent, not much, and not at all). If they rate their mood change as a lot or to some extent, the exercise will end, with a suggestion to keep the statement of balanced thinking and use it in their daily life; otherwise, they will be encouraged to try again with other evidence that does not support the thought or with an alternative statement of balanced thinking.

Intervention Group

Participants in the intervention group will be invited to access and study the SMART-CBT program for 10 weeks in total (ie, a 6-week main study period followed by a 4-week review period) after the baseline survey. Participants in the intervention study may quit participating in or continuing the intervention solely based on their decision. During the first 6 weeks, the intervention group will be notified every Monday via email that a new module is available for the study. When participants do not complete a module by that Friday, they will receive an email reminder to encourage them to complete the module. After the initial 6 weeks, those who complete all six modules (except for the COVID-19 module) will receive a weekly email to encourage them to review the modules. If participants do not complete any module (other than the COVID-19 module), they will receive an email reminder to encourage them to review the modules. Ten weeks after the baseline survey, the intervention program will be closed.

Control Group

Participants in the control group will not receive any intervention program during the study period. Participants in both the intervention group and the control group will be able to use an internal occupational health service and/or employee assistance program service, depending on the policy of their workplace. Participants in the control group will be provided a chance to use the intervention program after the study period.

Outcomes

All outcomes will be measured by using online questionnaires. Nonrespondents will receive a reminder email from the research center to participate in the surveys. Outcome measures other than the occurrence of an MDE will be assessed at baseline and at two follow-up time points, 3 and 6 months after the baseline survey. MDEs will be assessed at baseline, and 6- and 12-month follow-ups. Table 2 provides an overview of the outcome measures for each survey.

Table 2. Outcomes to be evaluate in this study: measures and timing of measurement.

Outcome	Measure	Baseline (T1)	3-month follow-up (T2)	6-month follow-up (T3)	12-month follow-up (T4)
Primary outcome					
Depression	BDI-II[a]	Yes	Yes	Yes	No
Secondary outcomes					
Psychological distress	K6[b]	Yes	Yes	Yes	No
COVID-19 fear	Fear of COVID-19 Scale	Yes	Yes	Yes	No
The total number of sickness absence days in the past 3 months	An original item	Yes	Yes	Yes	No
Major depressive episodes[c]	MINI[d] depression section: self-report	Yes	No	Yes	Yes

[a]BDI-II: Beck Depression Inventory II.

[b]K6: Kessler psychological distress scale.

[c]While major depressive episodes will be measured at 6- and 12-month follow-ups, the information will be combined to create a variable for major depressive episodes during the 12-month follow-up.

[d]MINI: Mini-International Neuropsychiatric Interview.

Primary Outcomes

The primary outcomes of the study are depression and psychological distress at 3- and 6-month follow-ups. Depression will be measured with the Japanese version of Beck Depression Inventory II (BDI-II) [46,47], a 21-item self-report inventory of depressive symptoms in the past 2 weeks, with each item to be scored from 0 to 3. The total scale score will be calculated and used as a measure of the severity of depressive symptoms.

Secondary Outcomes

The secondary outcomes include psychological distress, fear of COVID-19, sickness absence days at 3- and 6-month follow-ups, and MDEs at the 12-month follow-up. Psychological distress will be measured with the Japanese version of Kessler's psychological distress scale (K6) [48,49], a six-item scale of psychological distress (depression and anxiety) in the past 30 days, with a response option range from 0 (none of the time) to 4 (all of the time). The total scale score will be used as an indicator of the degree of psychological distress. Fear of COVID-19 will be measured with the Japanese version of the Fear of COVID-19 Scale (FCV-19S) [50,51], which is a seven-item scale to measure fear reactions to the COVID-19 infection. Each item is rated on a 5-point scale (1-5), and the total score (7-35) will be used as the measure of the degree of fear of COVID-19. Sickness absence days in the past 3 months will be measured using the following single-item question [37]: "How many days did you miss an entire work day because of problems with your health during the past 3 months? (please include only days missed for issues with your own health, not someone else's health.)." The presence of a MDE will be measured with a self-report scale developed based on the MINI [52] according to the Diagnostic and Statistical Manual of Mental Disorders-5 criteria [53]. The same set of nine questions from the MDE section of the MINI will be used to assess whether a participant has had a MDE in the past 12 months, followed by questions on the onset and the most recent time the participant has had symptoms of a MDE in the past 12 months. The sensitivity and specificity of this instrument for the clinical diagnosis of major depression were reported as 0.86 and 0.67, respectively, in a sample of psychiatric outpatients (n=31) in a pilot study. The self-report MINI for MDEs will be measured at 6- and 12-month follow-ups, as well as at baseline. Combining participants' responses to these two follow-up surveys, any MDE reported after baseline and the timing of onset (number of months since baseline) will be used as the MDE outcome during the 12-month follow-up period.

Process Evaluation

Information on the usage of the intervention program by participants in the intervention group will be collected from the records of the program. Questions will be asked in the baseline and follow-up questionnaires to gather information about respondents' self-reported knowledge and self-efficacy regarding stress management in general, as well as the CBT components of the program (cognitive restructuring, behavioral activation, assertive communication, problem solving, and relaxation training) as follows: for knowledge, "how much knowledge do you have about…" and for self-efficacy, "how confident are you that you can do…," with a 5-point scale ranging from 0 (none) to 4 (enough) [18].

Implementation Outcomes

Implementation outcomes will be measured with the user version of the Implementation Outcome Scales for Digital Mental Health (iOSDMH) (unpublished study "Implementation Outcome Scales for Digital Mental Health (iOSDMH): a scale development and cross-sectional study" by Sasaki et al, 2021), a 19-item scale, with a 4-point Likert-type response option, as follows: three items for acceptability, four items for appropriateness, six items for feasibility, five items for harms, and one item for overall satisfaction. Participants in the intervention group will be asked

to complete the questionnaire online at the 3-month follow-up. Participants in the intervention group will also be asked additional questions regarding the reasons for not participating in the program or discontinuing the program if they do so.

Demographic and Other Characteristics

Demographic data, such as sex, age, education, marital status, occupation, type of employment contract, type of work shift, frequency of remote work (working from home), treatment of chronic physical conditions and mental disorders, and overtime hours during the past month, will be collected.

Sample Size Calculation

The required sample size was calculated for one of the outcome variables, ie, depressive symptoms assessed by BDI-II. Previous meta-analyses of web-based universal prevention psychological interventions for improving depression and anxiety in the workplace yielded a summary effect size of 0.25 [8]; our previous study of a guided universal prevention iCBT program among workers reported a smaller effect size on depression (d=0.16) at a 6-month follow-up [18]. To detect a minimal effect size of 0.15 at an alpha of .05 and a power of 0.80, the estimated sample size is 699 participants in each group. The statistical power was calculated using the G*Power 3 program [54].

Randomization

Participants who meet the inclusion criteria will be randomly allocated to the intervention or control group, as well as stratified into two groups based on BDI-II scores at baseline (≥14 or <14) [46]. An independent biostatistician will generate a stratified permuted block random table by using SAS (SAS Institute Inc). The stratified permuted-block random table will be password protected and blinded to the researchers, and sent to the CRC by an independent research assistant. The assignment will be conducted by the CRC.

Statistical Methods

Effectiveness of the Intervention

For the primary and secondary outcomes, except for MDEs, a mixed model analysis for repeated measures will be used to test the intervention effect (group × time interactions) for 3- and 6-month follow-ups in the total sample (universal prevention), on an intention-to-treat basis. This model will handle and impute missing data with restricted maximum likelihood estimation assuming missing values at random. Effect sizes (Cohen ds) and 95% CIs at 3- and 6-month follow-ups will be calculated among those who complete the baseline and follow-up surveys. For MDEs at the 12-month follow-up, a Cox proportional hazard model will be used to estimate the preventive effect of the intervention program on MDEs. All statistical analyses will be conducted using SPSS Statistics v26.0 (IBM Corp).

Subgroup Analysis

The effectiveness of the program may be greater for participants with depression at baseline. We will conduct similar mixed model analyses for the effectiveness of the program among a subgroup of symptoms of depression at baseline (with a BDI-II score of ≥14; indicated prevention).

Data Monitoring

A data and safety monitoring board will consist of a chair and two members, independent of the research team. The board will meet every 3 months after the first participants are randomized. The purpose of the meetings will be to review the report prepared by the CRC to monitor recruitment progress and data collection.

Ethical Considerations

The researchers carefully developed the aims, design, and specific procedures of the study, and submitted a research application to the Research Ethics Review Board of the Graduate School of Medicine/Faculty of Medicine, The University of Tokyo. The board approved the application after a careful review and an interview with the researchers (number 3083-(6)). Informed consent will be obtained by the CRC from all participants included in this study after full disclosure and explanation of the purpose and procedures of the study. Candidate participants will be informed that their participation is totally voluntary, that even after voluntarily participating they can withdraw from the study at any time without stating the reason, and that neither participation nor withdrawal will cause any advantage or disadvantage to them. We expect no adverse health effects from this intervention, except possibly slight deterioration in depressive/anxiety symptoms [11]. We will provide an emergency phone number and email address at the research office. A research assistant will deal with the emergency calls or emails first and then consult with the clinical supervisor (NK) to provide appropriate care.

Data Confidentiality

Participants will complete baseline and follow-up online questionnaires on a specially designed website. Researchers will not know any personally identifying information about them; only the CRC will know this information. Collected data from the questionnaires will be anonymized, linked, and stored in a password-locked file by the CRC and sent to the researchers at the University of Tokyo (NK, KW, KI, and NSasaki) for further analysis.

Results

At the time this paper was submitted, the study was at the stage of recruitment of participants. The analysis of data will begin in January 2022 for the outcome variables, expect MDEs, and in July 2022 for MDEs. We expect to publish the results in 2022 or 2023.

Discussion

Strength of the Study

The strength of this study is its investigation of the effectiveness of a fully automated machine-guided iCBT for improving the subthreshold symptoms of depression among workers using an RCT design. The machine-guided iCBT is designed to incorporate several functions that were achieved by therapist support in previous guided iCBT programs [18], but are achieved by applying regression models, a scenario-based chatbot, and deep-learning technologies. The machine-guided

supports would enhance the effects of an iCBT program on depression alleviation and other outcomes to a level equivalent to or greater than that for guided iCBT programs.

Exercises after lectures (or homework assignments) are an important part of CBT, and they help participants practice skill-based knowledge learned in the session [55]. The present machine-supported iCBT provides participants with opportunities to practice cognitive restructuring skills guided by the AI algorithm, instead of a therapist. More specifically, the algorithms will be used to train participants to correctly distinguish concepts of the five-part CBT model, such as events, thoughts, moods, physical symptoms, and behavioral reactions. Another important CBT component of the present iCBT program is behavior activation, where practicing skills in real life is important for improving negative mood [21,22]. In the exercise for Module 3, a step-by-step procedure guides participants to list candidate behaviors, reconsider avoidance behaviors, select behaviors for practice in real life, set up a behavioral activation plan, and review and revise the plan afterwards, just like a procedure taken by a therapist [43,56], where machine-guided functions help participants to complete each step. These functions would encourage participants to practice behavior activation skills more frequently and intensively compared to an unguided self-help iCBT program where participants only read instructions on how to make a behavior activation plan [57].

The other function included in the present iCBT program is self-assessment of work-related stressors and emotional states, which also gives participants future projections of work-related and personal life–related outcomes based on the results of the assessment (Module 1), using regression models developed based on a large database. This would not only help participants to understand the concepts of the components of a stress model, but also increase their awareness of their own stress levels and motivate them to engage in the program. This may enhance the effectiveness of the present iCBT program on depression alleviation by enhancing participants' engagement in the program [58] or through improved self-monitoring for stress [36].

Dissemination of the Findings

A fully automated machine-guided iCBT program requires less involvement of mental health specialists such as psychologists. It can be provided at a low cost in a low-resource setting in which trained practitioners are seldom available. Thus, the present fully automated machine-guided iCBT program has a lot of potential for dissemination as a practical tool for the prevention of depression in small- and middle-sized enterprises, and also in the workplace in low- and middle-income countries that do not have a well-organized training system for CBT counselors. Once we find the machine-guided iCBT sufficiently effective, it will contribute to the dissemination of a stress management program to a large number of workers to improve depression online at a low cost in the COVID-19 era where close social contact is limited.

The main findings of this study will be disseminated via publications in peer-reviewed international journals. Study findings will also be presented at scientific conferences. If the present program is found to be effective, a future plan to disseminate the program to a large number of workers in the workplace will be discussed with the government, nonprofit organizations, and corporations.

Limitations

The major weaknesses of this study include that the study will not directly compare the effect of the machine-guided iCBT with that of a therapist-guided iCBT. While we can compare the effect size obtained from this study with past ones (Cohen d=0.16 to 0.25) [8,18], the comparison may be biased by differences between the studies in terms of the characteristics of participants, timing of the study, and other situational factors. The other weakness is that the machine-guided program developed in this study is not fully featured in terms of AI technologies. For instance, the program does not have a function to conduct natural conversations between a user and the system; additionally, the program is programmed based on machine learning of big data, but once fixed, the program will not learn any more to optimize the algorithm. The other problem related to the study design is that we will test the effectiveness of the program in healthy full-time workers. Thus, the study will not provide evidence for part-time workers. The study will not consider differences in work-related characteristics and major sources of stress among occupations. However, the study will provide a preliminary, but necessary, step toward establishing a machine-guided iCBT approach for preventing depression.

Conclusion

This is the first study to investigate the effectiveness of a fully automated machine-guided iCBT program applying AI technologies for the improvement of the symptoms of depression among workers, using an RCT design. The study will explore the potential of the machine-guided stress management program that can be disseminated online to a large number of workers with minimal cost in the post–COVID-19 era.

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Authors' Contributions

NK and KI conceived and designed the experiments. NK, KI, KW, YS, NSasaki, and NSato developed the intervention program, and members of the SMART-CBT Team provided basic data for the machine learning and gave critical comments to improve the program. NK, KI, KW, and YS wrote the paper. All authors read and approved the final paper.

Conflicts of Interest

NK reports grants from Fujitsu Ltd and TAK Ltd, and personal fees from Occupational Health Foundation, Japan Dental Association, Sekisui Chemicals, Junpukai Health Care Center, and Osaka Chamber of Commerce and Industry, outside the submitted work.

Multimedia Appendix 1
Demonstration of the SMART-CBT program.
[MP4 File (MP4 Video), 25685 KB - resprot_v10i9e30305_app1.mp4]

References

1. GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet 2020 Oct 17;396(10258):1204-1222 [FREE Full text] [doi: 10.1016/S0140-6736(20)30925-9] [Medline: 33069326]
2. Depression and other common mental disorders: global health estimates. World Health Organization. 2017. URL: https://apps.who.int/iris/handle/10665/254610 [accessed 2021-09-05]
3. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med 2006 Nov;3(11):e442 [FREE Full text] [doi: 10.1371/journal.pmed.0030442] [Medline: 17132052]
4. Cuijpers P, Pineda BS, Quero S, Karyotaki E, Struijs SY, Figueroa CA, et al. Psychological interventions to prevent the onset of depressive disorders: A meta-analysis of randomized controlled trials. Clin Psychol Rev 2021 Feb;83:101955 [FREE Full text] [doi: 10.1016/j.cpr.2020.101955] [Medline: 33333441]
5. Donker T, Blankers M, Hedman E, Ljótsson B, Petrie K, Christensen H. Economic evaluations of Internet interventions for mental health: a systematic review. Psychol Med 2015 Dec;45(16):3357-3376. [doi: 10.1017/S0033291715001427] [Medline: 26235445]
6. Zhou T, Li X, Pei Y, Gao J, Kong J. Internet-based cognitive behavioural therapy for subthreshold depression: a systematic review and meta-analysis. BMC Psychiatry 2016 Oct 21;16(1):356 [FREE Full text] [doi: 10.1186/s12888-016-1061-9] [Medline: 27769266]
7. Buntrock C, Ebert DD, Lehr D, Smit F, Riper H, Berking M, et al. Effect of a Web-Based Guided Self-help Intervention for Prevention of Major Depression in Adults With Subthreshold Depression: A Randomized Clinical Trial. JAMA 2016 May 03;315(17):1854-1863. [doi: 10.1001/jama.2016.4326] [Medline: 27139058]
8. Carolan S, Harris PR, Cavanagh K. Improving Employee Well-Being and Effectiveness: Systematic Review and Meta-Analysis of Web-Based Psychological Interventions Delivered in the Workplace. J Med Internet Res 2017 Jul 26;19(7):e271 [FREE Full text] [doi: 10.2196/jmir.7583] [Medline: 28747293]
9. Andersson G, Cuijpers P. Internet-based and other computerized psychological treatments for adult depression: a meta-analysis. Cogn Behav Ther 2009;38(4):196-205. [doi: 10.1080/16506070903318960] [Medline: 20183695]
10. Heber E, Ebert DD, Lehr D, Cuijpers P, Berking M, Nobis S, et al. The Benefit of Web- and Computer-Based Interventions for Stress: A Systematic Review and Meta-Analysis. J Med Internet Res 2017 Feb 17;19(2):e32 [FREE Full text] [doi: 10.2196/jmir.5774] [Medline: 28213341]
11. Imamura K, Kawakami N, Tsuno K, Tsuchiya M, Shimada K, Namba K. Effects of web-based stress and depression literacy intervention on improving symptoms and knowledge of depression among workers: A randomized controlled trial. J Affect Disord 2016 Oct;203:30-37. [doi: 10.1016/j.jad.2016.05.045] [Medline: 27280960]
12. Imamura K, Tran TTT, Nguyen HT, Sasaki N, Kuribayashi K, Sakuraya A, et al. Effect of smartphone-based stress management programs on depression and anxiety of hospital nurses in Vietnam: a three-arm randomized controlled trial. Sci Rep 2021 May 31;11(1):11353 [FREE Full text] [doi: 10.1038/s41598-021-90320-5] [Medline: 34059737]
13. Fu Z, Burger H, Arjadi R, Bockting CLH. Effectiveness of digital psychological interventions for mental health problems in low-income and middle-income countries: a systematic review and meta-analysis. Lancet Psychiatry 2020 Oct;7(10):851-864 [FREE Full text] [doi: 10.1016/S2215-0366(20)30256-X] [Medline: 32866459]
14. Institute of Medicine (US) Committee on Prevention of Mental Disorders. In: Mrazek PJ, Haggerty RJ, editors. Reducing Risks for Mental Disorders: Frontiers for Preventive Intervention Research. Washington, DC: National Academies Press; 1994.
15. Offord DR. Selection of levels of prevention. Addict Behav 2000;25(6):833-842. [doi: 10.1016/s0306-4603(00)00132-5] [Medline: 11125774]

16. Stockings EA, Degenhardt L, Dobbins T, Lee YY, Erskine HE, Whiteford HA, et al. Preventing depression and anxiety in young people: a review of the joint efficacy of universal, selective and indicated prevention. Psychol Med 2016 Jan;46(1):11-26. [doi: 10.1017/S0033291715001725] [Medline: 26315536]
17. Tan L, Wang M, Modini M, Joyce S, Mykletun A, Christensen H, et al. Preventing the development of depression at work: a systematic review and meta-analysis of universal interventions in the workplace. BMC Med 2014 May 09;12:74 [FREE Full text] [doi: 10.1186/1741-7015-12-74] [Medline: 24886246]
18. Imamura K, Kawakami N, Furukawa TA, Matsuyama Y, Shimazu A, Umanodan R, et al. Effects of an Internet-based cognitive behavioral therapy (iCBT) program in Manga format on improving subthreshold depressive symptoms among healthy workers: a randomized controlled trial. PLoS One 2014;9(5):e97167 [FREE Full text] [doi: 10.1371/journal.pone.0097167] [Medline: 24844530]
19. Chan AW, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. Ann Intern Med 2013 Feb 05;158(3):200-207 [FREE Full text] [doi: 10.7326/0003-4819-158-3-201302050-00583] [Medline: 23295957]
20. Padesky CA, Greenberger D. Clinician's Guide to Mind Over Mood. New York, NY: Guilford Press; 1995.
21. Lewinsohn PM. The Coping with Depression Course: A Psychoeducational Intervention for Unipolar Depression. Eugene, OR: Castalia Publishing Co; 1984.
22. Beck AT. Cognitive Therapy of Depression. New York, NY: Guilford Press; 1979.
23. Richardson KM, Rothstein HR. Effects of occupational stress management intervention programs: a meta-analysis. J Occup Health Psychol 2008 Jan;13(1):69-93. [doi: 10.1037/1076-8998.13.1.69] [Medline: 18211170]
24. Ellis A. Humanistic Psychotherapy: The Rational-emotive Approach. New York, NY: Julian Press; 1973.
25. Ellis A, Harper R. A Guide to Rational Living. Chatsworth, CA: Wilshire Book Company; 1975.
26. Bell AC, D'Zurilla TJ. Problem-solving therapy for depression: a meta-analysis. Clin Psychol Rev 2009 Jun;29(4):348-353. [doi: 10.1016/j.cpr.2009.02.003] [Medline: 19299058]
27. D'Zurilla TJ, Goldfried MR. Problem solving and behavior modification. J Abnorm Psychol 1971 Aug;78(1):107-126. [doi: 10.1037/h0031360] [Medline: 4938262]
28. Serrano-Ripoll MJ, Meneses-Echavez JF, Ricci-Cabello I, Fraile-Navarro D, Fiol-deRoque MA, Pastor-Moreno G, et al. Impact of viral epidemic outbreaks on mental health of healthcare workers: a rapid systematic review and meta-analysis. J Affect Disord 2020 Dec 01;277:347-357 [FREE Full text] [doi: 10.1016/j.jad.2020.08.034] [Medline: 32861835]
29. Giorgi G, Lecca LI, Alessio F, Finstad GL, Bondanini G, Lulli LG, et al. COVID-19-Related Mental Health Effects in the Workplace: A Narrative Review. Int J Environ Res Public Health 2020 Oct 27;17(21) [FREE Full text] [doi: 10.3390/ijerph17217857] [Medline: 33120930]
30. Hamouche S. COVID-19 and employees' mental health: stressors, moderators and agenda for organizational actions. Emerald Open Res 2020 Apr 20;2:15. [doi: 10.35241/emeraldopenres.13550.1]
31. Inoue A, Kawakami N, Shimomitsu T, Tsutsumi A, Haratani T, Yoshikawa T, et al. Development of a short questionnaire to measure an extended set of job demands, job resources, and positive health outcomes: the new brief job stress questionnaire. Ind Health 2014;52(3):175-189 [FREE Full text] [doi: 10.2486/indhealth.2013-0185] [Medline: 24492763]
32. Psychosocial factors at work and their relation to health. World Health Organization. 1987. URL: https://apps.who.int/iris/handle/10665/40996 [accessed 2021-09-08]
33. Daniels K, Harris C. Work, psychological well-being and performance. Occup Med (Lond) 2000 Jul;50(5):304-309. [doi: 10.1093/occmed/50.5.304] [Medline: 10975125]
34. Repetti R, Wang SW. Effects of job stress on family relationships. Curr Opin Psychol 2017 Feb;13:15-18. [doi: 10.1016/j.copsyc.2016.03.010] [Medline: 28813286]
35. Demerouti E. The spillover and crossover of resources among partners: the role of work-self and family-self facilitation. J Occup Health Psychol 2012 Apr;17(2):184-195. [doi: 10.1037/a0026877] [Medline: 22308969]
36. Wang J, Eccles H, Nannarone M, Schmitz N, Patten S, Lashewicz B. Does providing personalized depression risk information lead to increased psychological distress and functional impairment? Results from a mixed-methods randomized controlled trial. Psychol Med 2020 Nov 04:1-9. [doi: 10.1017/S0033291720003955] [Medline: 33143794]
37. Kessler RC, Barber C, Beck A, Berglund P, Cleary PD, McKenas D, et al. The World Health Organization Health and Work Performance Questionnaire (HPQ). J Occup Environ Med 2003 Feb;45(2):156-174. [doi: 10.1097/01.jom.0000052967.43131.51] [Medline: 12625231]
38. Kawakami N, Inoue A, Tsuchiya M, Watanabe K, Imamura K, Iida M, et al. Construct validity and test-retest reliability of the World Mental Health Japan version of the World Health Organization Health and Work Performance Questionnaire Short Version: a preliminary study. Ind Health 2020 Aug 07;58(4):375-387 [FREE Full text] [doi: 10.2486/indhealth.2019-0090] [Medline: 32173661]
39. Sherstinsky A. Fundamentals of Recurrent Neural Network (RNN) and Long Short-Term Memory (LSTM) network. Physica D: Nonlinear Phenomena 2020 Mar;404:132306. [doi: 10.1016/j.physd.2019.132306]
40. U2plus. URL: https://u2plus.jp/ [accessed 2021-09-05]
41. Janome v0.4 documentation. Mocobeta GitHub. URL: https://mocobeta.github.io/janome/ [accessed 2021-09-05]
42. Adam: A Method for Stochastic Optimization. arXiv. 2014. URL: https://arxiv.org/abs/1412.6980 [accessed 2021-09-05]

43. Hopko DR, Lejuez CW, Ruggiero KJ, Eifert GH. Contemporary behavioral activation treatments for depression: procedures, principles, and progress. Clin Psychol Rev 2003 Oct;23(5):699-717. [doi: 10.1016/s0272-7358(03)00070-9] [Medline: 12971906]
44. Chui E. Synergy between Western Practice and Chinese Culture. Asia Pacific Journal of Social Work and Development 2004 Jun;14(1):51-64. [doi: 10.1080/21650993.2004.9755942]
45. Interian A, Allen LA, Gara MA, Escobar JI. A Pilot Study of Culturally Adapted Cognitive Behavior Therapy for Hispanics with Major Depression. Cognitive and Behavioral Practice 2008 Feb;15(1):67-75. [doi: 10.1016/j.cbpra.2006.12.002]
46. Beck A, Steer R, Brown G. Manual for the Beck Depression Inventory-II. San Antonio, TX: Psychological Corporation; 1996.
47. Hiroe T, Kojima M, Yamamoto I, Nojima S, Kinoshita Y, Hashimoto N, et al. Gradations of clinical severity and sensitivity to change assessed with the Beck Depression Inventory-II in Japanese patients with depression. Psychiatry Res 2005 Jun 30;135(3):229-235. [doi: 10.1016/j.psychres.2004.03.014] [Medline: 15996749]
48. Furukawa TA, Kawakami N, Saitoh M, Ono Y, Nakane Y, Nakamura Y, et al. The performance of the Japanese version of the K6 and K10 in the World Mental Health Survey Japan. Int J Methods Psychiatr Res 2008;17(3):152-158 [FREE Full text] [doi: 10.1002/mpr.257] [Medline: 18763695]
49. Kessler RC, Andrews G, Colpe LJ, Hiripi E, Mroczek DK, Normand SLT, et al. Short screening scales to monitor population prevalences and trends in non-specific psychological distress. Psychol Med 2002 Aug;32(6):959-976. [doi: 10.1017/s0033291702006074] [Medline: 12214795]
50. Ahorsu DK, Lin C, Imani V, Saffari M, Griffiths MD, Pakpour AH. The Fear of COVID-19 Scale: Development and Initial Validation. Int J Ment Health Addict 2020 Mar 27:1-9 [FREE Full text] [doi: 10.1007/s11469-020-00270-8] [Medline: 32226353]
51. Wakashima K, Asai K, Kobayashi D, Koiwa K, Kamoshida S, Sakuraba M. The Japanese version of the Fear of COVID-19 scale: Reliability, validity, and relation to coping behavior. PLoS One 2020;15(11):e0241958 [FREE Full text] [doi: 10.1371/journal.pone.0241958] [Medline: 33152038]
52. Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry 1998;59 Suppl 20:22-33;quiz 34. [Medline: 9881538]
53. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 5th Edition: DSM-5. Arlington, VA: American Psychiatric Publishing; 2013.
54. Faul F, Erdfelder E, Buchner A, Lang A. Statistical power analyses using G*Power 3.1: tests for correlation and regression analyses. Behav Res Methods 2009 Nov;41(4):1149-1160. [doi: 10.3758/BRM.41.4.1149] [Medline: 19897823]
55. Conklin LR, Curreri AJ, Farchione TJ, Barlow DH. Homework Compliance and Quality in Cognitive Behavioral Therapies for Anxiety Disorders and Obsessive-Compulsive Disorder. Behav Ther 2021 Jul;52(4):1008-1018. [doi: 10.1016/j.beth.2021.01.001] [Medline: 34134818]
56. Lejuez CW, Hopko DR, Hopko SD. A brief behavioral activation treatment for depression. Treatment manual. Behav Modif 2001 Apr;25(2):255-286. [doi: 10.1177/0145445501252005] [Medline: 11317637]
57. Cuijpers P, Schuurmans J. Self-help interventions for anxiety disorders: an overview. Curr Psychiatry Rep 2007 Aug;9(4):284-290. [doi: 10.1007/s11920-007-0034-6] [Medline: 17880859]
58. Donkin L, Christensen H, Naismith SL, Neal B, Hickie IB, Glozier N. A systematic review of the impact of adherence on the effectiveness of e-therapies. J Med Internet Res 2011 Aug 05;13(3):e52 [FREE Full text] [doi: 10.2196/jmir.1772] [Medline: 21821503]

Abbreviations

AI: artificial intelligence
BDI-II: Beck Depression Inventory II
CBT: cognitive behavioral therapy
CRC: clinical research coordinator
iCBT: internet-based cognitive behavioral therapy
LSTM: long short-term memory
MDE: major depressive episode
MINI: Mini-International Neuropsychiatric Interview
RCT: randomized controlled trial
TAU: treatment as usual

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Protocol

Promoting Adolescent Healthy Relationships (The About Us Program): Protocol for a Randomized Clinical Trial

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Abstract

Background: Romantic relationships play a critical role in adolescent development, and by middle adolescence, most young people have been involved in at least one romantic relationship, a context in which most sexual interactions occur. Research suggests adolescents lack positive models and skills related to building healthy relationships.

Objective: This project aims to test the impact of an innovative healthy relationships intervention, called About Us, implemented in school-based health centers (SBHCs) in California in a randomized controlled trial.

Methods: About Us is being tested using a 7-site, 2-group, parallel randomized controlled trial with a treatment versus control allocation ratio of 3:2 to assess the impact of the intervention relative to the standard of care among adolescents aged 14 to 18 years. Adolescents with active parental consent provide study assent at each of the 3 survey time points: baseline, 3 months postintervention, and 9 months postintervention. A stratified randomization procedure was used to ensure balance in key covariates and screening criteria across intervention groups. Through benchmark intent-to-treat analyses, we will examine the primary outcome of this study—the impact of About Us relative to the standard of care 9 months following the end of the intervention on the prevalence of vaginal or anal sex without condoms in the past 3 months. The secondary outcomes are four-fold: what is the impact of About Us relative to the standard of care 3 and 9 months following the end of the intervention, on (1) the prevalence of abstinence from vaginal or anal sex in the past 3 months, (2) composite scores of relationship communication and positive conflict resolution among participants involved in a relationship at baseline, (3) the prevalence of SBHC service use or information receipt in the past 3 months, and (4) composite scores of condom use intentions and attitudes regarding condoms and other birth control? Additionally, as part of our sensitivity analyses, two additional analyses will be implemented: modified intent-to-treat and complete case analysis.

Results: This project (ClinicalTrials.gov #NCT03736876) was funded in 2016 through the Family Youth Services Bureau as part of the Personal Responsibility Education Innovative Strategies program. Baseline data collection took place between February 2018 and March 2020, yielding a total of 5 cohorts and 533 study participants: 316 assigned to treatment and 217 assigned to control. Ongoing follow-up data collection continued through May 2021.

Conclusions: About Us draws on developmental science to create a contextually and developmentally relevant program that addresses motivation and emotional influences in sexual decision-making. The intervention was designed for implementation within SBHCs, an understudied venue for relationship and sexual health promotion interventions. Unfortunately, COVID-19 pandemic restrictions led to school closures, interrupting ongoing programming, and in-person follow-up data collection, which has affected study attrition.

Trial Registration: ClinicalTrials.gov NCT03736876; https://clinicaltrials.gov/ct2/show/NCT03736876
International Registered Report Identifier (IRRID): DERR1-10.2196/30499

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KEYWORDS

adolescents; youth; teens; healthy relationships; unintended pregnancy; teen pregnancy; sexually transmitted infections; sexually transmitted diseases; sexual health education; school-based health center; randomized controlled trial

Introduction

Background and Rationale

Romantic relationships play a critical role in adolescent development [1]. By middle adolescence, most young people have been involved in at least one romantic relationship [2], a context associated with greater odds of sexual intercourse [3] and in which most sexual interactions occur [4]. Research suggests adolescents lack positive models as well as norms and skills related to building healthy relationships [5]. Nonetheless, developmental psychologists emphasize that adolescence represents a new period in which past models of relationships may be reshaped, priming young people for healthier adult relationships [6]. Additionally, research suggests adolescents' views on relationships may be influenced by discussions with peers [7], highlighting the importance of promoting positive normative beliefs and sexual behavior within the context of relationships.

Opportunities for sexual experimentation and status attainment are often at the forefront of adolescents' initial views of romantic relationships [8], providing leverage points for interventions to guide adolescents in setting sexual boundaries and identifying potentially unsafe sexual situations. Accordingly, adolescents with experience in relationships are primed for prevention programs that address critical relationship skills, such as communication in intimate relationships and navigating different sexual boundaries. Using a targeted approach that involves identifying and engaging adolescents with increased vulnerabilities maximizes resources and prioritizes serving them. This project centers on promoting healthy relationships and expanding the typical prevention education foci in sexual health.

Focusing on romantic relationships aligns with developmental science underscoring the importance of relationships in adolescence. Because of continued disparities in sexually transmitted infections (STI) and unintended pregnancies in the United States, there remains a need for addressing pregnancy and disease prevention. Among adolescents aged 15 to 19 years, the teen birth rate declined 7% from 2017 to 2018, from 18.8 to 17.4 births per 1000; however, the teen birth rate remained approximately twice as high for Hispanic and Black teens compared to non-Hispanic White teens [9]. Additionally, 75% of teen pregnancies are unintended [10,11]. Further, rural counties observe higher teen birth rates compared to urban and suburban areas [12]. Very few evidence-based program models addressing sexual risk have been developed and tested with targeted populations, such as Hispanic adolescents or those residing in more rural areas [13,14].

Not all young people are at equal risk of experiencing an unplanned pregnancy or STI. Indeed, some contextual factors, such as experience with romantic relationships or even exposure to violence, place adolescents at greater risk for engaging in sexual activity, including unprotected (eg, condomless) sex that could lead to an unplanned pregnancy or STI. In addition, exposure to violence, both directly and indirectly, is associated with risky behaviors (eg, unprotected sex), lack of self-efficacy, anxiety, depression, challenges developing and maintaining healthy relationships with prosocial peers, and increased associations with peers who endorse unsafe norms and behaviors [5,15]. Estimates suggest that 60% of children and adolescents younger than 18 years have been exposed to at least one form of violence in the previous year [16], meaning these adolescents are at increased vulnerability for other poor outcomes.

Most existing evidence-based programs (EBPs) for adolescents are delivered in community-based settings or schools (eg, Making Proud Choices; Reducing the Risk) [17,18]. A few are delivered through health clinics (eg, Seventeen Days) [19], but none to our knowledge have been developed and tested expressly for implementation via school-based health centers (SBHCs). SBHCs are clinics initially created in response to adolescent health needs that operate on or near school campuses and provide a range of age-appropriate health-related services to adolescents. Today, most SBHCs also offer a comprehensive array of services, including primary care, mental health services, and health education. In most high school SBHCs, reproductive health is a core service [20]. As SBHCs become more common across the United States, the role SBHCs play in prevention and health promotion interventions will also grow in importance [21]. SBHCs are uniquely positioned, both physically and philosophically, to reach young people. SBHCs' location on or near a school campus offers easy access to large groups of adolescents. More importantly, however, SBHCs focus on building trust and meeting young people "where they are" developmentally. Thus, SBHCs offer a unique opportunity to deliver health interventions that integrate prevention education and clinical care [20].

This original paper outlines the rigorous evaluation of About Us, an innovative healthy relationships intervention implemented in SBHCs to reduce the prevalence of unprotected sex and promote stronger relationships among adolescents facing disparities in sexual health outcomes.

Intervention

Developed from a piloted intervention, About Us is an innovative healthy relationships intervention that promotes positive adolescent romantic relationships, condom use, and highly effective contraceptives if participants are having sex.

The program includes 10 lessons (2 lessons are 30-45 minutes long and 8 are 50 minutes long) that blend group-based activities with online activities implemented in a small group format with students in grades 9 or 10 who have parental consent and provide assent to participate.

About Us draws on the latest research on developmental neuroscience to shape content and strategies. Part of the innovative design of About Us stems from the use of positive youth development (PYD) principles and adolescent development literature as core elements that are foundational to the curriculum. PYD is a strength-based approach used to promote adolescents' prosocial competencies and skill-building related to their positive health and well-being [22]. The adolescent development literature, such as that reported by Collins [23], guides the relationship development content and helps ensure it is age-appropriate.

The program also draws on dual-process theories to address socioemotional well-being and cognitive influences on sexual decision-making [24]. For example, in a lesson on correct and consistent condom use, the program addresses adolescents' explicit intentions to use a condom during sexual intercourse and has them explore which circumstances might precipitate their decision to have sexual intercourse without condoms, prompting them to recognize and navigate these experiences to avoid condomless sex. Finally, the program draws from social cognitive theory [25], both in terms of key constructs in skill acquisition, such as building self-efficacy or confidence in one's ability to perform a behavior and shaping the process of learning through observational learning or modeling during instruction. Bandura [25] posited that self-efficacy is influenced in 4 ways: mastery experiences (successful completion of a task), modeling (observing others similar to oneself perform a task successfully), social persuasion (information from others that one can perform a task successfully), and physiological arousal states (information from one's physiological state, such as anxiety). The program draws on these strategies in the skills-based sessions to maximize its impact on self-efficacy. For example, to apply the concept of mastery experiences, the program includes role-play exercises in which adolescents practice in context (small groups and online) and receive feedback on their use of the skills.

Each About Us session includes an initial soap opera-like story to build interest and illustrate key concepts, 2-3 group-based activities with reflection, individual app-based work on computer tablets (to allow for personalization of the content), and a group-based debrief to reflect on the session and reinforce key messages. To maximize the relevancy of the content and strategies, we engaged adolescents in developing the About Us curriculum, and they contributed to its naming, cast of characters, and storylines.

For this study, the group-based content was delivered by trained facilitators (eg, health educators) from participating SBHCs. The app-based content was housed on a secure website and accessed through tablets with unique logins for each participant. Online activities were completed individually during each session (eg, completing a poll or watching and responding to a brief video). Several lessons also included homework activities that encouraged communication between students and a caring adult. Additional details of About Us are displayed in Table 1.

Participants assigned to the treatment group attended group sessions at the designated space. Health educators followed up with students who missed a session to engage them and remind them of the next session. Participants assigned to the treatment group received a US $30 incentive if they attended 6 or more sessions.

Table 1. About Us intervention components.

Component	Amount, duration, and intended dosage	Content	Who delivers	Setting
Group-based sessions	10 (2 prelessons and 8 regular lessons) over 4-9 weeks for a total of 10 hours of programming.	Characteristics of healthy and unhealthy relationships, communication skills (having difficult conversations, such as sexual consent, sexual boundaries, and condoms; using "I" statements); personal and sexual boundaries and sexual consent; condom and contraceptive use; influences on sexual decisions in relationships; ending relationships.	Trained health educators from the school-based health centers.	During school (students pulled out of class to come to the health center or other agreed-upon space on the school campus).
Online work during regular group-based sessions	Approximately 15 minutes in each regular lesson; students are able to revisit content from prior lessons outside of group sessions during the implementation period.	Same as above; online activities allow for the review and application of key concepts and the personalization of content for each lesson.	Trained health educators from the school-based health centers will prompt and support students using the tablets and the application during the group sessions.	Same as above.
Parent/other adult-adolescent homework	2 homework activities.	Brief conversation-based homework activities focused on healthy relationship values and influences related to sexual expectations in relationships.	Trained health educators "assign" homework activities as part of the group-based sessions; adolescents are asked to bring back a sign-off sheet acknowledging they completed the activity, which will be included in the implementation log.	These were assigned during the program implementation, but the setting for completion was out of school.

Study Objectives

The overall goal of this project is to test the impact of the About Us blended learning healthy relationships intervention, implemented in SBHCs in a randomized controlled trial (RCT), on reducing unintended pregnancies and STI in adolescents facing disparities in sexual health outcomes.

Research Questions and Hypotheses

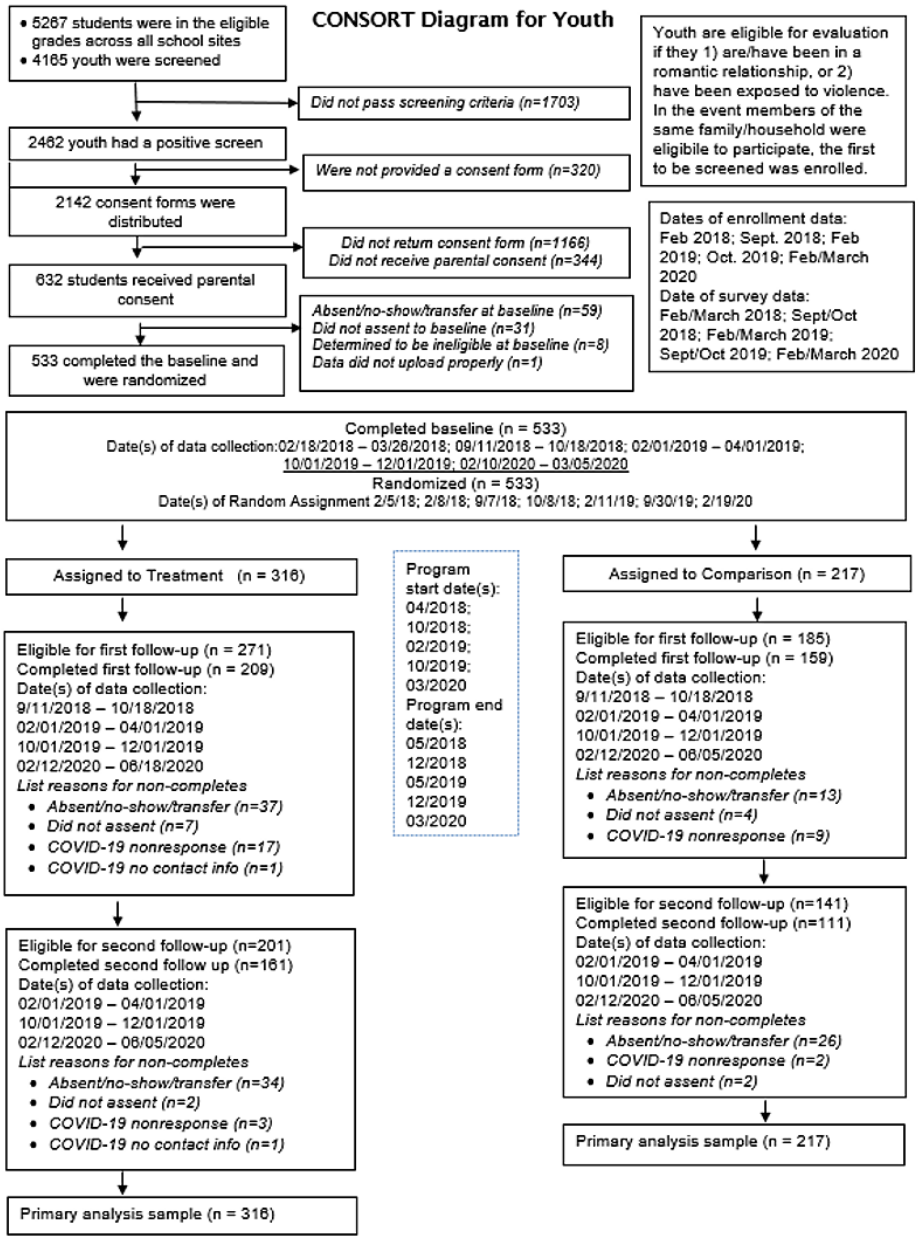
1. During the 9 months following the end of the program, what is the impact of About Us relative to the standard of care on the prevalence of vaginal or anal sex without condoms in the past 3 months? We hypothesize that at the final follow-up, the prevalence of self-reported unprotected vaginal or anal sexual intercourse (ie, without condoms) in the past 3 months will be lower among adolescents in the intervention group than students in the control group.
2. During the 3 months and 9 months following the end of the program, what is the impact of About Us relative to the standard of care on (1) the prevalence of abstinence from vaginal or anal sex in the past 3 months, (2) composite scores of relationship communication and positive conflict resolution among participants involved in a relationship at baseline, (3) the prevalence of school-based health center service use or information receipt in the past 3 months, and (4) composite scores of condom use intentions and attitudes regarding condoms and other birth control? At each follow-up, we hypothesize that, compared to the control group, students in the intervention condition will have: (1) a higher prevalence of sexual abstinence in the past 3 months, (2) higher composite scores showing stronger relationship communication and more positive conflict resolution (3) a higher prevalence of SBHC services utilization or information receipt, and (4) higher composite scores showing stronger intentions and more positive attitudes regarding condom use and other forms of birth control.

Methods

Study Design Overview

This study is a 7-site, 2-group, parallel RCT with a treatment versus control allocation ratio of 3:2, assessing the impact of the About Us program relative to the standard of care among adolescents aged 14 to 18 years. Figure 1 summarizes study screening, eligibility assessments, enrollment, randomization, and follow-up results.

Figure 1. CONSORT diagram for the About Us evaluation (as of October 2020).



Study Funding and Ethics Approval

This study was funded in 2016 through the Family Youth Services Bureau (FYSB) as part of the Personal Responsibility Education Innovative Strategies (PREIS) program as an award to ETR. This project was approved by the San Diego State University (SDSU) institutional review board (IRB) in March 2017. In June 2020, Indiana University approved an IRB reliance (protocol 2004100675) on the SDSU IRB approval (protocol HS-2017-0121). The study is registered with clinicaltrials.gov (NCT03736876).

Study Setting

This project was implemented in 7 SBHCs in rural or suburban communities throughout California with large Hispanic populations. The California School-Based Health Alliance (CSHA) assisted the About Us project team in recruiting participating sites and supporting the clinic screening process used as part of assessing eligibility. The CSHA supports the entire network of SBHCs in California.

Eligibility Criteria

Students in the 9th and 10th grades between the ages of 14 and 18 years were eligible to participate if they met at least one of two eligibility criteria: (1) had ever witnessed a serious injury or homicide or (2) had a girlfriend, boyfriend, or partner before or during the study consent process (prior or current experience with a romantic relationship). In addition, a student would be considered ineligible if a sibling or step-sibling had already enrolled in the study to avoid contaminating participants in different conditions.

Recruitment

Power Analyses

For a statistical power of 80%, to detect a 9% difference (effect size: prevalence ratio=0.74, 95% CI 0.60-0.91 equivalent to an

odds ratio [OR] of 0.65 or Cohen's *d*=0.24) in the prevalence of condomless sex at 9 months between intervention and control group participants with an allocation ratio of 3:2, we needed to have a sample size of 508 and 339 subjects in the intervention and control groups, respectively, based on a simple two-tailed proportion difference test at a Type I error of 5%.

We selected a minimum detectable effect of Cohen's *d*=0.2. The rationale for this selection is two-fold: (1) in our R21 pilot test of a less robust version of the About Us curriculum with a very small (<100) sample, we achieved an estimated effect size of *d*=0.15 for our unprotected sex outcome, and (2) in a meta-analysis of group-based pregnancy or STI interventions, the average effect size across multiple studies was OR 0.70, which corresponds to a small Cohen's *d*=0.19 [26,27].

Screening

Study sites administered a grade-wide or school-wide screening questionnaire to assess adolescents' exposure to violence and relationship status (two of the eligibility criteria noted above). For screening, sites used a variety of customized approaches based on their school protocols. All of the sites opted to include additional items on their screening questionnaires to learn more about the general health and well-being of 9th or 10th grade students (eg, "Do you have a primary doctor?" or "Do you eat fruits and vegetables daily?").

Consent and Assent Process

Per California law, we sought active parental consent for study participation through either a signed copy of the consent form or verbal confirmation via telephone calls (by research staff) when there was a parent signature, but the permission checkmark was ambiguous. Consent forms were available in both English and Spanish. The consent process began in one of two ways: (1) either an in-class presentation about the study was delivered by an SBHC representative or (2) students who met the screening criteria were sent invitations through a required class at school to attend an informational event, where, if interested, they received more information about the study, and parental consent forms were distributed. A single high school differed from other sites in that it provided consent forms to students ahead of the screening procedure. Students were informed that they would receive a US $10 incentive for returning a parental consent form regardless of their parent's decision. They were directed to return parental consent forms to their respective SBHC.

For students whose parents provided study consent and met the screening criteria, site liaisons compiled an eligibility log with the following data: student's last name, first name, and middle initial; student ID (optional); student's sex assigned at birth; student's reported gender identity; the number of screening criteria met (selected from a dropdown menu); school (selected from a dropdown menu); agency (selected from a dropdown menu); whether students have a sibling or step-sibling at the school; and whether that sibling participated in About Us in the past (criterion for exclusion). Evaluation data collectors (EDCs) used this log onsite to determine which students were fully eligible for the assent process.

The study's EDCs administered the study assent process on the day of the baseline survey administration at a given site. At the time of assent, prospective participants of consenting parents who met all the other eligibility criteria and agreed to study participation were enrolled in the study.

Baseline Data Collection

At the time of assent and prior to randomization, adolescents completed the baseline survey on a self-administered tablet device via the Qualtrics Offline Surveys application (version 1.4.06) [28]. Following survey administration, EDCs promptly uploaded responses to the QualtricsXM server as soon as a secure internet connection could be achieved. EDCs were provided Verizon Jetpack MiFi devices (7730L and 8800L) for this purpose.

Participants were enrolled and completed baseline surveys on a rolling basis during the spring and fall semesters of 2018 and 2019 and spring of 2020. The targeted enrollment was approximately 173 students per site over 5 semesters (34 to 35 students per semester) for a total of 865 students.

At the completion of baseline surveys for a given cohort at a given site, the EDCs submitted a baseline survey administration log to the evaluation project manager for review and transferred data to the evaluation statistician for randomization into either About Us (intervention) or standard of care (control).

Baseline data collection consisted of two separate instruments: a computer tablet-based survey designed to capture adolescent knowledge, attitudes, and experiences regarding sexual behavior, contraception, STI, and HIV/AIDS; and a brief survey that collected contact information for study follow-up purposes. EDCs were selected and trained by the evaluation team to represent the study in the local communities and schools within which About Us was being implemented and evaluated.

Randomization

Following baseline survey completion, eligible adolescents who had already received parental consent and assented to study participation were randomized to either the intervention or control group.

To assign participants to study groups (intervention or control), we used a stratified permuted block randomization procedure to ensure balance in key covariates and experience factors across intervention conditions given our need to randomize in smaller cohorts within schools by semester (ie, blocks). Specifically, eligible and consented adolescents were subdivided into strata defined by the sex assigned at birth (male or female) and whether they had one or two of the screening experience factors, followed by permuted block randomization for each stratum. Within each stratum, participants were assigned to either the intervention or control group using a 60/40 split. The goal was to create a balance of sex assigned at birth and experience factors to ensure that the intervention and control groups had an equal distribution of these factors that may affect our primary outcome of interest (ie, having vaginal or anal sex without condoms). In other words, the stratification was done to avoid the potential imbalances or confounding due to the sex assigned at birth and the number of baseline experience factors.

Students randomized to the control group received business as usual (BAU) care only. Students assigned to the control group received no special services beyond BAU provided through the schools. To measure the control group experience, we included a set of general exposure items on the impact survey to assess self-reported dosage from or exposure to teen pregnancy programming or sex education during the study period in the school and community (eg, have you had a guest speaker come to your school to provide any of the following information: abstinence information, sexuality information, pregnancy prevention information, STI or HIV information, etc). We also collected data from our schools (on a "needs and resources assessment") to evaluate content from BAU education during the study period using a brief, web-based survey collected from our site liaisons and the schools' health education teachers.

Random assignment duties were limited to the study statistician and conducted within one week of baseline data collection at a particular study site. A participant's random assignment to the intervention group was communicated to the evaluation project manager, who then transmitted this information to the respective SBHCs study site coordinators.

Follow-up Data Collection

Follow-up surveys were administered at 2 separate time points following the completion of the About Us intervention (approximately 3 months and 9 months postprogram implementation). Similar to baseline data collection for cohort 1 (spring 2018), cohort 2 (fall 2018), and cohort 3 (spring 2019), most follow-up surveys were conducted in-person on school or SBHC grounds. Upon receipt of a signed assent form, adolescents completed the survey on a self-administered tablet device via the Qualtrics Offline Surveys application and in the presence of an EDC. For any adolescents who transferred or were absent, a follow-up contact protocol was used to locate and provide an opportunity to complete the survey. Specifically, using contact data provided by the adolescent at the baseline or 3-month survey, EDCs would undertake a series of contacts through email, text message, cell phone calls, home phone calls, and/or social media messaging, sending the adolescent a unique link to the follow-up survey. Adolescents received a US $10 incentive for each survey completed up to the end of March 2020.

Follow-up surveys for cohorts 4 and 5 were affected by the COVID-19 pandemic due to school closures and travel restrictions preventing evaluation staff from traveling to study sites to administer the surveys. As a result, the study team adopted an online follow-up protocol as the primary approach to administering follow-up surveys and increased the online survey incentive to US $25, as the literature shows this amount is more effective in increasing response rates [29].

Throughout the study and depending on whether the cohort was surveyed during the pandemic, it was possible for participants in both the intervention and control groups to receive incentives totaling as little as US $10 and as much as US $60. Survey incentives offered to all participants were different than program incentives offered only to those in the intervention group who completed About Us program sessions.

Measures

Primary measures to be analyzed are listed below in Textbox 1. All secondary measures to be analyzed along with sources are provided in Multimedia Appendix 1 [30-36].

Textbox 1. Behavioral outcomes used for the primary research question.

Outcome name: Condomless vaginal or anal sex in the past 3 months (core measures for Personal Responsibility Education Innovative Strategies grantees) [36].

Source item(s):

- When you had vaginal sex in the past 3 months, how often did you or a partner use a condom? Vaginal sex is when a penis is put in a vagina.
- When you had anal sex in the past 3 months, how often did you or a partner use a condom? Anal sex is when a penis is put in a rectum, ass, or butt.
- Original response options for vaginal or anal sex include 1 (all of the time), 2 (some of the time), or 3 (none of the time).

Constructed measure:

- Construct a single, dichotomous outcome coded as 1 if the respondent indicated they had vaginal or anal sex without a condom in the past 3 months, 0 if they did not, or missing otherwise.
- To be recoded into a single dichotomous variable (vaginal or anal sex) with response options as follows: 0=all of the time (1), as well as participants who reported not having vaginal or anal sex in the past 3 months; 1=some (2) or none of the time (3); and (?)=missing response for vaginal or anal sex without a condom in the past 3 months.

Timing of measure: 9 months following the completion of the program.

Data Cleaning

Phase I

Data cleaning is being implemented in three phases. At the baseline, 3-month, and 9-month surveys, the evaluation team engages in a screening process beginning during data entry and using built-in checks for participant entries via Qualtrics. We are using predefined expectations about normal ranges (eg, aged 14 to 18 years), flagging of dubious data entry and patterns (eg, using prompts to confirm an entry), and skip patterns (eg, if students reported having been in a relationship, they received an additional branch of questions not given to those who never were in a relationship).

After retrieving Qualtrics data from each participant survey from the EDCs, project staff transfers the files to a password-protected shared drive. Participant data are transferred and warehoused in SPSS (version 27; IBM) by data wave (ie, baseline, 3 months, and 9 months). Using SPSS, we are recoding variables, creating new variables (eg, check-all variables, such as race and sexuality, recoded into one categorical variable), and labeling and formatting variables for analysis.

For each data wave and merged data sets, data are checked to ensure they meet predefined range expectations, logical skip patterns, and consistency checks and missing data patterns by examining variable descriptive summary statistics (eg, minimum, maximum, mean, median, and SD), frequency distributions, cross-tabulations, and graphical explorations of variable distributions (eg, box plots, histograms, and scatter plots). Data are also checked against expected data collections (based on the number of randomized participants, lags between baseline, and follow-up surveys) and errors in transferring data from Qualtrics (eg, duplicate entries and inadvertent deletions). This process is implemented using SPSS and SAS (version 9.4; SAS Institute).

Phase II

At this phase, we are going back to the original Qualtrics data files for any inconsistent data points and patterns to verify entries and add justifications for any changes made to the warehoused SPSS data.

Phase III

We will flag inconsistencies for further discussion and, if decisions are made to adjust reported values, those decision rules will be fully documented for reporting purposes. These rules will be informed by the literature, What Works Clearinghouse (WWC) standards, or best practice guidance. We will check for within-time point and across-time point inconsistencies and set up cleaning rules for both. For example, within a time point (eg, baseline), if a participant reports no history of anal sex but reports using a condom during anal sex in the last 3 months, both responses would be edited as missing values. Similarly, across time points (ie, baseline, 3-month, and 9-month assessments), if someone reports that they have never had anal sex at 9 months, but report having had anal sex at the 3-month evaluation, we will carry out two sensitivity analyses with (1) recoded 3-month data to match 9-month data and (2) recoded 9-month data to match 3-month data [37]. However, it is important to note that such inconsistencies are not expected due to the built-in skip patterns in our Qualtrics survey but are planned for nonetheless.

Additionally, any response values that were not supposed to have been provided based on built-in skip patterns will be recoded as "not applicable." Overall, missing values will be differentiated with appropriate coding as "nonresponse," "do not know," and "not applicable" as needed, and some anomalies (if plausible) will be left unchanged (eg, true extreme values such as age at 18 years). Finally, original respondents' data will be kept as a backup, and we will explore sensitivity analyses to check to what extent data cleaning edits influence our results, including the use of multiple imputation procedures described below.

Primary Outcome

The primary outcome of this study is the impact of About Us relative to the standard of care 9 months following the end of the intervention on the prevalence of vaginal or anal sex without condoms in the past 3 months. Items specifically examine condom use during vaginal and anal sex independently (Textbox 1).

Secondary Outcomes

The secondary outcomes are four-fold: 3 months and 9 months following the end of the intervention, what is the impact of About Us relative to the standard of care on (1) the prevalence of abstinence from vaginal or anal sex in the past 3 months, (2) composite scores of relationship communication and positive conflict resolution among participants involved in a relationship at baseline, (3) the prevalence of school-based health center service use or information receipt in the past 3 months, and (4) composite scores of condom use intentions and attitudes regarding condoms and other types of birth control? These secondary outcomes are summarized in Tables S1-S4 in Multimedia Appendix 1.

Generalities of Statistical Analysis Methods

Statistical analysis will be undertaken using SPSS and SAS. All participants randomized to either intervention (About Us) or BAU will be included in the analyses using the intent-to-treat (ITT) principles. Our benchmark analysis data set will include all randomized participants with imputed data for missing covariate and outcome variables.

As part of our sensitivity analyses, two additional types of analyses will be implemented: modified intent-to-treat (modified ITT) and complete case analysis.

Modified ITT analysis (ie, analysis based on a data set that includes all randomized subjects who provide baseline measurements on primary and secondary outcomes and have at least one follow-up assessment) will also be implemented under different conditions for missing data adjustment (described below).

Assessment of Baseline Equivalence

Equivalence between the intervention and control groups will be assessed for demographic characteristics and primary and secondary outcomes at 3 time points: baseline, 3-month, and 9-month follow-up. At the 3-month and 9-month time points, baseline characteristics and outcomes will be compared between participants who completed each assessment separately. For example, if 400 out of 533 randomized participants completed the 3-month assessment, their baseline characteristics and outcome measures will be compared between intervention and control group participants (n=400). The baseline equivalence results will be used to help identify issues such as a potential lack of equivalence due to attrition (study or program attrition). Baseline demographic characteristics and primary and secondary outcome measures that are statistically different between the treatment and control groups will be controlled in our primary and secondary outcome analyses as described below.

Demographic characteristics of interest include age, sex assigned at birth, and race and ethnicity. The mean age and its corresponding SD for intervention and control groups will be calculated. Frequencies and proportions will be produced for categorical outcomes such as sex assigned at birth and race and ethnicity. Race will be categorized into non-Hispanic White, non-Hispanic Black, Hispanic, and other races.

A Pearson's Chi-square test (or Fisher's exact test as needed) will be used to examine baseline differences between categorical variables (sex assigned at birth, race and ethnicity, primary and secondary outcomes, and group assignment at baseline, 3-month, and 9-month assessment time points separately.

A two-sample independent t-test (or a Mann-Whitney test, nonparametric test as needed) will be used to examine baseline differences between continuous variables (age and secondary outcomes) and group assignment at baseline, 3-month, and 9-month assessment time points separately.

Baseline equivalence analyses will be conducted using SAS, and statistical significance will be assessed at an alpha (Type I error) of 5%.

Preliminary Data Analysis

Preliminary data analysis will involve routine range checks for continuous variables and frequencies and cross-tabulations for categorical variables. If necessary, continuous outcomes (eg, score-based measures) will be corrected using the least powerful transformations possible to meet our statistical modeling assumptions (ie, "normalize" univariate data that might be skewed or "straighten out" a bivariate curvilinear relationship) of outcome and covariate relationships for linear regression [38]. In addition, bivariate analyses will be performed to identify potential nonlinear relationships (eg, between 9-month continuous outcomes and baseline characteristics and measures such as age and composite scores) that may need to be modeled. Preliminary analysis of score-based (or instrument-based) outcomes will include examining evidence of construct validity and reliability. Construct validity refers to the degree to which an instrument or measure assesses the underlying theoretical construct it is supposed to measure (ie, the test is measuring what it is purported to measure). This will be examined via confirmatory factor analysis for score-based outcomes. Reliability refers to the degree of interrelationship or homogeneity among question items on a test (questionnaire), such that they are consistent with one another and measure the same construct; this will be examined by generating an internal consistency index–Cronbach's alpha for our score-based outcomes.

Statistical Analysis Models

For dichotomous outcomes at 9 months, we will use logistic regression models with covariates (see Textbox 2) for the intervention, baseline outcome variables, strata variables (sex assigned at birth and number of screening experience factors present), sociodemographic characteristics (age and race and ethnicity), the time elapsed between baseline and the follow-up survey (at 3-month and 9-month follow-up), cohort, and school. For continuous outcomes, we will use linear regression models with covariates for the intervention, baseline outcome variables, strata variables (sex and number of screening risk factors present), sociodemographic characteristics (age and race and ethnicity), the time elapsed between baseline and follow-up surveys (at 3-month and 9-month follow-up), cohort, and school. Additional (exploratory) analyses will test for 3-way and 2-way statistical interactions and adjust for prognostic factors such as potential confounders of intervention effects. Similarly, we will include a covariate that captures whether our outcome data were collected pre-COVID-19 versus during the COVID-19 pandemic. Potential 2-way interactions involving this covariate and intervention group, age and grade, and relationship status will be examined to test the differential effects of the pandemic on outcomes of interest.

Textbox 2. Covariates included in impact analyses.

Screening factor: one or two screening factors present (categorical variable).

Age (years): baseline date to DOB (continuous variable).

Sex: sex assigned at birth; 1=male, 2=female (dichotomous variable).

Race and ethnicity: White, Black, Hispanic, other (categorical variable).

Number of days between baseline and the follow-up survey (3 or 9 months): follow-up date to baseline date (continuous variable).

Cohort: cohort 1 (spring 2018), cohort 2 (fall 2018), cohort 3 (spring 2019), cohort 4 (fall 2019), and cohort 5 (spring 2020; categorical variable).

School: high schools 1 to 7.

We will also take advantage of all measurement time point data and appropriately model the data hierarchy by exploring the use of generalized linear mixed models (GLMM) [39,40] to evaluate intervention effectiveness. The GLMM will allow us to use all data available and adjust for multilevel dependencies (eg, repeated measures, such as baseline and follow-up at 3 months and 9 months, within an individual participant nested within the intervention or control group, within a cohort (block) and study site). Additional analyses to account for multilevel effects will be explored as secondary or sensitivity analyses.

Presentation of Continuous Outcomes

Least squares (LS) means, corresponding SEs, 95% 2-sided CIs, and 2-tailed *P* values will be presented for the within-group (ie, intervention and control) outcome measures. For each between-group, the difference in LS means, corresponding SE, 2-sided 95% CI, and 2-tailed *P* value will also be derived from the linear regression model and presented. Standard model diagnostics will be performed to assess the validity of the proposed model. These diagnostics will include examining the residuals for normality and homoscedasticity as well as testing

for the significance of the intervention by baseline outcome interaction terms.

Presentation of Categorical Outcomes

The estimated odds ratio, SE, 95% Wald CI, and *P* value will be presented for each between-group comparison of interest. Standard model diagnostics will be performed to assess the validity of the proposed model. These diagnostics will include testing the goodness of fit with the Hosmer-Lemeshow test and examining influence statistics for potentially outlying observations. In addition, the number and percentage of subjects with a primary outcome (eg, condomless vaginal or anal sex) will be presented for each treatment group, including model estimated probabilities and statistical significance of differences observed (at α=.05).

Handling Missing Data

Our general approach to missing data will involve taking advantage of all observed information while not exaggerating the precision of findings based on incomplete data [41,42].

All variables described for our final regression models will be used in our imputation procedures. That is, outcome measures (at 3-month and 9-month follow-up analyzed separately), treatment condition, baseline outcome variables, strata variables (sex and number of screening experience factors present), sociodemographic characteristics (age, race, and ethnicity), the time elapsed between baseline and follow-up survey (at 3-month or 9-month follow-up), and school. The treatment and control group participant data will be imputed separately [43].

Multivariate imputation by chained equations [44] methods using PROC MI and MIANALYZE procedures in SAS will be used to create multiple imputations (replacement values) for multivariate missing data (eg, continuous, binary, unordered categorical, and ordered categorical data) based on a fully conditional specification [45], where each incomplete variable is imputed by a separate model [46]. All missingness (nonresponse, program attrition, or study loss to follow-up) will be treated the same way for our benchmark analysis. Additional analyses (see Sensitivity Analysis) will be explored where reasons for program attrition are accounted for in the generation of imputed covariate and outcome values. All variables (ie, outcome and baseline characteristics) described in the above analysis models will be used for the imputation procedures. The number of data sets to be imputed will be determined using the quadratic rule recommended by von Hippel [47]. In addition to the baseline value of the outcome of interest, age, race and ethnicity, the sex assigned at birth, and the number of screening experience factors (1 or 2; ie, adolescents had either exposure to violence or a prior or current experience with a romantic relationship or both), and time (days) between baseline and 3-month or 9-month follow-up will be included in our final analysis models (ie, linear and logistic regression).

Sensitivity Analysis

In addition to the benchmark analyses described above (3-month and 9-month follow-up examined separately), two types of analyses (ie, complete case analysis—no imputation for missing data—and modified ITT with imputed data) will be implemented using procedures similar to the benchmark analyses (linear and logistic regression models). The robustness of the inferential findings will be assessed by comparing differences in analytical findings across the three types of analyses (ITT with imputed data, complete case analysis, and modified ITT).

Results

Baseline data collection commenced in February 2018 and was completed in March 2020, yielding 5 cohorts and 533 study participants, with 316 assigned to the intervention group and 217 assigned to the control group. Though the project team anticipated an additional semester of implementation in the fall of 2020, the COVID-19 pandemic and subsequent school closures interfered with the scheduling of additional programming. We continued with online data collection and anticipate the completion of follow-up data collection by May 2021.

Discussion

Support for the Intervention

Most of the existing EBPs yield relatively short-term gains [48] and were developed using normative decision-making models [49]. These models describe decision-making as a deliberate and analytic process and are useful for predicting behaviors that are typically unemotional [50]; the utility of these models is limited for sexual behaviors, which are inherently emotional. Findings stemming from developmental neuroscience experts suggest that changes in relational, emotional, and social processing play a critical role in influencing adolescent behavior, highlighting the potential of integrating emotionally relevant learning strategies into sexual health programs; by doing so, the content becomes more meaningful and relevant to adolescents, and better supports the development of decision-making skills [51]. Further, most existing interventions are inherently cognitive, teaching adolescents how to refuse unwanted or unprotected sexual intercourse, but do not address the circumstances or situations under which adolescents might be willing to engage in certain sexual behaviors [51]. About Us draws on this body of research to create a more contextually and developmentally relevant program that addresses motivation and emotional influences in sexual decision-making.

The lack of student interactivity is a major pedagogical issue facing learning environments today [52]. EBPs for teen pregnancy and STI prevention share similar interactive instructional strategies (eg, mini-lectures, games, role-playing, and simulations); however, other strategies could extend the program's impact. Strategies include storytelling and the use of blended learning. Stories have been recognized for centuries as a powerful tool for organizing and transmitting information [53]. They are one way to pique students' curiosity and build interest while framing new concepts, illustrating consequences, modeling skills, and providing context. Neuroscience supports the use of stories as anchors of information assisting in the learning process [54]. In addition, educators now emphasize the importance of blended learning, which incorporates the use of new online technologies in face-to-face settings to engage students in active and interactive learning [55]. The potential

of using technology in changing sexual behaviors is highlighted in research with computer-based or blended learning programs [56,57].

Further, technology provides young people with opportunities to gain virtual experiences related to relationships. Some research suggests there is an association between emotional experience gained in virtual environments with emotional experiences lived in real-life contexts, which can provide a safe and low-risk venue for emotional learning [58]. We draw on both of these strategies in this project.

Limitations

This study is not without limitations. The COVID-19 global pandemic severely impacted this project. As a result, policies enacted by state and local governments, by school sites participating in About Us, and by the research institutions conducting the evaluation were implemented to protect as many people as possible from the virus. This included suspending in-person intervention delivery, recruitment, and data collection and necessitated the transition to online-only follow-up survey administrations beginning in March 2020. These changes reduced the number of students recruited and prevented those who had already been recruited from receiving the intervention.

Implementation of the intervention was also impacted by instances of turnover within schools and health centers, which sometimes confused all stakeholders. For example, new administrators frequently had no knowledge of the research study because it had not been communicated to them by the outgoing administrators. Similarly, new health center staff were often overwhelmed by “inheriting” this new program from a predecessor, thus slowing the pace of required implementation and evaluation activities. These instances of turnover combined with the challenges of scheduling intervention delivery to occur during the already limited regular school day or after school resulted in lower enrollment in the study.

Another limitation was the incompleteness of the contact information provided by adolescents participating in the study. For example, in some instances, adolescents either initially provided incorrect information or did not provide updated information for study team members to use for follow-up contact attempts. This reduced our follow-up survey response rate and resulted in participants being lost to follow-up. When possible, study team members worked with SBHC staff to reach students with outdated or incorrect contact information and encourage them to participate in scheduled survey administration.

The study was also impacted by a lower-than-expected number of returned consent forms, which resulted in lower-than-expected enrollment. SBHC staff utilized various methods for distributing the consent forms (eg, individually to each student during screening visits or in a welcome packet for parents at the beginning of school term), but the collection of consent forms may have been negatively impacted by lack of follow-up with adolescents about returning the forms to the SBHC. While our study team employed methods previously shown to be associated with improved consent form return in youth samples (eg, providing incentives for consent form return or utilizing school staff for consent form collection) [59,60], additional approaches such as greater engagement with parents or using an opt-out versus an opt-in approach where appropriate may improve consent form return rates.

In some cases, adolescents transferred to different school sites that were not involved in the study. In these instances, we could not rely on SBHC staff to reach out to adolescents if their contact information was incorrect or incomplete, and they were lost to follow-up.

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Conflicts of Interest

None declared.

Multimedia Appendix 1
Supplementary tables.
[DOCX File , 35 KB - resprot_v10i9e30499_app1.docx]

References

1. Feiring C. Other-sex friendship networks and the development of romantic relationships in adolescence. Journal of Youth and Adolescence 1999 Aug;28(4):495-512. [doi: 10.1023/a:1021621108890]
2. Carver K, Joyner K, Udry J. Adolescent Romantic Relations and Sexual Behavior: Theory, Research and Practical Implications. Florsheim P, editor. National Estimates of Adolescent Romantic Relationships Internet Mahwah, N. J.: Lawrence Erlbaum Associates; 2003. URL: https://www.cpc.unc.edu/resources/publications/bib/2156/ [accessed 2021-01-13]
3. Manning WD, Longmore MA, Copp J, Giordano PC. The complexities of adolescent dating and sexual relationships: fluidity, meaning(s), and implications for young adults' well-being. New Dir Child Adolesc Dev 2014;2014(144):53-69 [FREE Full text] [doi: 10.1002/cad.20060] [Medline: 24962362]

4. Manning W, Giordano P, Longmore M. Hooking up: The relationship contexts of "nonrelationship" sex. Journal of Adolescent Research 2006;21(5):459-483. [doi: 10.1177/0743558406291692]
5. Coyle K, Guinosso S, Glassman J, Anderson P, Wilson H. Exposure to violence and sexual risk among early adolescents in urban middle schools. The Journal of Early Adolescence 2017;37(7):889-909 [FREE Full text] [doi: 10.1177/0272431616642324]
6. Collins W, van Dulmen M. 'The Course of True Love(s)...': Origins and Pathways in the Development of Romantic Relationships. In: Romance and Sex in Adolescence and Emerging Adulthood: Risks and Opportunities. Mahwah, NJ, US: Lawrence Erlbaum Associates Publishers; 2006:63-86.
7. Buhi ER, Goodson P. Predictors of adolescent sexual behavior and intention: a theory-guided systematic review. J Adolesc Health 2007 Jan;40(1):4-21. [doi: 10.1016/j.jadohealth.2006.09.027] [Medline: 17185201]
8. Bouchey H, Furman W. Dating and Romantic Experiences in Adolescence. In: Blackwell Handbook of Adolescence. Oxford, UK: Blackwell Publishers; 2006:312-329.
9. Martin J, Hamilton B, Osterman M, Driscoll A. Births: Final data for 2018. National Vital Statistics Reports; vol 68, no 13. Hyattsville, MD: National Center for Health Statistics; 2019. URL: https://www.cdc.gov/nchs/data/nvsr/nvsr68/nvsr68_13-508.pdf [accessed 2021-03-08]
10. Unintended Pregnancy in the United States [Fact Sheet]. Guttmacher Institute. 2019 Jan. URL: https://www.guttmacher.org/sites/default/files/factsheet/fb-unintended-pregnancy-us.pdf [accessed 2021-01-14]
11. Finer LB, Zolna MR. Declines in unintended pregnancy in the United States, 2008-2011. N Engl J Med 2016 Mar 03;374(9):843-852 [FREE Full text] [doi: 10.1056/NEJMsa1506575] [Medline: 26962904]
12. Hamilton BE, Rossen LM, Branum AM. Teen birth rates for urban and rural areas in the United States, 2007-2015. NCHS Data Brief 2016 Nov(264):1-8 [FREE Full text] [Medline: 27849147]
13. Lugo-Gil J, Lee A, Vohra D, Harding J, Ochoa L, Goesling B. Updated findings from the HHS Teen Pregnancy Prevention Evidence Review: August 2015 through October 2016. U.S. Department of Health and Human Services: Office of the Assistant Secretary for Planning and Evaluation. 2018 Apr. URL: https://tppevidencereview.youth.gov/pdfs/Summary_of_findings_2016-2017.pdf [accessed 2021-01-13]
14. Goesling B. Making Sense of Replication Studies: Guidance for Teen Pregnancy Prevention Researchers. ASPE Research Brief. Washington, DC: U.S. Department of Health and Human Services, Office of Human Services Policy, Office of the Assistant Secretary for Planning and Evaluation; 2015 May 12. URL: https://tinyurl.com/dc845s8t [accessed 2021-01-14]
15. Wilson HW, Woods BA, Emerson E, Donenberg GR. Patterns of violence exposure and sexual risk in low-income, urban African American girls. Psychol Violence 2012 Apr;2(2):194-207 [FREE Full text] [doi: 10.1037/a0027265] [Medline: 24563808]
16. Finkelhor D, Turner H, Ormrod R, Hamby SL. Violence, abuse, and crime exposure in a national sample of children and youth. Pediatrics 2009 Nov;124(5):1411-1423. [doi: 10.1542/peds.2009-0467] [Medline: 19805459]
17. Reducing the Risk. Program Success Center for Sexual & Reproductive Health. Scotts Valley, CA: ETR URL: https://www.etr.org/ebi/programs/reducing-the-risk/ [accessed 2021-01-14]
18. Making Proud Choices!. Program Success Center Internet. Scotts Valley, CA: ETR URL: https://www.etr.org/ebi/programs/making-proud-choices/ [accessed 2021-01-14]
19. About. Seventeen Days. URL: http://seventeendays.org/about/ [accessed 2014-01-14]
20. Services Provided by SBHCs. California School-Based Health Alliance. 2011. URL: https://www.schoolhealthcenters.org/school-health-centers-in-ca/what-types-of-health-services-do-schools-provide/ [accessed 2021-01-13]
21. Brown M, Bolen L. The school-based health center as a resource for prevention and health promotion. Psychology in the Schools 2008;45(1):28-38 [FREE Full text] [doi: 10.1002/pits.20276]
22. Damon W. What is positive youth development? The ANNALS of the American Academy of Political and Social Science 2016 Sep 08;591(1):13-24. [doi: 10.1177/0002716203260092]
23. Collins W. More than myth: The developmental significance of romantic relationships during adolescence. Journal of Research on Adolescence 2003;13(1):1-24 [FREE Full text] [doi: 10.1111/1532-7795.1301001]
24. Reyna VF, Brainerd CJ. Dual processes in decision making and developmental neuroscience: A fuzzy-trace model. Dev Rev 2011 Sep;31(2-3):180-206 [FREE Full text] [doi: 10.1016/j.dr.2011.07.004] [Medline: 22096268]
25. Bandura A. Social Foundations of Thought and Action: A Social Cognitive Theory. 1st edition. Englewood Cliffs, NJ: Prentice Hall; 1985.
26. Marseille E, Mirzazadeh A, Biggs MA, P Miller A, Horvath H, Lightfoot M, et al. Effectiveness of school-based teen pregnancy prevention programs in the USA: A systematic review and meta-analysis. Prev Sci 2018 May;19(4):468-489. [doi: 10.1007/s11121-017-0861-6] [Medline: 29374797]
27. Goesling B, Colman S, Trenholm C, Terzian M, Moore K. Programs to reduce teen pregnancy, sexually transmitted infections, and associated sexual risk behaviors: a systematic review. J Adolesc Health 2014 May;54(5):499-507. [doi: 10.1016/j.jadohealth.2013.12.004] [Medline: 24525227]
28. Qualtrics. Provo, Utah, USA: Qualtrics; 2020. URL: https://www.qualtrics.com/ [accessed 2021-01-14]

29. Zheng G, Oksuzyan S, Hsu S, Cloud J, Jewell MP, Shah N, et al. Self-reported interest to participate in a health survey if different amounts of cash or non-monetary incentive types were offered. J Urban Health 2018 Dec;95(6):837-849 [FREE Full text] [doi: 10.1007/s11524-018-0237-7] [Medline: 29654397]
30. Taylor BG, Mumford EA. A national descriptive portrait of adolescent relationship abuse: Results from the national survey on teen relationships and intimate violence. J Interpers Violence 2016 Mar;31(6):963-988. [doi: 10.1177/0886260514564070] [Medline: 25548142]
31. Arellano C, Markman H. The managing affect and differences scale (MADS): A self-report measure assessing conflict management in couples. Journal of Family Psychology 1995 Sep;9(3):319-334. [doi: 10.1037/0893-3200.9.3.319]
32. Cleland J. Illustrative Questionnaire for Interview-Surveys with Young People. World Health Organization. 2001. URL: https://www.scirp.org/(S(czeh2tfqyw2orz553k1w0r45))/reference/ReferencesPapers.aspx?ReferenceID=1950110 [accessed 2021-05-13]
33. Escribano S, Espada JP, Orgilés M, Morales A. Implementation fidelity for promoting the effectiveness of an adolescent sexual health program. Eval Program Plann 2016 Dec;59:81-87. [doi: 10.1016/j.evalprogplan.2016.08.008] [Medline: 27614301]
34. Starosta AJ, Berghoff CR, Earleywine M. Factor structure and gender stability in the multidimensional condom attitudes scale. Assessment 2015 Jun 18;22(3):374-384. [doi: 10.1177/1073191114547887] [Medline: 25139383]
35. Kyes K. Contraceptive attitude scale. In: Davis C, Yarber W, Bauserman R, Schreer G, Davis S, editors. Handbook of Sexuality-related Measures. Thousand Oaks, CA: SAGE Publications, Inc; 1998:164-165.
36. Prep Studies of Performance Measures and Adults Preparation Subjects. Core Measures for PREIS Grantees' Local Evaluations. 2016. URL: https://omb.report/icr/201609-0970-004/doc/68048501 [accessed 2021-08-03]
37. Wellman RJ, O'Loughlin J. Data dilemmas and difficult decisions: on dealing with inconsistencies in self-reports. J Adolesc Health 2015 Apr;56(4):365-366. [doi: 10.1016/j.jadohealth.2015.01.015] [Medline: 25797629]
38. Box G, Cox D. An analysis of transformations. Journal of the Royal Statistical Society: Series B (Methodological) 2018 Dec 05;26(2):211-243. [doi: 10.1111/j.2517-6161.1964.tb00553.x]
39. Breslow NE, Clayton DG. Approximate inference in generalized linear mixed models. Journal of the American Statistical Association 1993 Mar;88(421):9. [doi: 10.2307/2290687]
40. McCullagh P, Nelder J. Generalized Linear Models. Second Edition. London: Chapman and Hall; 1989.
41. Rubin DB. Inference and missing data. Biometrika 1976 Dec;63(3):581. [doi: 10.2307/2335739]
42. Rubin D. Multiple Imputation for Nonresponse in Surveys. New York: John Wiley & Sons, Inc; 1987.
43. Sullivan TR, White IR, Salter AB, Ryan P, Lee KJ. Should multiple imputation be the method of choice for handling missing data in randomized trials? Stat Methods Med Res 2018 Sep;27(9):2610-2626 [FREE Full text] [doi: 10.1177/0962280216683570] [Medline: 28034175]
44. van Buuren S, Groothuis-Oudshoorn K. mice: multivariate imputation by chained equations in R. J. Stat. Soft 2011;45(3):1-67. [doi: 10.18637/jss.v045.i03]
45. van Buuren S. Multiple imputation of discrete and continuous data by fully conditional specification. Stat Methods Med Res 2007 Jun;16(3):219-242. [doi: 10.1177/0962280206074463] [Medline: 17621469]
46. van Buuren S, Brand JP, Groothuis-Oudshoorn CG, Rubin DB. Fully conditional specification in multivariate imputation. Journal of Statistical Computation and Simulation 2006 Dec;76(12):1049-1064. [doi: 10.1080/10629360600810434]
47. von Hippel PT. How many imputations do you need? a two-stage calculation using a quadratic rule. Sociological Methods & Research 2018 Jan 18;49(3):699-718. [doi: 10.1177/0049124117747303]
48. Coyle K, Anderson P, Laris B. Schools and sexuality education. In: Ponzetti J, editor. Evidence-based Approaches to Sexuality Education: A Global Perspective. 1st Edition. Routledge: Taylor & Francis Group; 2016.
49. Kirby D, Laris B. Effective curriculum-based sex and STD/HIV education programs for adolescents. Child Development Perspectives 2009;3(1):21-29 [FREE Full text] [doi: 10.1111/j.1750-8606.2008.00071.x]
50. Halpern-Felsher B. Adolescent Decision-Making. In: Bradford B, Prinstein M, editors. Encyclopedia of Adolescence. New York, NY: Elsevier Academic Press; 2011:30-37.
51. Ballonoff Suleiman A, Brindis CD. Adolescent school-based sex education: using developmental neuroscience to guide new directions for policy and practice. Sex Res Soc Policy 2014 Feb 14;11(2):137-152. [doi: 10.1007/s13178-014-0147-8]
52. Draper S, Brown M. Increasing interactivity in lectures using an electronic voting system. Journal of Computer Assisted Learning 2004;20(2):81-94 [FREE Full text] [doi: 10.1111/j.1365-2729.2004.00074.x]
53. Hsu J. The secrets of storytelling. Sci Am Mind 2008 Aug;19(4):46-51. [doi: 10.1038/scientificamericanmind0808-46]
54. Immordino-Yang M, Damasio A. We feel, therefore we learn: The relevance of affective and social neuroscience to education. Mind, Brain, and Education 2007;1(1):3-10 [FREE Full text] [doi: 10.1111/j.1751-228x.2007.00004.x]
55. Dziuban C, Harmtan J, Moskal P. Blended learning. Educause. 2004. URL: https://library.educause.edu/resources/2004/3/blended-learning [accessed 2021-01-14]
56. Lightfoot M, Comulada WS, Stover G. Computerized HIV preventive intervention for adolescents: indications of efficacy. Am J Public Health 2007 Jun;97(6):1027-1030. [doi: 10.2105/AJPH.2005.072652] [Medline: 16670219]

57. Tortolero SR, Markham CM, Peskin MF, Shegog R, Addy RC, Escobar-Chaves SL, et al. It's your game: keep it real: delaying sexual behavior with an effective middle school program. J Adolesc Health 2010 Feb;46(2):169-179 [FREE Full text] [doi: 10.1016/j.jadohealth.2009.06.008] [Medline: 20113923]
58. Riva G, Mantovani F, Capideville CS, Preziosa A, Morganti F, Villani D, et al. Affective interactions using virtual reality: the link between presence and emotions. Cyberpsychol Behav 2007 Feb;10(1):45-56. [doi: 10.1089/cpb.2006.9993] [Medline: 17305448]
59. Rodgers P. Maximizing the Return of Parent Consent Forms.: American Foundation for Suicide Prevention; 2006. URL: https://www.yumpu.com/en/document/read/28735978/maximizing-the-return-of-parent-consent-forms-suicide- [accessed 2021-08-03]
60. Fletcher AC, Hunter AG. Strategies for obtaining parental consent to participate in research. Family Relations 2003 Jul;52(3):216-221. [doi: 10.1111/j.1741-3729.2003.00216.x]

Abbreviations

BAU: business as usual
CSHA: California School-Based Health Alliance
EBP: evidence-based practice
EDC: evaluation data collector
GLMM: generalized linear mixed model
ITT: intent-to-treat
LS: least squares
OR: odds ratio
PREIS: Personal Responsibility Education Innovative Strategies
PYD: positive youth development
RCT: randomized controlled trial
SBHC: school-based health center
STI: sexually transmitted infections

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Protocol

Disability-Inclusive Diabetes Self-management Telehealth Program: Protocol for a Pilot and Feasibility Study

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Abstract

Background: Individuals with disabilities and type 2 diabetes require self-management programs that are accessible, sustainable, inclusive, and adaptable. Health coaching has been shown to be an effective approach for improving behavioral changes in self-management. Health coaching combined with telehealth technology has the potential to improve the overall quality of and access to health services.

Objective: This protocol outlines the study design for implementing the Artificial Intelligence for Diabetes Management (AI4DM) intervention. The protocol will assess the feasibility, acceptability, and preliminary efficacy of the AI4DM telehealth platform for people with disabilities.

Methods: The AI4DM study is a 2-arm randomized controlled trial for evaluating the delivery of a 12-month intervention, which will involve telecoaching, diabetes educational content, and technology access, to 90 individuals with diabetes and physical disabilities. The hypothesis is that this pilot project is feasible and acceptable for adults with permanently impaired mobility and type 2 diabetes. We also hypothesize that adults in the AI4DM intervention groups will have significantly better glycemic control (glycated hemoglobin) and psychosocial and psychological measures than the attention control group at the 3-, 6-, and 12-month follow-ups.

Results: The AI4DM study was approved by the university's institutional review board, and recruitment and enrollment will begin in October 2021.

Conclusions: The AI4DM study will improve our understanding of the feasibility and efficacy of a web-based diabetes self-management program for people with disabilities. The AI4DM intervention has the potential to become a scalable and novel method for successfully managing type 2 diabetes in people with disabilities.

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KEYWORDS

telehealth; health coaching; artificial intelligence; diabetes mellitus; mobile phone

Introduction

Background

Diabetes mellitus is one of the most common metabolic disorders; it affects approximately 12.2% of the overall adult population in the United States and 25.25% of the population aged above 65 years [1]. One-third of the US adult population is affected by prediabetes. Diabetes can increase the overall risk of premature death and has been linked to several complications, including cardiovascular, renal, and neurological issues. Although diabetes is a major problem among all populations, people with disabilities are more prone to diabetes. According to the Behavioral Risk Factor Surveillance System 2017 report, nearly 1 in 4 people with disabilities are diagnosed with diabetes, whereas approximately 1 in 10 people without a disability are diagnosed with some form of diabetes [2].

Although physical disabilities increase the risk of developing diabetes, an inverse may also occur. Diabetes is associated with a significant increase in the risk of mobility disability [3]. It has been suggested that individuals with diabetes have an increased risk of disability because of multiple factors, such as obesity, depression, and stroke, when compared with individuals with no diabetes [4]. Similarly, numerous studies have indicated that diabetes may lead to disabling disorders, including cardiovascular disease [5], renal dysfunction [6], retinopathy [7,8], and peripheral vascular disease [8]. Older adults with diabetes are also less likely to engage in physical activity (PA) [9], and some are unable to perform minor physical tasks.

In diabetes management, PA, medication adherence, and glucose tracking have been shown to be effective in reducing glycated hemoglobin (HbA_{1c}) in both the general population and people with intellectual and developmental disabilities [10-15]. Recent meta-analyses have indicated that diabetes prevention and management programs emphasizing community engagement and tracking of food consumption, especially in the context of a low-carbohydrate diet, were more successful than medications in effective diabetes management [16,17]. Studies that investigated the effect of health promotion initiatives and lifestyle interventions on participants with disabilities also indicate that such efforts can promote healthy diets, regular exercise, and reduce sedentary lifestyle, thereby improving the management of chronic health conditions including obesity and diabetes among individuals with disabilities [15,18,19].

Diabetes education is essential for the treatment and management of diseases. Better education and knowledge can reduce the risk of developing diabetes complications while reducing morbidity and mortality. However, based on the 2014 Behavioral Risk Factor Surveillance System data, 47.3% of adults with disabilities did not receive diabetes education, and 10.86% did not visit health professionals for diabetes in the past year. This problem has been amplified by racial minorities. Low health literacy (LHL) is another major problem among people with disabilities [20,21]. Similarly, older adults, people with less than a high school degree, racial and ethnic minorities, people with low-income levels, and nonnative speakers of English are most likely to experience LHL [22]. Approximately 80 million adults in the United States are estimated to have LHL [23]. People with LHL are more prone to low diabetes knowledge levels [24-27] and limited glycemic control [26], resulting from unhealthy dietary habits, low PA levels, poor medication adherence, and poor blood glucose monitoring [23-27]. People with low literacy skills are not illiterate; however, using plain language is necessary to improve their health literacy and make written and oral information easier to understand [22]. Improving health literacy among participants with LHL would be beneficial for the education, treatment, and management of chronic diseases.

However, people with disabilities face inordinate barriers to achieving a healthy diet and recommended PA levels [28-31]. People with disabilities remain to be one of the least active populations in society [31-33]. Nationwide, 46% of people with disabilities have been categorized as physically inactive [32]. Maintaining a healthy diet is also a challenge for people with disabilities. There are several barriers to this process, such as feeling too tired to cook, organic or healthy, and nutrition foods being expensive, and lack of desire or willpower to cook [29]. All of these issues can be resolved using a systematic approach. However, accessible, inclusive, and adapted diabetes management programs for people with disabilities do not exist. Programs that are not designed with people with disabilities in mind (ie, noninclusive) pose various physical, programmatic, and attitudinal barriers. A few studies have examined diabetes management for people with disabilities, but they have all been singular studies that have not led to the creation of sustainable and scalable diabetes management programs for people with disabilities. For example, the National Center on Health, Physical Activity and Disability created the first *Prevent T2 for ALL*, an inclusive adaptation of the CDC's *Prevent T2 program*. However, the Prevent T2 program is a diabetes prevention program (not a diabetes management program), and the primary focus is on BMI control, not glycemic control.

As our next step toward diabetes management for people with disabilities, we propose the development of an inclusive telecoaching self-management program for diabetes management in people with disabilities. To make the telecoaching approach sustainable and scalable, artificial intelligence techniques are employed to reduce the time health coaches spend on each participant.

Objectives

The primary objective of this project is to evaluate the preliminary efficacy and feasibility of an accessible and inclusive artificial intelligence–assisted, individualized, family-focused lifestyle modification intervention (the Artificial Intelligence for Diabetes Management [AI4DM] intervention) for glycemic control in people with disabilities.

We hypothesize that the clinical outcome (HbA_{1c}) associated with type 2 diabetes mellitus (T2DM) self-management and self-efficacy outcomes would have a greater effect in the AI4DM intervention arm than in the attention control arm at the 3-, 6-, and 12-month follow-ups. We also hypothesize that the AI4DM intervention is feasible and acceptable for adults with permanent impaired mobility and T2DM, their caregivers, and health coaches and that the fidelity of the program will be maintained. A fidelity monitoring protocol was developed by the research

team for the AI4DM study based on the five domains recommended by the National Institutes of Health Behavior Change Consortium [34].

Methods

Overview

The AI4DM study is a 2-arm randomized controlled trial. Eligible participants will be randomly assigned to one of two groups: (1) the AI4DM intervention group with telecoaching support and (2) the attention control group. The active intervention will include 6 months of telecoaching followed by 6 months of follow-up and access to the technology but with no telecoaching calls (Table 1). For the study, 4 weeks is considered a month, thereby making the study duration 48 weeks. Study activities involving participants with disabilities will be primarily conducted on the web nationally in the United States.

Table 1. Research design.

Group	Enrollment (weeks 1-2)	Pretest (weeks 2-3)	Weeks 4-15[a]	AI4DM[b] intervention		Posttest (weeks 52-53)
				Weeks 16-27[a]	Weeks 28-51	
AI4DM intervention	✓[c]	✓	Weekly calls and technology access	Biweekly calls and technology access	Only technology access	✓
Attention control	✓	✓	Weekly courtesy calls	Biweekly courtesy calls	No technology access	✓

[a]Follow-up data collected at the end of weeks 15 and 27 as well (for both arms of the study).

[b]AI4DM: Artificial Intelligence for Diabetes Management.

[c]Study activity present.

Explanation for Choice of Comparators

The AI4DM intervention is designed to evaluate the feasibility and preliminary efficacy of a web-based diabetes self-management program for people with disabilities. Participants will either be assigned to the intervention group, which includes telehealth coaching calls, a technology package, and access to diabetes educational content, or an attention control group, which will receive the same number of telecoaching calls at the same frequency as the intervention group. These calls generally serve as courtesy calls or general wellness calls.

Eligibility Criteria

Eligible participants must meet the following inclusion criteria: (1) a diagnosis of T2DM; (2) an HbA_{1c} level of ≥8%; (3) an age of 18-65 years; (4) individuals living with a permanent physical disability such as spinal cord injury, spina bifida, multiple sclerosis, or stroke and (5) the ability to speak and read English. To screen for permanently impaired mobility, the NHANES Physical Functioning Survey [35] will be used.

Exclusion criteria include (1) the use of insulin medication for diabetes treatment; (2) current enrollment in any diabetes-related intervention; (3) severe cognitive impairment; (4) severe untreated depression in the past 6 months; (5) a major cardiac event in the past 12 months; (6) uncontrolled blood pressure; (7) resting tachycardia; (8) renal failure; (9) severe peripheral neuropathy; and (10) the unavailability of a smartphone.

Interventions

The total study duration for both groups is 12 months. The protocol includes both groups receiving weekly health coaching calls weekly for 12 weeks, and one biweekly coaching call (every other week) for 12 weeks, for a total of 18 coaching calls. The intervention group, AI4DM, will receive access to home and web-based technology and diabetes-specific educational content through a telehealth app. The attention control group will serve as an untreated comparison group for the AI4DM intervention group. Both groups will also receive 4 HbA_{1c} kits for glucose data collection.

Study Survey Packets

After enrolling in the study, participants will automatically be emailed a Health Insurance Portability and Accountability Act (HIPAA)–compliant Research Electronic Data Capture (REDCap) link to a survey packet. REDCap is a secure program developed by a collaboration between Vanderbilt University and the National Institutes of Health National Center for Research Resources that manages and stores clinical trial data. This survey packet included a demographic survey and the secondary outcome measures listed in Table 2. Participants will be asked to complete this survey packet 4 times during the 12-month study period (excluding the demographics in the first survey packet). The timepoints included baseline, 3 months, 6 months, and postintervention (12 months).

Table 2. Measures of efficacy.

Variables	Instruments	Time points
Glycemic management	HbA_{1c}[a] (clinical and primary outcome)	B,[b] 3,[c] 6,[d] P[e]
Psychological distress	Diabetes Distress Scale	B, 3, 6, P
Quality of life	Diabetes Quality of Life Measure	B, 3, 6, P
Self-efficacy	Diabetes Empowerment Scale	B, 3, 6, P
Family support	Diabetes Family Behavior Scale	B, 3, 6, P
Physical activity	Godin leisure-time exercise questionnaire	B, 3, 6, P
Dietary intake	The UK Diabetes and Diet Questionnaire	B, 3, 6, P
Medication adherence	Medication Adherence Rating Scale	B, 3, 6, P
Telehealth dashboard usability	System Usability Scale & Health Information Technology Usability Evaluation Scale	3, 6, P
Health information technology	The eHealth Literacy Scale	B, 3, 6, P
Medication and dosage	Instruments for controlling medication and dosage during the analysis of the clinical outcome	B, 3, 6, P

[a]HbA_{1c}: glycated hemoglobin.

[b]B: baseline.

[c]3: 3-month follow-up.

[d]6: 6-month follow-up.

[e]P: 12-month post–follow-up.

Welcome Call

After the first survey packet is emailed to the participants, a study team member will call the participants. The purpose of this call is to welcome them into the study and explain the study elements. During the call, the staff will inform the participant that they will receive a package within the next few days (see the section *HbA_{1c} Kits*).

HbA_{1c} Kits

All participants, regardless of study arm allocation, will receive 4 HbA_{1c} kits. The HbA_{1c} kits will be shipped from a clinical diagnostic laboratory testing company. Research personnel will have access to an account through the testing company website and will send an HbA_{1c} kit 4 times during the study duration: baseline (after the welcome call), 3 months, 6 months, and postintervention (12 months). The HbA_{1c} kit will include a testing kit and return packaging materials. Participants will be asked to complete and return the kit at their earliest convenience.

Randomization

A randomization sequence will be generated and stored within REDCap, which automatically assigns a participant to the AI4DM intervention group or the attention control group. Randomization will only occur after the baseline survey packet and baseline HbA_{1c} kit are completed.

Orientation Call

After randomization, a study health coach will be notified from REDCap that a participant has been randomized to one of the study arms and will conduct an orientation call with the participant. The purpose of this call is to introduce themselves to the participants as their primary health coach and to schedule the first weekly coaching call. The first weekly call, regardless of the study arm assignment, will be scheduled for the next calendar week.

Intervention Package

If a participant is randomized into the AI4DM intervention group, the research staff will coordinate the shipment of a technology package that will be delivered to the participant's residence within 1 to 2 days after randomization. The contents of this intervention package will include (1) an Amazon Echo, (2) a Fitbit Flex device, and (3) a wireless glucometer. Participants will also be given supplemental instructions for signing in to the mobile health (mHealth) app and device setup instructions. This package is used for intervention delivery and not for outcome measurements.

AI4DM Intervention Group Coaching Calls (First 12 Weeks)

Coaching calls for the intervention group will be guided by a prepared outline of diabetes-related content that will be delivered to the participant through the mHealth app. This content will be delivered at the beginning of each week before the coaching call. The educational content is derived from using the Partnership to Improve Diabetes Education program and delivered to the participant as multimedia content [36]. Other health-related areas covered during the coaching call will include nutrition and eating habits, exercise and PA, glucose monitoring, and medication adherence. Questions outside the scope of the health coaching content will be provided to the study clinician or registered dietician. If the study team determines that the questions require collecting a participant's detailed medical profile, the participant will be guided to communicate with their primary care physician. Finally, the health coach will address other health-related questions that the participant may have. For each call, the health coach will be able to record notes in the telehealth app regarding topics discussed with the participant

for future calls, as needed. Coaching calls are expected to last for up to 60 minutes.

AI4DM Intervention Group Coaching Calls (Second 12 Weeks)

Biweekly coaching calls during the following 12 weeks will cover nutrition and eating habits, exercise and PA, glucose monitoring, medication adherence, general well-being, and Partnership to Improve Diabetes Education content, as needed.

Attention Control Group Coaching Call

The coaching content for the attention control group will refrain from any diabetes-specific content; rather, the health coach will only focus on general well-being. This will apply to all phone calls during weekly and biweekly coaching calls.

Exit Interviews

After the study duration, up to 30 participants from the AI4DM intervention group will be contacted for a follow-up interview to obtain their experiences and feedback with the AI4DM telehealth platform. These interviews will be conducted virtually.

Outcome Measures

Primary and secondary outcome measures will be assessed at baseline, 3 months, 6 months, and postintervention (12 months). The primary clinical outcome measure is HbA_{1c} with the secondary outcome measures described in Table 2.

Data Collection Methods

HbA_{1c} Collection

HbA_{1c} kits will be distributed and received by a clinical at-home laboratory testing service. Study personnel will use the company's web-based resources to ship at-home test kits to all participants. The test kit will contain all necessary items to collect, prepare, and mail dried blood specimens to the laboratory for testing. Upon receiving the kit, the testing company will report the values through their network, and study personnel will obtain the values and record them directly into REDCap.

All other measures, including demographic data and secondary outcome measures, will be retrieved and automatically stored through electronic surveys delivered by REDCap. All self-reported items within the questionnaires will be required to prevent missing data. The questionnaire packet will be delivered electronically to the participants at 4 time points during the study (Table 2).

Psychological Distress

To measure psychological distress, participants will complete the Diabetes Distress Scale (DDS). This 17-item questionnaire assesses diabetes-related emotional distress using Likert-style questions for the previous month. The DDS has been shown to be a valid and reliable tool for measuring diabetes-related emotional distress [37,38].

Quality of Life

Participants will complete the Diabetes Quality of Life Measure, which is a 15-item questionnaire asking about perceptions of one's ability to manage their diabetes in conjunction with other life areas [39].

Self-efficacy

To measure psychosocial self-efficacy in diabetes management, participants will complete the Diabetes Empowerment Scale Short Form (DES-SF). The DES-SF is an 8-item questionnaire asking about attitudes toward diabetes and the ability to successfully manage diabetes. The DES-SF has been shown to be a valid and reliable measure of psychosocial self-efficacy [40].

Family Support

Participants will complete the Diabetes Social Support Questionnaire, which is a 52-item questionnaire that asks questions related to familial support for individuals with diabetes [41]. This questionnaire was originally designed for adolescents with diabetes; however, the original version was modified to reflect questions appropriate for adults. Thus, the Diabetes Social Support Questionnaire used will be a 33-item questionnaire.

Physical Activity

To measure PA, participants will complete the Godin Leisure-Time Exercise Questionnaire. This short questionnaire asks three questions related to strenuous, moderate, and light exercises performed during the past seven days [42].

Dietary Intake

Participants will complete the UK Diabetes and Diabetes Questionnaire to assess nutrition and dietary behaviors within the past month [43]. This 24-item questionnaire includes foods that are common in the United Kingdom; therefore, those items that are specific to the United Kingdom will be replaced with items equivalent in the United States to reduce confusion for participants.

Medication Adherence

To measure medication adherence, participants completed the Medication Adherence Rating Scale. The Medication Adherence Rating Scale is a general, 10-item binary questionnaire that asks questions related to regularly taking medication [44].

Health Information Technology Literacy

Participants will complete the eHealth Literacy Scale, which is an 8-item survey that measures perceived knowledge, comfort, and skill when using technology to address overall health [45].

Telehealth Dashboard Usability

To measure the usability of the telehealth dashboard, participants will complete the System Usability Scale and the Health Information Usability Evaluation Scale. These Likert scales include items asking about the dashboard's effectiveness (ability to complete tasks), efficiency (level of dashboard use), and satisfaction (subjective reactions to the dashboard) [46,47].

Medication and Dosage

Participants will be asked to provide current medications and dosages throughout the study duration to control medication data during the statistical analysis.

Feasibility Measures

This study will obtain measures related to the feasibility and acceptability of the AI4DM intervention on diabetes self-management. Measures will include process, resource, scientific, and management feasibility outcomes. All elements of intervention delivery will be collected, including but not limited to adherence, retention, attrition, coach and participant communication needs, staff preparation, and adverse events. Obtaining these measures will inform future considerations in the delivery of a web-based diabetes self-management program for people with disabilities.

Participant Timeline

The study duration for those enrolled in the study will be 12 months, regardless of study arm allocation.

Sample Size

A total of 90 participants will be enrolled. The sample size for this protocol is based on a primary analytic strategy of analysis of covariance, a two-sided test, type 1 error rate of 0.05, and intention-to-treat analysis with multiple imputations. Assuming a correlation between baseline and follow-up outcomes of at least 0.7, we will have 80% power to detect an effect size of 0.65.

Recruitment

The entire recruitment will be conducted on the web nationally through the National Center on Health, Physical Activity and Disability website and its associated social media. Through these mechanisms, interested individuals will be directed to a landing website page that will have promotional media content and information about the study. From there, participants will be directed to a separate link through HIPAA-compliant REDCap and complete a screening eligibility form. If deemed eligible, the participants will be sent an electronic consent form to be completed using the HIPAA-compliant REDCap. On the basis of our recruitment methods, we expect that approximately 180 individuals will be screened for eligibility.

Allocation

Participants will be randomized to the two study arms in a 1:1 allocation ratio using a computer-generated randomization procedure. The allocation sequence will be implemented after the baseline surveys, and the baseline HbA_{1c} kit has been completed by the participant. The computer-generated randomization process will be implemented in REDCap after the data from the baseline surveys and HbA_{1c} kit are entered into the REDCap database. This will trigger the allocation procedure to randomly assign participants to one of the two study arms. The health coach will be notified about the randomization through the telecoaching dashboard and will inform the participants about their randomization into the AI4DM intervention or the attention control arm during the orientation call.

Blinding (Masking)

The principal investigator and primary statistician will be blinded to the randomization of the participants into the study arms. All other study staff will be unblinded for purposes of recruitment, consent, orientation calls, welcome calls, coaching calls, and intervention package shipping. There are no circumstances in which the principal investigator or statistician will become unblinded during this protocol.

Data Management

All data collected will be entered directly into REDCap. Participants will be assigned a subject number upon enrollment in the study. Only approved study personnel will have access to the REDCap program, where data will be stored. Data checking will involve confirming that surveys, questionnaires, and HbA_{1c} values are completed.

Statistical Methods

All data will be examined for normality violations, outliers, errors, and patterns of missing values. For primary and secondary outcome measures, the sample and variables will be described using frequency distributions and appropriate summary statistics. Randomization across the study arms will be checked. If any baseline variable differs by group, it will be included as a covariate in subsequent analyses. Our primary analysis for the hypothesis that adults in the AI4DM intervention group will result in better glycemic control than the attention control group will be tested using analysis of covariance with baseline measurement as a covariate. Multiple imputations will be used to impute missing data. The study data will also explore the pattern and missing mechanism, and additional sensitivity analyses will be performed to test parametric assumptions as well as assumptions of missingness. Outliers and normality of quantitative variables will be evaluated. This study is powered to enable the estimation of effect sizes. Analysis of the clinical outcome (HbA_{1c}) will control for the impact of medication and dosage during the intervention period.

Data Monitoring

This project is a pilot feasibility and efficacy study that has duration of 12 months and only has minimal risks. Therefore, we believe that a data monitoring committee is not required. The principal investigator will be responsible for protocol fidelity and data collection throughout the study. The biostatistician will oversee data analysis in preparation for publication.

Harms

The AI4DM study will monitor all adverse events. Adverse events will be assessed for severity and causality and will be reported to the institutional review board and all other relevant regulatory bodies as needed.

Auditing

All elements of the study protocol will be evaluated at regular intervals (ie, weekly, monthly, or quarterly) to ensure proper and consistent adherence to the study design and implementation. Elements of auditing will include checklists, coaching call logs, audio recordings or coaching calls, content resource banks, telehealth platform reviews and event logs, review of participant food, PA, medication, glucose entries, time spent on the platform, and team meetings to discuss participant progress and protocol adherence.

Research Ethics Approval

All proposed elements of this protocol will be approved by the university's institutional review board before beginning the study.

Protocol Amendments

Any changes deemed necessary by the principal investigator will be submitted as amendments to the university's institutional review board and will only make changes after approval.

Consent or Assent

All consent processes will be conducted on the web through predetermined screening questionnaires provided through the landing website and REDCap link. If a participant is deemed eligible through the web-based process, an electronic consent form will be sent to the participant to complete. Only approved study staff will have access to complete records of the consent form.

Confidentiality

Personal information will be collected in this study. All personal information shared, such as demographic details, will be collected and stored through HIPAA-compliant REDCap. Only approved study staff will have access to securely stored personal information. All information will be subject to the university's institutional review board and the policies of affiliated entities surrounding confidentiality.

Declaration of Interests

There are no declarations of interests for all study staff for this protocol.

Ancillary and Posttrial Care

This is not applicable. No provisions for posttrial care are included in the study.

Dissemination Policy

The results of this study will be disseminated publicly through publications in peer-reviewed journals and presented at regional and national conferences.

Appendices: Biological Specimens

Blood samples will be collected for HbA_{1c} analysis at 4 different time points (baseline, 3-month, 6-month, and 12-month). The laboratory testing service will be responsible for mailing, receiving, and processing completed HbA_{1c} kits. The study personnel will not interact or have access to blood samples at the testing laboratory.

Results

The AI4DM protocol has been approved by the university's institutional review board and has been registered at ClinicalTrials.gov (trial number: NCT04927377). The mHealth app (dashboard and educational content) and landing website are currently under development by the study technical support team, and research personnel are developing the database (REDCap) that will store data and communication mechanisms (ie, emails and text notifications). We estimate that enrollment for the study will begin in October 2021.

Discussion

Although diabetes mellitus is one of the most common metabolic disorders affecting millions in the US population, this disorder has become more prevalent in people with disabilities [2]. Compared with nondisabled individuals, people with disabilities experience higher rates of diabetes, which leads to several health-related complications. In addition, people with disabilities experience and face barriers that prevent the ability to successfully manage their diabetes through exercise and healthy eating [28-31]. Therefore, the development of an inclusive diabetes management program for people with disabilities is warranted.

As multiple barriers exist that would hinder a person's ability to successfully manage diabetes, AI4DM seeks to create a sustainable, scalable, accessible, and inclusive diabetes management program for people with disabilities, which currently does not exist. This study will examine the feasibility and preliminary efficacy of AI4DM for glycemic control (HbA_{1c}) for people with disabilities using mobile and web-based apps, telehealth coaching sessions, and diabetes-related educational multimedia content. The AI4DM study will also focus on quality-of-life measures during the intervention and will include qualitative interviews following the intervention to provide a holistic evaluation of the intervention program as a viable mode of diabetes management. Next, to reduce barriers experienced by people with disabilities, the AI4DM program will be conducted completely on the web with all coaching sessions taking place over the telephone, thereby allowing all participants to manage their diabetes in a home environment. Finally, the results of this feasibility study will inform how web-based chronic disease management programs can be improved for future studies.

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Authors' Contributions

EE, AZ, and MT contributed substantially to the conception and design of the work, drafted and revised the manuscript critically for important intellectual content, were responsible for final approval of the version to be published, and agreed to be accountable for all aspects of the work.

AH, HQ, AW, and AC were responsible for the design and analysis of the work, revised the work critically for important intellectual content and for the final approval of the version to be published, and agreed to be accountable for all aspects of the work.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Peer-reviewer report from the National Institute on Disability, Independent Living, and Rehabilitation Research.
[PDF File (Adobe PDF File), 297 KB - resprot_v10i9e31689_app1.pdf]

References

1. National Diabetes Statistics Report. Centers for Disease Control and Prevention. 2017. URL: https://dev.diabetes.org/sites/default/files/2019-06/cdc-statistics-report-2017.pdf [accessed 2021-08-05]
2. Behavioral Risk Factor Surveillance System (BRFSS). Centers for Disease Control and Prevention. 2017. URL: https://www.cdc.gov/brfss/index.html [accessed 2021-08-05]
3. Wong E, Backholer K, Gearon E, Harding J, Freak-Poli R, Stevenson C, et al. Diabetes and risk of physical disability in adults: a systematic review and meta-analysis. Lancet Diabet Endocrinol 2013 Oct;1(2):106-114. [doi: 10.1016/s2213-8587(13)70046-9]
4. Gregg E, Menke A. Diabetes and disability. In: Cowie C, Casagrande S, Menke A, editors. Diabetes in America. 3rd Edition. Bethesda: National Institute of Diabetes and Digestive and Kidney Diseases (US); 2018.
5. Fox CS, Coady S, Sorlie PD, Levy D, Meigs JB, D'Agostino RB, et al. Trends in cardiovascular complications of diabetes. J Am Med Assoc 2004 Nov 24;292(20):2495-2499. [doi: 10.1001/jama.292.20.2495] [Medline: 15562129]
6. Retnakaran R, Cull CA, Thorne KI, Adler AI, Holman RR, UKPDS Study Group. Risk factors for renal dysfunction in type 2 diabetes: U.K. Prospective Diabetes Study 74. Diabetes 2006 Jun 26;55(6):1832-1839 [FREE Full text] [doi: 10.2337/db05-1620] [Medline: 16731850]
7. Nentwich MM, Ulbig MW. Diabetic retinopathy - ocular complications of diabetes mellitus. World J Diabetes 2015 Apr 15;6(3):489-499 [FREE Full text] [doi: 10.4239/wjd.v6.i3.489] [Medline: 25897358]
8. Stratton I, Adler A, Neil H, Matthews DR, Manley SE, Cull CA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. Br Med J 2000 Aug 12;321(7258):405-412 [FREE Full text] [doi: 10.1136/bmj.321.7258.405] [Medline: 10938048]
9. Zhao G, Ford E, Li C, Balluz L. Physical activity in U.S. older adults with diabetes mellitus: prevalence and correlates of meeting physical activity recommendations. J Am Geriatr Soc 2011 Jan;59(1):132-137. [doi: 10.1111/j.1532-5415.2010.03236.x] [Medline: 21226683]
10. World Health Organization. Global Report on Diabetes. Geneva: World Health Organization; 2016:1-83.
11. Ali MK, Echouffo-Tcheugui JB, Williamson DF. How effective were lifestyle interventions in real-world settings that were modeled on the Diabetes Prevention Program? Health Aff (Millwood) 2012 Jan;31(1):67-75. [doi: 10.1377/hlthaff.2011.1009] [Medline: 22232096]
12. Rollo ME, Aguiar EJ, Williams RL, Wynne K, Kriss M, Callister R, et al. eHealth technologies to support nutrition and physical activity behaviors in diabetes self-management. Diabetes Metab Syndr Obes 2016 Nov;9:381-390 [FREE Full text] [doi: 10.2147/DMSO.S95247] [Medline: 27853384]
13. Mokdad AH, Ford ES, Bowman BA, Dietz WH, Vinicor F, Bales VS, et al. Prevalence of obesity, diabetes, and obesity-related health risk factors, 2001. J Am Med Assoc 2003 Jan 01;289(1):76-79. [doi: 10.1001/jama.289.1.76] [Medline: 12503980]
14. Smyth S, Heron A. Diabetes and obesity: the twin epidemics. Nat Med 2006 Jan;12(1):75-80. [doi: 10.1038/nm0106-75] [Medline: 16397575]
15. Taggart L, Truesdale M, Dunkley A, House A, Russell AM. Health promotion and wellness initiatives targeting chronic disease prevention and management for adults with intellectual and developmental disabilities: recent advancements in type 2 diabetes. Curr Dev Disord Rep 2018 Jun 23;5(3):132-142 [FREE Full text] [doi: 10.1007/s40474-018-0142-5] [Medline: 30148038]
16. Feinman RD, Pogozelski WK, Astrup A, Bernstein RK, Fine EJ, Westman EC, et al. Dietary carbohydrate restriction as the first approach in diabetes management: critical review and evidence base. Nutrition 2015 Jan;31(1):1-13 [FREE Full text] [doi: 10.1016/j.nut.2014.06.011] [Medline: 25287761]
17. Snorgaard O, Poulsen GM, Andersen HK, Astrup A. Systematic review and meta-analysis of dietary carbohydrate restriction in patients with type 2 diabetes. BMJ Open Diabetes Res Care 2017 Feb 23;5(1):e000354 [FREE Full text] [doi: 10.1136/bmjdrc-2016-000354] [Medline: 28316796]
18. Dunkley A, Tyrer F, Doherty Y, Martin-Stacey L, Patel N, Spong R, STOP Diabetes Team. Development of a multi-component lifestyle intervention for preventing type 2 diabetes and cardiovascular risk factors in adults with intellectual disabilities. J Public Health (Oxf) 2018 Jun 01;40(2):141-150. [doi: 10.1093/pubmed/fdx067] [Medline: 28985308]

19. Emerson E, Hatton C. Addressing the health inequalities faced by people with intellectual disabilities. In: Health Inequalities and People with Intellectual Disabilities. Cambridge: Cambridge University Press; 2013:83-107.
20. Chinn D. Critical health literacy health promotion and people with intellectual disabilities. Asia-Pacific J Health Sport Phys Educ 2014 Sep 17;5(3):249-265. [doi: 10.1080/18377122.2014.940811]
21. Erickson K, Koppenhaver D, Yoder D. Literacy and adults with developmental disabilities. NCAL Technical Report TR94–15. 1994. URL: https://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.20.5666&rep=rep1&type=pdf [accessed 2021-08-05]
22. Quick guide to health literacy. Office of Disease Prevention and Health Promotion. 2019. URL: https://health.gov/our-work/health-literacy/health-literacy-online [accessed 2021-08-05]
23. Berkman N, Sheridan S, Donahue K, Halpern DJ, Viera A, Crotty K, et al. Health literacy interventions and outcomes: an updated systematic review. Evid Rep Technol Assess (Full Rep) 2011 Mar(199):1-941. [Medline: 23126607]
24. Gazmararian JA, Williams MV, Peel J, Baker DW. Health literacy and knowledge of chronic disease. Patient Edu Counsel 2003 Nov;51(3):267-275. [doi: 10.1016/S0738-3991(02)00239-2]
25. Kim S, Love F, Quistberg DA, Shea JA. Association of health literacy with self-management behavior in patients with diabetes. Diabetes Care 2004 Dec 23;27(12):2980-2982. [doi: 10.2337/diacare.27.12.2980] [Medline: 15562219]
26. Schillinger D, Grumbach K, Piette J, Wang F, Osmond D, Daher C, et al. Association of health literacy with diabetes outcomes. J Am Med Assoc 2002 Jul 24;288(4):475-482. [doi: 10.1001/jama.288.4.475] [Medline: 12132978]
27. Williams MV, Baker DW, Parker RM, Nurss JR. Relationship of functional health literacy to patients' knowledge of their chronic disease. A study of patients with hypertension and diabetes. Arch Intern Med 1998 Jan 26;158(2):166-172. [doi: 10.1001/archinte.158.2.166] [Medline: 9448555]
28. Common barriers to participation experienced by people with disabilities. Centers for Disease Control and Prevention. 2019. URL: https://www.cdc.gov/ncbddd/disabilityandhealth/disability-barriers.html [accessed 2021-08-05]
29. Hall L, Colantonio A, Yoshida K. Barriers to nutrition as a health promotion practice for women with disabilities. Int J Rehabil Res 2003 Sep;26(3):245-247. [doi: 10.1097/00004356-200309000-00013] [Medline: 14501578]
30. Putnam M, Geenen S, Powers L, Saxton M, Finey S, Dautel P. Health and wellness: People with disabilities discuss barriers and facilitators to well being. J Rehab 2003;69(1):37-45 [FREE Full text]
31. Rimmer JH, Riley B, Wang E, Rauworth A, Jurkowski J. Physical activity participation among persons with disabilities: barriers and facilitators. Am J Prev Med 2004 Jun;26(5):419-425. [doi: 10.1016/j.amepre.2004.02.002] [Medline: 15165658]
32. Carroll DC, Stevens A, Sloan M, Lullo C, Visser S, Fox M, et al. Vital signs: disability and physical activity - United States, 2009-2012. Morbidity and Mortality Weekly Report (MMWR). 2014. URL: https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6318a5.htm [accessed 2021-08-05]
33. Altman B, Bernstein A. Disability and Health in the United States, 2001–2005. Hyattsville, MD: National Center for Health Statistic; 2008.
34. Zengul AG, Evans E, Hall A, Qu H, Willig A, Cherrington A, et al. Telehealth behavioral intervention for diabetes management in adults with physical disabilities: intervention fidelity protocol for a randomized controlled trial. JMIR Res Protoc 2021 Sep 10;10(9):e31695 [FREE Full text] [doi: 10.2196/31695]
35. Bowen P, Lee L, Martin M, Clay O. Depression and physical functioning among older Americans with diabesity: NHANES 2009-2010. J Am Assoc Nurse Pract 2017 Feb;29(2):70-76. [doi: 10.1002/2327-6924.12393] [Medline: 27472244]
36. Wolff K, Chambers L, Bumol S, White RO, Gregory BP, Davis D, et al. The PRIDE (Partnership to Improve Diabetes Education) Toolkit: Development and evaluation of novel literacy and culturally sensitive diabetes education materials. Diabetes Educ 2016 Feb 07;42(1):23-33 [FREE Full text] [doi: 10.1177/0145721715620019] [Medline: 26647414]
37. Polonsky WH, Fisher L, Earles J, Dudl RJ, Lees J, Mullan J, et al. Assessing psychosocial distress in diabetes: development of the diabetes distress scale. Diabetes Care 2005 Mar 25;28(3):626-631. [doi: 10.2337/diacare.28.3.626] [Medline: 15735199]
38. Fisher L, Glasgow RE, Mullan JT, Skaff MM, Polonsky WH. Development of a brief diabetes distress screening instrument. Ann Fam Med 2008 May 01;6(3):246-252 [FREE Full text] [doi: 10.1370/afm.842] [Medline: 18474888]
39. The DCCT Research Group. Reliability and validity of a diabetes quality-of-life measure for the diabetes control and complications trial (DCCT). Diabetes Care 1988 Oct;11(9):725-732. [doi: 10.2337/diacare.11.9.725] [Medline: 3066604]
40. Anderson RM, Funnell MM, Fitzgerald JT, Marrero DG. The Diabetes Empowerment Scale: a measure of psychosocial self-efficacy. Diabetes Care 2000 Jun 01;23(6):739-743 [FREE Full text] [doi: 10.2337/diacare.23.6.739] [Medline: 10840988]
41. La Greca AM, Bearman K. The diabetes social support questionnaire-family version: evaluating adolescents' diabetes-specific support from family members. J Pediatr Psychol 2002 Dec;27(8):665-676. [doi: 10.1093/jpepsy/27.8.665] [Medline: 12403857]
42. Godin G. The Godin-Shephard Leisure-Time Physical Activity Questionnaire. Health Fit J Can 2011;4(1):18-22. [doi: 10.14288/hfjc.v4i1.82]
43. England CY, Thompson JL, Jago R, Cooper AR, Andrews RC. Development of a brief, reliable and valid diet assessment tool for impaired glucose tolerance and diabetes: the UK Diabetes and Diet Questionnaire. Public Health Nutr 2016 Sep 09;20(2):191-199. [doi: 10.1017/s1368980016002275]

44. Thompson K, Kulkarni J, Sergejew A. Reliability and validity of a new Medication Adherence Rating Scale (MARS) for the psychoses. Schizoph Res 2000 May;42(3):241-247. [doi: 10.1016/s0920-9964(99)00130-9]
45. Norman CD, Skinner HA. eHEALS: The eHealth Literacy Scale. J Med Internet Res 2006 Nov;8(4):e27 [FREE Full text] [doi: 10.2196/jmir.8.4.e27] [Medline: 17213046]
46. Brooke J. SUS: A 'Quick and Dirty' usability scale. In: Usability Evaluation In Industry. Boca Raton, Florida, United States: CRC Press; 1996:4-7.
47. Schnall R, Cho H, Liu J. Health Information Technology Usability Evaluation Scale (Health-ITUES) for usability assessment of mobile health technology: validation study. JMIR Mhealth Uhealth 2018 Jan 05;6(1):e4 [FREE Full text] [doi: 10.2196/mhealth.8851] [Medline: 29305343]

Abbreviations

AI4DM: Artificial Intelligence for Diabetes Management
DES-SF: Diabetes Empowerment Scale Short Form
HbA_{1c}: glycated hemoglobin
HIPAA: Health Insurance Portability and Accountability Act
LHL: low health literacy
mHealth: mobile health
PA: physical activity
REDCap: Research Electronic Data Capture
T2DM: type 2 diabetes mellitus

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Protocol

Telehealth Behavioral Intervention for Diabetes Management in Adults With Physical Disabilities: Intervention Fidelity Protocol for a Randomized Controlled Trial

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Abstract

Background: Diabetes mellitus is a major health problem among people with physical disabilities. Health coaching has been proven to be an effective approach in terms of behavioral changes, patient self-efficacy, adherence to treatment, health service use, and health outcomes. Telehealth systems combined with health coaching have the potential to improve the quality of health care by increasing access to services. Treatment fidelity is particularly important for behavior change studies; however, fidelity protocols are inadequately administered and reported in the literature.

Objective: The aim of this study is to outline all the intervention fidelity strategies and procedures of a telecoaching intervention—artificial intelligence for diabetes management (AI4DM)—which is a randomized controlled trial to evaluate the feasibility, acceptability, and preliminary efficacy of a telehealth platform in adults with type 2 diabetes and permanent impaired mobility. AI4DM aims to create a web-based disability-inclusive diabetes self-management program. We selected the National Institutes of Health Behavior Change Consortium (NIH BCC) fidelity framework to describe strategies to ensure intervention fidelity in our research.

Methods: We have developed fidelity strategies based on the five fidelity domains outlined by the NIH BCC—focusing on study design, provider training, treatment delivery, treatment receipt, and enactment of treatment skills. The design of the study is grounded in the social cognitive theory and is intended to ensure that both arms would receive the same amount of attention from the intervention. All providers will receive standardized training to deliver consistent health coaching to the participants. The intervention will be delivered through various controlling and monitoring strategies to reduce differences within and between treatment groups. The content and structure of the study are delivered to ensure comprehension and participation among individuals with low health literacy. By constantly reviewing and monitoring participant progress and protocol adherence, we intend to ensure that participants use cognitive and behavioral skills in real-world settings to engage in health behavior.

Results: Enrollment for AI4DM will begin in October 2021 and end in October 2022. The results of this study will be reported in late 2022.

Conclusions: Developing and using fidelity protocols in behavior change studies is essential to ensure the internal and external validity of interventions. This study incorporates NIH BCC recommendations into an artificial intelligence embedded telecoaching platform for diabetes management designed for people with physical disabilities. The developed fidelity protocol can provide guidance for other researchers conducting telehealth interventions within behavioral health settings to present more consistent and reproducible research.

Trial Registration: ClinicalTrials.gov NCT04927377; http://clinicaltrials.gov/ct2/show/NCT04927377.

International Registered Report Identifier (IRRID): PRR1-10.2196/31695

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KEYWORDS

telehealth; health coaching; artificial intelligence; diabetes mellitus; intervention fidelity; mobile phone

Introduction

Background

Although diabetes mellitus (DM) is a significant problem among all populations, people with disabilities are more likely to be affected by DM. According to the 2017 Behavioral Risk Factor Surveillance System report, 23.6% of people with disabilities are diagnosed with diabetes, whereas 9% of people without a disability are diagnosed with diabetes [1]. DM can increase the overall risk of premature death and is linked to a number of complications, including heart attack, stroke, kidney failure, leg amputation, vision loss, and nerve damage [2]. Current science has enabled multiple approaches to manage type 2 diabetes (T2D) and its related complications [2-5]. Glycemic control through a combination of diet, physical activity (PA), medication adherence, and glucose monitoring have been shown to reduce glycated hemoglobin and be effective in T2D management for both the general population and people with intellectual and developmental disabilities [2,4,6,7].

Behavioral weight loss programs, such as the lifestyle interventions used in the Diabetes Prevention Program, have proven successful in DM management [8]. However, there is no accessible, inclusive, and adapted diabetes management program for people with disabilities. Programs that are not designed with people with disabilities in mind (ie, noninclusive) pose various physical, programmatic, and attitudinal barriers. To address various barriers, such as lack of time and transportation, and to reach millions of more people, several studies have successfully used technology-mediated interventions for DM management [4,6,9-11]. However, these technology-mediated intervention solutions are not inclusive and usually have static content delivered through websites, emails, or mobile apps with no personalized interaction with the client.

To address these deficiencies, we are developing a platform that combines human synchronous telecoaching with mobile health (mHealth) technologies to promote T2D self-management for people with disabilities. In this artificial intelligence (AI)–assisted, individualized, family-focused, lifestyle modification telehealth intervention (AI for DM [AI4DM]), we use an AI-embedded telecoaching dashboard to promote the fidelity of coaching sessions and reduce the workload required to personalize telecoaching.

Importance of Reporting Fidelity

Fidelity in health behavior change studies is an essential factor in ensuring that the intervention program is delivered as intended [12]. Telehealth behavior change studies usually include similar strategies to deliver the treatment, such as using guidelines or manuals, monitoring audio and video materials, and adherence to the intervention protocols. However, several systematic reviews of health behavior interventions indicate that there is inconsistency in the use of these strategies. In addition, most of these interventions did not incorporate effective fidelity protocols to monitor the validity of their research [12-16]. To report their fidelity, studies usually focus on monitoring intervention delivery but poorly report and discuss other fidelity components, such as design, training, and intervention receipt strategies to enhance intervention fidelity [17]. Inadequate reporting of fidelity can lead to misinterpretation of the results because of the increased type 1 and type 2 errors due to the residual confounding bias, which would contribute to difficulty replicating and translating findings of the study into practice [12].

The complexity of research designs, working with diverse populations, and maintaining credibility when testing the feasibility of innovative interventions are common challenges faced by behavior change studies. The methodological challenges in designing, conducting, and reporting health behavior change studies eventually led to the formation of the Treatment Fidelity Workgroup of the National Institutes of Health Behavior Change Consortium (NIH BCC) [14]. In 2004, NIH BCC published recommendations to guide and encourage researchers to incorporate treatment fidelity concepts and strategies in the field of health behavior change. The recommendations focus on five domains: study design, provider training, delivery of treatment, receipt of treatment, and enactment of treatment. These recommendations include advancing the definition, methodology, and measurement of treatment fidelity to enhance the internal and external validity of the interventions.

Considering the importance of developing and using treatment fidelity in behavioral change interventions, we aim to describe and report the fidelity protocol for the AI4DM study. AI4DM combines mHealth technologies with telecoaching sessions to create the first-ever web-based diabetes self-management program for people with disabilities. The fidelity protocol was developed to address the five domains of intervention fidelity outlined by the NIH BCC. Considering the complexity of our intervention design, the development and use of the fidelity protocol is essential to document our fidelity measures to present more consistent and reproducible research.

Methods

Overview of the Study and the Intervention Fidelity Protocol

This project aims to develop and assess a telehealth framework, AI4DM, paired with inclusive diabetes self-management content. AI4DM is grounded in the social cognitive theory (SCT) [18] and is designed to serve as a support system and communication platform among health coaches, participants with disabilities and their caregivers, and health care providers. AI4DM consists of (1) a telecoaching dashboard, (2) a participant-specific mHealth app, (3) a caregiver-specific

mHealth app, and (4) a conversational agent, Amazon Echo (Amazon).

At the center of AI4DM, there is an AI-embedded coaching dashboard. This dashboard will assist health coaches in offering consistent and personalized health coaching for participants. The AI engine will be connected to a commercial ingredient and recipe database and use a food recommendation engine to offer personalized nutrition tips that take into account a given participant's recommended diet, the participants' and caregivers' cuisine preferences, time and food availability, financial limitations, cooking skills (accessibility), and other preferences and limitations. The AI engine will also feature a rule-based expert system to offer personalized PA recommendations based on the participants' physical conditions, environmental conditions, and preferences. All data generated by the AI engine will be delivered to the participants and their caregivers after approval and tailoring from health coaches. The delivery of information to participants and caregivers will be enabled through multiple channels—smartphones (mHealth apps), conversational agents (eg, Amazon Echo), and telecoaching phone calls—thereby enhancing accessibility to the information. The design and educational content of mHealth apps will be tailored and inclusive of people with all forms of disabilities. Collectively, these AI-assisted and user-centered design features will reduce the time and effort required by health coaches and promote sustained use of the intervention by participants, eventually enabling self-management.

The primary aim of AI4DM is to evaluate the feasibility (ie, process, resource, management, and scientific feasibility), acceptability (based on surveys and interviews with participants, their caregivers, and health coaches), and preliminary efficacy of AI4DM in adults with type 2 DM (T2DM) and permanent impaired mobility. We will use a randomized controlled pilot study design in which 90 adults with T2DM and permanent impaired mobility will be randomized to the AI4DM intervention arm or an attention control arm. The entire recruitment will be conducted nationally, on the web, through the National Center on Health, Physical Activity, and Disability website, associated social media, and ResearchMatch website. The inclusion criteria were as follows: (1) diagnosis of T2DM; (2) glycated hemoglobin ≥8%; (3) 18 to 65 years of age; (4) living with a permanent physical disability such as a spinal cord injury, spina bifida, multiple sclerosis, or stroke; (5) can speak and read English; and (6) availability of a smartphone. This study was approved by the institutional review board, and all screened participants provided informed consent before enrollment.

For the intervention, each participant will be randomly assigned to one of two treatment conditions: (1) AI4DM intervention with telecoaching support and (2) attention control. We planned an active (coach contact) intervention period of 24 weeks (6 months) with 18 coaching calls during that period, followed by a passive period of 24 weeks (6 months) with only technology access to see if self-management behaviors were sustained. Table 1 presents the study design. For further information on the methods for the parent study, see the research protocol paper [19].

Table 1. The research design.

Group	Enrollment; weeks 1-2	Pretest; weeks 2-3	AI4DM[a] intervention			Posttest; weeks 52-53
			Weeks 4-15[b]	Weeks 16-27[b]	Weeks 28-51	
Intervention	✓[c]	✓	Weekly calls and technology access	Biweekly calls and technology access	Only technology access	✓
Attention control	✓	✓	Weekly courtesy calls with no technology access	Biweekly courtesy calls with no technology access	No technology access	✓

[a]AI4DM: artificial intelligence for diabetes mellitus.

[b]Follow-up data collected at the end of weeks 15 and 27 as well (for both arms of the study).

[c]Study activity present.

We have developed methodological strategies to monitor and enhance fidelity based on the NIH BCC Treatment Fidelity recommendations, focusing on *study design, provider training, treatment delivery, treatment receipt, and enactment of treatment skills* [14]. Monitoring intervention fidelity is essential to ensure the internal and external validity of the intervention.

Study Design

Overview

On the basis of the Behavior Change Consortium treatment fidelity recommendations, study designs must ensure that (1) the procedures and implementation are congruent with the presented theory and clinical practices, (2) participants receive the equal *dose* of the treatments, and (3) all procedures would address possible setbacks in implementation. Textbox 1 presents the fidelity of study design and monitoring plan for AI4DM.

Textbox 1. Fidelity of study design and monitoring plan.

Goal

- Intervention will be congruent with presented theory and practice
- Equal treatment dose will be given within and across conditions
- Addressing implementation setbacks

Description from the National Institutes of Health Behavior Change Consortium

- Operationalize treatment to optimally reflect theoretical roots; precisely define variables most relevant to "active ingredients" of the intervention
- Ensure equal treatment "dose" (measured by number, frequency, and length of contact) is adequately described and is the same for each subject within and across treatment conditions
- Address possible setbacks in implementation (eg, treatment providers dropping out)

Fidelity monitoring plan for artificial intelligence for diabetes mellitus

- Monthly review of coaching call checklist and call logs
- Quarterly review of randomly selected coaching calls
- Quarterly review of content resource bank
- Team meetings to discuss participant progress and protocol adherence
- Review of telecoaching platform and its event log
- Review of adverse event log

Ensure That the Procedures and Implementation Are Congruent With the Presented Theory and Clinical Practices

AI4DM is grounded in the SCT view that self-management is not under the complete control of an individual but rather occurs in the context of a larger social environment involving the individual [18]. Thus, AI4DM systematically focuses on improving social support (friend and family support for PA participation), self-efficacy (confidence in one's ability to be physically active in various situations), outcome expectancies for PA, and self-regulation (exercise goal setting) to understand how the intervention is effective will be systematically targeted through both the features of the app and the content used for in the app and telecoaching. The participant's app dashboard will focus on the actions the participant needs to take, such as completing blood glucose logging and nutrition logging, whereas the content will be grounded in the SCT [18].

Ensure That Participants Receive an Equal Dose of the Treatments

The attention control group will be used to provide an untreated comparison for the AI4DM intervention group and will receive phone calls from the telecoach at the same frequency as the intervention group. These *courtesy calls* are devised to ensure that both groups received the same amount of attention from the telecoach, thereby not influencing or inflating the effect size for future research. Thus, both groups will receive one weekly call for 12 weeks and one biweekly call for the next week. The AI4DM intervention and attention control groups will be exposed to the same data collection measures and protocols.

Ensure That All Procedures Would Address Possible Setbacks in Implementation

We will collect evidence on reporting and handling constraints of adverse events, serious adverse events, and clinical emergencies, as well as participant experiences, burdens, and compliance during the assessment experience and intervention. Assessment experience will be documented through participant self-reports of time to complete the baseline intake. Intervention experience will be documented by having participants self-report parameters of coaching sessions in participant logs and through an evaluation of staff logs.

Provider Training

The project team of the study has the appropriate experience and training needed for the successful completion of all the proposed activities. We have assembled a multidisciplinary team of academic, technical, and programmatic professionals that are uniquely positioned with the necessary technical, disability, diabetes, PA, nutrition, behavior change, content development, and coaching-related skills and knowledge. During the intervention, health coaches will be formally trained in a PA-, nutrition-, or nursing-related health profession and pay special attention to regular blood sugar monitoring, setting nutrition goals, and PA goals in weekly calls (up to 60 minutes). The dashboard in the developed platform will assist health coaches in offering consistent and personalized health coaching for participants. The Behavior Change Consortium recommends four strategies to monitor and improve provider training: (1) standardize training, (2) ensure provider skill acquisition, (3) minimize *drift* in provider skills, and (4) accommodate provider differences. Textbox 2 outlines the fidelity of the provider or health coach training strategies and the monitoring plan for AI4DM.

Textbox 2. Fidelity of health coach training strategies.

Goal

- Standardized training
- Ensure provider skill acquisition
- Minimize “drift” in provider skills
- Accommodate provider differences

Description from the National Institutes of Health Behavior Change Consortium

- Training must be conducted similarly for all providers
- Train providers to well-defined performance criteria
- Ensure provider skills do not decay over time
- Ensure adequate level of training in providers of different skills level, experience, or professional background

Strategies used in artificial intelligence for diabetes mellitus

- The coaches will receive American Council on Exercise health coaching training
- Review of coaching calls checklists and call logs
- Recording coaching calls
- Quarterly review of random selection of calls
- Team meetings to discuss participant progress and protocol adherence

Delivery of Treatment

Overview

Another essential strategy provided by NIH BCC is to ensure that treatment or intervention is delivered as planned. As recommended by NIH BCC, we designed our protocol to address four major goals for fidelity of treatment delivery: *control for provider differences,reduction of differences within treatment groups,ensure adherence to treatment protocols*, and *minimize contamination between conditions* [12,14] (see Textbox 3 for the fidelity of intervention delivery strategies of AI4DM).

Textbox 3. Fidelity of intervention delivery strategies.

Goal

- Control for provider differences
- Reduce differences within treatment
- Ensure adherence to treatment protocol
- Minimize contamination between treatments

Description from the National Institutes of Health Behavior Change Consortium

- Monitor and control for subjects’ perceptions of nonspecific treatment effects (eg, warmth and credibility) across conditions
- Ensure that providers in the same condition are delivering the same intervention
- Ensure that the treatments are being delivered in the way in which they were conceived with regard to content and dose
- Minimize contamination

Strategies used in artificial intelligence for diabetes mellitus

- Coaching call checklists and call logs
- Random audit of audio recording of coaching calls
- Review of randomly selected coaching sessions
- Having different supervisors to evaluate the content and coaching sessions
- Team meetings to discuss participant progress and protocol adherence
- Review of telecoaching platform and its event log

Control for Provider Differences

To deliver the intervention protocol effectively, we plan to incorporate various strategies, including reporting and monitoring participants' and health coaches' complaints, having health coaches working with participants in both arms, audiotaping coaching sessions, and auditing and monitoring of random selection of coaching calls by an expert to evaluate the sessions. Although the platform and REDCap (Research Electronic Data Capture) [20] will provide data regarding adherence and retention, an exit survey will be conducted to provide information about the satisfaction and perceptions of the participants. On the basis of the exit survey results and the data on REDCap and platform, 15 participants will be chosen to interview to ask the reason for their low-high adherence, low-high satisfaction, or dropping out.

Reduce Differences Within Treatment Groups

AI4DM, as a telecoaching platform, uses an artificial engine–embedded telecoaching dashboard to promote the fidelity of coaching sessions and reduce the workload required to personalize telecoaching. The dashboard will assist the coach in effectively preparing for and conducting calls and acting as a proxy for the participants' self-management activities if needed. While using a scripted intervention protocol and detailed coaching manuals to reduce human error, we will also use standard materials and resources scheduled for each week based on the PRIDE (Partnership to Improve Diabetes Education) toolkit that has 30 comprehensive interactive education modules [21].

All procedures for delivering treatment goals will be standardized according to the group assignment to reduce the differences within treatment groups. For the coaching sessions, health coaches will focus on four domains: healthy eating, exercise, glucose monitoring, and medication adherence. Although the attention control arm will receive phone calls from the telecoach at the same frequency as the intervention group, these *courtesy calls* will only focus on the general well-being of the participants. Besides the coaching sessions, the platform will involve an abundance of videos, graphical and textual content, and technical features to deliver the intervention effectively. We will maximize the use of short video clips and infographics, paired with appropriate alternate access strategies. Educational content will be provided through the app and reinforced through telecoaching sessions and conversational agents (Amazon Echo). Conducting weekly team meetings to discuss participant progress and protocol adherence and having different supervisors evaluate the content and coaching sessions will also help ensure adequate treatment delivery.

Ensure Adherence to Treatment Protocols

In addition to the quarterly audio recording of coaching calls, coaching call checklists and coaching call logs will be used to improve adherence to the intervention protocols. Call logs will include information regarding the calls made, attempted, missed, and voicemails. Scheduled calls and summary notes will also be recorded in these logs. Coaching call checklists are intended to remind health coaches to prepare for scheduled content delivery. The call logs and coaching checklists will be audited monthly. Moreover, a detailed scripted missed call protocol will be provided for health coaches to follow.

Minimize Contamination Between Conditions

Upon randomization, participants will be assigned to either the attention control arm or the intervention arm. The coaches will be provided with a scripted protocol for both groups. The coaches will be given standardized training and supplied with the PRIDE manual. The review of recorded phone calls and the trackable progress of the participants on the platform will act as a monitoring step to detect contamination.

Receipt of Treatment

The success of an intervention depends on its clarity and applicability. Receipt of treatment strategy focuses on the participant's ability to understand the given content and perform the related behavioral activities during the intervention. The structure of AI4DM was created according to the three goals that NIH BCC suggests: (1) ensure participant comprehension, (2) ensure participant ability to use cognitive skills, and (3) ensure participants' ability to perform behavioral skills [14].

AI4DM is developed for people with disabilities who are more prone to experiencing low health literacy (LHL) [22,23]. Similarly, older adults, people with less than a high school degree, racial and ethnic minorities, people with low-income levels, and nonnative speakers of English are most likely to experience LHL [24]. Using plain language is necessary to improve health literacy and make written and oral information easier to understand [24]. Improving health literacy among participants with LHL would be beneficial for the education, treatment, and management of chronic diseases. Therefore, all contents of the AI4DM were designed to target the reading level of fifth grade or below (Textbox 4).

In addition, participants will be counseled using techniques drawn from cognitive behavioral therapy [25]. The cognitive behavioral therapy materials in AI4DM will help the participant and caregiver to focus on motivation for change, increasing healthy behaviors (including appropriate diet and exercise), teaching positive coping strategies, and stress management skills. They will also guide the telecoach in using motivational interviewing techniques to introduce the program, assess how ready and willing the participants are to change, and help finalize relevant goals associated with the psychosocial aspects of behavior change (Textbox 4).

Textbox 4. Fidelity of receipt of treatment strategies.

Goal

- Ensure participant comprehension
- Ensure participant ability to use cognitive skills
- Ensure participant ability to perform behavioral skills

Description from the National Institutes of Health Behavior Change Consortium

- Ensure that participants understand the information provided by the intervention
- Make sure that participants are able to use the cognitive skills taught in the intervention
- Make sure that participants are able to use behavioral skills taught in the intervention

Strategies used in artificial intelligence for diabetes mellitus

- Target reading level of fifth grade or below for the content
- Review of recorded coaching sessions
- Review of participant food, physical activity, medication, and glucose journals
- Review of participant log-ins and time spent on platform
- Team meetings to discuss participant progress and protocol adherence

Enactment of Treatment Skills

According to NIH BCC, enactment of treatment skills is one of the most challenging aspects of intervention fidelity. It involves applying the proposed theories and protocols to *real-world* settings. To ensure participants' use of cognitive and behavioral skills, the content for the proposed program will be adapted from a variety of sources. The Diabetes Literacy and Numeracy Education Toolkit [26] and the PRIDE toolkit [21] will form the underlying basis for creating the content. The majority of our efforts will focus on packing the content in a highly accessible yet engaging format. We will maximize the use of short video clips and infographics, paired with appropriate alternate access strategies. Educational content will be provided through mHealth apps and reinforced through telecoaching sessions and conversational agents (Amazon Echo).

Participants in the intervention arm would also receive a wireless blood glucose monitor and a Fitbit Flex (Google LLC), which are used for intervention delivery and not for outcome measurement. This program involves an abundance of videos, graphical and textual content, and technical features such as AI-assisted dietary planning and tracking, sensor-based PA tracking, and context-aware recommendations to help participants understand and adopt the related cognitive and behavioral skills. Having access to digital content (texts and videos) and one-to-one interaction with a health coach is expected to improve the cognitive and behavioral performance of the participants. Textbox 5 presents the strategies that will be used in the AI4DM for the enactment of treatment skills.

Textbox 5. Fidelity of enactment of treatment strategies.

Goal

- Ensure participant use of cognitive skills
- Ensure participant use of behavioral skills

Description from the National Institutes of Health Behavior Change Consortium

- Ensure that participants actually use the cognitive skills provided in the intervention in appropriate life settings
- Ensure that participants actually use the behavioral skills provided in the intervention in appropriate life settings

Strategies used in artificial intelligence for diabetes mellitus

- Review of participant food, physical activity, medication, and glucose journals
- Review of participant log-ins and time spent on platform
- Team meetings to discuss participant progress and protocol adherence
- Review of coaching notes

Results

Enrollment for AI4DM began in August 2021 and will end in August 2022. The results of this study will be reported in late 2022.

Discussion

Treatment fidelity refers to strategies for monitoring and enhancing the consistency and accuracy of an intervention. Reporting treatment fidelity is an essential component to ensure that the intervention is implemented as planned [14,27]. A behavior change intervention must be consistently administered throughout the trial to obtain valid conclusions from the study. Maintaining high intervention fidelity would provide valuable information on the feasibility of the intervention in real-world settings. It can help to minimize experimenter bias and the reactivity of observations by ensuring that any changes observed during an intervention reflect the subject's behavior only [28,29]. This paper aims to present an overview of the intervention protocol for an ongoing randomized controlled trial that aims to develop and assess a telehealth platform, AI4DM, paired with inclusive diabetes self-management content. AI4DM is grounded in the SCT [18] and will be designed to serve as a support system and communication platform between health coaches, participants with disabilities, and health care providers.

This study applied treatment fidelity strategies and recommendations from NIH BCC, which includes five fidelity domains [14]. We have outlined the strategies for assessing, monitoring, and enhancing our intervention fidelity based on each of these domains. NIH BCC acts as an important and comprehensive resource for providing essential strategies to ensure the internal and external validity of health behavior change studies [30]. AI4DM will be the first web-based diabetes self-management program for people with disabilities that is accessible, inclusive, scalable, and sustainable. Therefore, by reporting the intervention fidelity protocol in accordance with NIH BCC recommendations, this paper provides guidance for other researchers conducting telehealth interventions within behavioral health settings by serving as an example to develop fidelity protocols.

Following the NIH BCC framework, we generated detailed protocols regarding the design, training, delivery, receipt, and enactment components for the management and implementation of our program. One of the challenges that we encountered was using different platforms to manage and monitor the fidelity of the intervention. Comprehensive protocols that use both an AI-assisted telecoaching platform and a data management tool, that is, REDCap, to manage and deliver the intervention. To prevent potential setbacks in the implementation of the intervention and increase the applicability of the procedures, we collaborated with our tech team before finalizing our protocols. Thus, we expected no drastic changes in the fidelity processes during the intervention.

We have observed extensive preparatory and postwork before and after a call through several of our earlier health coaching–related projects. This often involves reading call notes, search recipes, manually emailing reminders, and follow-up messages. Similarly, some studies have pointed out that variations between coaches are a major limitation for health coaching [16,31]. All AI-related features and fidelity-related features also aim to reduce the time required by the coaches, thereby leading to scalability and sustainability of self-management behavior by the participants. However, including telecoaching sessions in the intervention introduces some challenges, such as *therapist drift*, which can lead to lower treatment engagement. In this phenomenon, health coaches may unintentionally or unknowingly shift from the main topic by making small changes to the administration of the intervention [27,32]. In this study, we generated detailed and standardized health coaching protocols and checklists and provided standardized training to prevent potential coaching drifts and maintain intervention integrity. This will help to structure more effective coaching sessions and potentially affect the internal validity of the study. Such standardization can contribute to creating evidence-based coaching sessions that can be incorporated into other behavior change studies.

Although there is always a threat to fidelity assessment that participants can provide desirable responses to the coaches, having a protocol based on NIH BCC criteria will positively affect the study's internal or external validity, which will eventually affect the outcomes and interpretation of the results. Consistently monitoring fidelity can also provide valuable insights regarding the implementation of the intervention. Therefore, in this study, we outlined all the intervention fidelity strategies and procedures of the AI4DM project to evaluate its feasibility, acceptability, and preliminary efficacy in adults with T2DM and permanent impaired mobility.

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Authors' Contributions

AZ, EE, and MT contributed substantially to the conception and design of the work, drafted and revised the manuscript critically for important intellectual content, were responsible for final approval of the version to be published, and agreed to be accountable for all aspects of the work. AH, HQ, AW, and AC were responsible for the design and analysis of the work, revised the work critically for important intellectual content, provided final approval of the version to be published, and agreed to be accountable for all aspects of the work.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Peer-reviewer report from the National Institute on Disability, Independent Living, and Rehabilitation Research.
[PDF File (Adobe PDF File), 297 KB - resprot_v10i9e31695_app1.pdf]

References

1. Behavioral risk factor surveillance system: 2017 BRFSS Survey data and documentation. Centers for Disease Control and Prevention. 2017 Apr 27. URL: https://www.cdc.gov/brfss/annual_data/annual_2017.html [accessed 2021-08-05]
2. Diabetes. World Health Organization. URL: https://www.who.int/health-topics/diabetes#tab=tab_1 [accessed 2021-08-05]
3. Guariguata L, Whiting D, Hambleton I, Beagley J, Linnenkamp U, Shaw J. Global estimates of diabetes prevalence for 2013 and projections for 2035. Diabetes Res Clin Pract 2014 Feb;103(2):137-149. [doi: 10.1016/j.diabres.2013.11.002] [Medline: 24630390]
4. Ali MK, Echouffo-Tcheugui JB, Williamson DF. How effective were lifestyle interventions in real-world settings that were modeled on the Diabetes Prevention Program? Health Aff (Millwood) 2012 Jan;31(1):67-75. [doi: 10.1377/hlthaff.2011.1009] [Medline: 22232096]
5. Riazi H, Larijani B, Langarizadeh M, Shahmoradi L. Managing diabetes mellitus using information technology: a systematic review. J Diabetes Metab Disord 2015 Jun 3;14(1):49 [FREE Full text] [doi: 10.1186/s40200-015-0174-x] [Medline: 26075190]
6. Rollo ME, Aguiar EJ, Williams RL, Wynne K, Kriss M, Callister R, et al. eHealth technologies to support nutrition and physical activity behaviors in diabetes self-management. Diabetes Metab Syndr Obes 2016 Nov;9:381-390. [doi: 10.2147/dmso.s95247]
7. Taggart L, Truesdale M, Dunkley A, House A, Russell AM. Health promotion and wellness initiatives targeting chronic disease prevention and management for adults with intellectual and developmental disabilities: recent advancements in type 2 diabetes. Curr Dev Disord Rep 2018 Jun 23;5(3):132-142 [FREE Full text] [doi: 10.1007/s40474-018-0142-5] [Medline: 30148038]
8. Diabetes Prevention Program (DPP) Research Group. The Diabetes Prevention Program (DPP): description of lifestyle intervention. Diabetes Care 2002 Dec 01;25(12):2165-2171 [FREE Full text] [doi: 10.2337/diacare.25.12.2165] [Medline: 12453955]
9. Bian RR, Piatt GA, Sen A, Plegue MA, De Michele ML, Hafez D, et al. The effect of technology-mediated diabetes prevention interventions on weight: a meta-analysis. J Med Internet Res 2017 Mar 27;19(3):e76 [FREE Full text] [doi: 10.2196/jmir.4709] [Medline: 28347972]
10. Block G, Azar KM, Romanelli RJ, Block TJ, Hopkins D, Carpenter HA, et al. Diabetes prevention and weight loss with a fully automated behavioral intervention by email, web, and mobile phone: a randomized controlled trial among persons with prediabetes. J Med Internet Res 2015 Oct 23;17(10):e240 [FREE Full text] [doi: 10.2196/jmir.4897] [Medline: 26499966]
11. Hartz J, Yingling L, Powell-Wiley TM. Use of mobile health technology in the prevention and management of diabetes mellitus. Curr Cardiol Rep 2016 Dec 8;18(12):130. [doi: 10.1007/s11886-016-0796-8] [Medline: 27826901]
12. Sineath A, Lambert L, Verga C, Wagstaff M, Wingo BC. Monitoring intervention fidelity of a lifestyle behavioral intervention delivered through telehealth. Mhealth 2017 Aug 25;3:35 [FREE Full text] [doi: 10.21037/mhealth.2017.07.04] [Medline: 28894745]
13. Shingleton RM, Palfai TP. Technology-delivered adaptations of motivational interviewing for health-related behaviors: a systematic review of the current research. Patient Educ Couns 2016 Jan;99(1):17-35 [FREE Full text] [doi: 10.1016/j.pec.2015.08.005] [Medline: 26298219]
14. Bellg AJ, Borrelli B, Resnick B, Hecht J, Minicucci DS, Ory M, Treatment Fidelity Workgroup of the NIH Behavior Change Consortium. Enhancing treatment fidelity in health behavior change studies: best practices and recommendations from the NIH Behavior Change Consortium. Health Psychol 2004 Sep;23(5):443-451. [doi: 10.1037/0278-6133.23.5.443] [Medline: 15367063]
15. Blackman KC, Zoellner J, Berrey LM, Alexander R, Fanning J, Hill JL, et al. Assessing the internal and external validity of mobile health physical activity promotion interventions: a systematic literature review using the RE-AIM framework. J Med Internet Res 2013 Oct 04;15(10):e224 [FREE Full text] [doi: 10.2196/jmir.2745] [Medline: 24095951]
16. Willard-Grace R, Chen EH, Hessler D, DeVore D, Prado C, Bodenheimer T, et al. Health coaching by medical assistants to improve control of diabetes, hypertension, and hyperlipidemia in low-income patients: a randomized controlled trial. Ann Fam Med 2015 Mar 09;13(2):130-138 [FREE Full text] [doi: 10.1370/afm.1768] [Medline: 25755034]
17. Slaughter SE, Hill JN, Snelgrove-Clarke E. What is the extent and quality of documentation and reporting of fidelity to implementation strategies: a scoping review. Implement Sci 2015 Sep 07;10(1):129 [FREE Full text] [doi: 10.1186/s13012-015-0320-3] [Medline: 26345357]

18. Bandura A. Social cognitive theory (social learning theory). In: International Encyclopedia of Communications. Hoboken, New Jersey, United States: John Wiley & Sons, Ltd; 2008:92-95.
19. Evans E, Zengul A, Hall A, Qu H, Willig A, Cherrington A, et al. Disability-inclusive diabetes self-management telehealth program: protocol for a pilot and feasibility study. JMIR Res Protoc 2021 Sep 10;10(9):e31689 [FREE Full text] [doi: 10.2196/31689]
20. Patridge EF, Bardyn TP. Research Electronic Data Capture (REDCap). J Med Libr Assoc 2018 Jan 12;106(1):142. [doi: 10.5195/jmla.2018.319]
21. Wolff K, Chambers L, Bumol S, White RO, Gregory BP, Davis D, et al. The PRIDE (Partnership to Improve Diabetes Education) Toolkit: Development and evaluation of novel literacy and culturally sensitive diabetes education materials. Diabetes Educ 2016 Feb 07;42(1):23-33 [FREE Full text] [doi: 10.1177/0145721715620019] [Medline: 26647414]
22. Chinn D. Critical health literacy health promotion and people with intellectual disabilities. Asia-Pacific Journal of Health, Sport and Physical Education 2014 Sep 17;5(3):249-265. [doi: 10.1080/18377122.2014.940811]
23. Erickson K. Literacy and persons with developmental disabilities: why and how. paper commissioned for the EFA Global Monitoring Report. 2006. URL: https://scholar.google.com/citations?view_op=view_citation&hl=en&user=QmuhdlwAAAAJ&citation_for_view=QmuhdlwAAAAJ:aqlVkmm33-oC [accessed 2021-08-05]
24. Health Literacy Online: A guide to simplifying the user experience. U.S. Department of Health and Human Services, Office of Disease Prevention and Health Promotion. 2015. URL: https://health.gov/our-work/health-literacy/health-literacy-online [accessed 2021-08-05]
25. Rothbaum B, Meadows E, Resick P, Foy D. Cognitive-behavioral therapy. In: Foa E, Keane T, Friedman M, Cohen J, editors. Effective Treatments for PTSD: Practice Guidelines From the International Society for Traumatic Stress Studies. New York: Guilford Press; 2000:320-325.
26. Wolff K, Cavanaugh K, Malone R, Hawk V, Gregory BP, Davis D, et al. The Diabetes Literacy and Numeracy Education Toolkit (DLNET): materials to facilitate diabetes education and management in patients with low literacy and numeracy skills. Diabetes Educ 2009 Feb 09;35(2):233-245 [FREE Full text] [doi: 10.1177/0145721709331945] [Medline: 19240246]
27. Hinckley JJ, Douglas NF. Treatment Fidelity: Its importance and reported frequency in aphasia treatment studies. Am J Speech Lang Pathol 2013 May;22(2):0092. [doi: 10.1044/1058-0360(2012/12-0092)]
28. Smith SW, Daunic AP, Taylor GG. Treatment Fidelity in Applied Educational Research: Expanding the adoption and application of measures to ensure evidence-based practice. Edu Treat Child 2007;30(4):121-134. [doi: 10.1353/etc.2007.0033]
29. Schlosser R. On the importance of being earnest about treatment integrity. Augment Altern Comm 2009 Jul 12;18(1):36-44. [doi: 10.1080/aac.18.1.36.44]
30. Eaton LH, Doorenbos AZ, Schmitz KL, Carpenter KM, McGregor BA. Establishing treatment fidelity in a web-based behavioral intervention study. Nurs Res 2011;60(6):430-435 [FREE Full text] [doi: 10.1097/NNR.0b013e31823386aa] [Medline: 22048559]
31. Sharma AE, Willard-Grace R, Hessler D, Bodenheimer T, Thom DH. What happens after health coaching? Observational study 1 year following a randomized controlled trial. Ann Fam Med 2016 May 16;14(3):200-207 [FREE Full text] [doi: 10.1370/afm.1924] [Medline: 27184989]
32. Waller G. Evidence-based treatment and therapist drift. Behav Res Ther 2009 Feb;47(2):119-127. [doi: 10.1016/j.brat.2008.10.018] [Medline: 19036354]

Abbreviations

AI: artificial intelligence
AI4DM: artificial intelligence for diabetes mellitus
DM: diabetes mellitus
LHL: low health literacy
mHealth: mobile health
NIH BCC: National Institutes of Health Behavior Change Consortium
PA: physical activity
PRIDE: Partnership to Improve Diabetes Education
REDCap: Research Electronic Data Capture
SCT: social cognitive theory
T2D: type 2 diabetes
T2DM: type 2 diabetes mellitus

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Protocol

The Finding My Way UK Clinical Trial: Adaptation Report and Protocol for a Replication Randomized Controlled Efficacy Trial of a Web-Based Psychological Program to Support Cancer Survivors

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Abstract

Background: Cancer survivors frequently report a range of unmet psychological and supportive care needs; these often continue after treatment has finished and are predictive of psychological distress and poor health-related quality of life. Web-based interventions demonstrate good efficacy in addressing these concerns and are more accessible than face-to-face interventions. *Finding My Way* (FMW) is a web-based, psycho-educational, and cognitive behavioral therapy intervention for cancer survivors developed in Australia. Previous trials have demonstrated that *FMW* is acceptable, highly adhered to, and effective in reducing the impact of distress on quality of life while leading to cost savings through health resource use reduction.

Objective: This study aims to adapt the Australian *FMW* website for a UK cancer care context and then undertake a single-blinded, randomized controlled trial of *FMW UK* against a treatment-as-usual waitlist control.

Methods: To an extent, our trial design replicates the existing Australian randomized controlled trial of *FMW.* Following a comprehensive adaptation of the web resource, we will recruit 294 participants (147 per study arm) from across clinical sites in North West England and North Wales. Participants will have been diagnosed with cancer of any type in the last 6 months, have received anticancer treatment with curative intent, be aged ≥16 years, be proficient in English, and have access to the internet and an active email address. Participants will be identified and recruited through the National Institute for Health Research clinical research network. Measures of distress, quality of life, and health economic outcomes will be collected using a self-report web-based questionnaire at baseline, midtreatment, posttreatment, and both 3- and 6-month follow-up. Quantitative data will be

analyzed using intention-to-treat mixed model repeated measures analysis. Embedded semistructured qualitative interviews will probe engagement with, and experiences of using, *FMW UK* and suggestions for future improvements.

Results: The website adaptation work was completed in January 2021. A panel of cancer survivors and health care professionals provided feedback on the test version of *FMW UK*. Feedback was positive overall, although minor updates were made to website navigation, inclusivity, terminology, and the wording of the *Improving Communication* and *Sexuality and Intimacy* content. Recruitment for the clinical trial commenced in April 2021. We aim to report on findings from mid-2023.

Conclusions: Replication studies are an important aspect of the scientific process, particularly in psychological and clinical trial literature, especially in different geographical settings. Before replicating the *FMW* trial in the UK setting, content updating was required. If *FMW UK* now replicates Australian findings, we will have identified a novel and cost-effective method of psychosocial care delivery for cancer survivors in the United Kingdom.

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International Registered Report Identifier (IRRID): DERR1-10.2196/31976

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KEYWORDS

cancer; survivorship; psychosocial intervention; digital health; quality of life; protocol; mobile phone

Introduction

Background

Cancer survivorship rates in the United Kingdom have increased such that up to 57% of cancer patients in the United Kingdom can now expect to survive for 10 years [1]. However, there is regional discrepancy, and survival rates differ across geographic regions and treatment center catchment areas. Recently published screening studies suggest a prevalence of distress of up to 41.5% in adolescents and young adults [2] and 46% in adult [3] cancer populations. Anxiety, depression, and other psychological comorbidities significantly impact quality of life [4]. If left untreated, distress can escalate [5], and a pooled analysis of 163,363 cancer survivors demonstrated that distress in some cancer groups predicted higher mortality risk, even after controlling for age, sex, education, socioeconomic status, BMI, smoking, and alcohol intake [6]. Our own work in people diagnosed with the four most common cancers demonstrates that cognitive and emotional responses to diagnosis can predict distress [4] and that psychological variables, such as psychological flexibility, are predictive of distress-related outcomes *independent* of clinical and sociodemographic characteristics [7]. Unmet psychological and supportive care needs are prevalent in cancer survivors [8-11]; we found that 54% of hematological patients report five or more unmet supportive care needs [10], and 46% of colorectal patients report at least one specific psychological need [12]. Therefore, there is a crucial need to develop effective interventions to manage psychological distress in cancer survivors.

A recent review of psychological interventions for patients with cancer [13] concluded that although cognitive behavioral therapy remains the gold standard treatment choice, we need more methodologically robust research to determine efficacy and scope for implementation. There is an excess of small-scale studies where fully powered trials exploring moderators and mediators of effects are needed. Research in non–breast cancer populations is recommended, along with the inclusion of health economic outcomes, to provide powerful data for clinical service commissioners. Given the high cost and time invested in developing new intervention content and delivery formats, one effective strategy is to adapt *existing* interventions rather than waste finite resources to develop novel and competing interventions. Furthermore, replication studies are important to demonstrate consistency and generalizability of outcomes and are recommended in response to the replication crisis in psychology [14].

A recent systematic review highlighted that one of the top barriers to accessing psychosocial support identified by patients with cancer is difficulty with transport to the health service delivery center [15], although other types of access issues have been reported elsewhere. To overcome this barrier, recent research has increasingly investigated the feasibility and efficacy of web-based psychosocial interventions for patients with cancer [16]. Web-based delivery methods are also recommended to overcome the expense of delivering psychological support [17-19]. Given the recent increases in home-based internet access in the United Kingdom, especially through the rapid development and uptake of smartphone and tablet technologies [20], web-based interventions may address access issues by widening the potential pool of beneficiaries [21]. They also overcome the stigma associated with overtly seeking psychological support [22], and (as demonstrated through the current COVID-19 pandemic) are a way to ensure continuation of service where there may be barriers to continued face-to-face care [23]. Digital psychosocial interventions confer many potential benefits, including greater convenience, reduced burden on patients with cancer and caregivers, and reduced resource use and health care costs, as compared with traditional face-to-face interventions [24]. However, most clinically measurable differences associated with web-based psychosocial interventions for this population fail to meet statistical significance, a phenomenon likely attributable to study design rather than a lack of real effect [16]. In addition, there is a need to identify treatment components involving active user engagement with web-based exercises to mitigate the lack of face-to-face interaction.

One of the most promising web-based interventions for cancer survivors is *Finding My Way* (FMW), developed by Beatty et al [25] in Australia. FMW is the second iteration of a six-module, web-based, self-guided intervention, initially titled *Cancer Coping Online* [26]. It uses psycho-educational and cognitive behavioral therapy–based theoretical frameworks and includes exercises from third-wave approaches, for example, mindfulness and values clarification work exercises. Early pilot work demonstrated benefits for physical functioning and distress outcomes [18]. Although between-group differences were not replicated in a recent, larger, randomized controlled trial (RCT) [27], this trial compared the intervention group with a low-dose active control group (identical psychoeducation and video-based content), with both groups reporting reductions in distress over time. As such, the lack of significant between-group findings may be related more to the overlap of content between treatment groups rather than a lack of efficacy in the web-based intervention group. This recent RCT found significantly better emotional functioning and lowered health care use in the FMW arm, demonstrating both (1) that distress had less functional impact on quality of life and (2) health service cost reduction [27]. Adherence was also high [26]. A number of replication studies of FMW are underway across the world, and FMW has been adapted for women with advanced breast cancer [28], demonstrating the flexibility of the program for different demographic groups and clinical contexts. As such, FMW is a good candidate for effective support in the UK cancer care setting, but some adaptation was necessary before implementation.

Objective

This paper reports on our work undertaken to adapt the intervention, and the protocol for the ongoing RCT, which tests its efficacy in a UK National Health Service (NHS) setting. We aim to test (1) whether outcome effects are replicated or improved and (2) whether intervention uptake, use, and acceptability meet feasibility thresholds for implementation in standard care.

Methods

Trial Design

We will conduct a single-blinded RCT of FMW UK compared with treatment-as-usual control. Mixed methods data collection—using self-report questionnaires, quantitative clinical data extraction, and in-depth interviews—will be undertaken to investigate efficacy and acceptability. Where possible, trial design and outcomes replicate the key features of the Australian RCT of FMW by Beatty et al [27].

All aspects of study design and governance are planned to involve the expert voices of people affected by cancer as active partners in the research study. The University of Chester hosted the study with scrutiny provided by a trial steering group comprising grant coapplicants (including a cancer survivor coapplicant), the local research team, a patient, a caregiver, and a health care professional stakeholder representative. The steering group meets twice per year, with a smaller project management group meeting bimonthly to provide operational oversight. The funder peer-review report is presented in Multimedia Appendix 1.

The FMW UK Intervention

The FMW UK intervention is designed as a six-week, self-administered, modularized, web-based program. Written and video-based information about a range of cancer care topics and the provision of psychological intervention materials are supplemented with testimonials from cancer survivors sharing their experiences and advice. Interactive exercises, including worksheets, assessment tools, and prerecorded self-guided mindfulness meditations are included; these experiential components are likely to boost efficacy [27]. The modules, released one per week, address common psychosocial concerns and unmet needs among cancer survivors and are structured around (1) treatment and communication with treatment teams; (2) coping with physical symptoms and side effects; (3) managing distress; (4) challenges to identity, body image, and sexuality; (5) social support and family concerns; and (6) issues that arise after treatment. On first accessing the site, users are prompted to choose the order in which they wish to access modules to meet their self-determined need priorities. A booster module is released one month after completion, which recaps program content and signposts back to earlier modules.

Contextual Adaptation

We began our adaptation of FMW with our local research team reviewing the information provided to determine which aspects needed to change for the UK cancer care setting. This included referencing standard care pathways and services available to patients with cancer in the United Kingdom and adapting some terminology to avoid confusion. We reviewed all website content to identify Australian-specific resources and treatment information and then worked with our steering group (including academics, clinicians, and patient and caregiver representatives) to systematically identify equivalent British information and signposting resources with which to replace them. Our adaptation plan was approved by the trial steering group.

Video Content

Each module included an information video, and in the Australian version, these were recorded by either an oncologist or a psychologist. In rerecording these videos, we chose to include a wider variety of professionals, including psychologists, oncologists, surgeons, and managers of local cancer support centers with a cancer-nursing background. This change was undertaken to (1) better represent the multidisciplinary nature of cancer care in the UK setting and (2) as a tool to increase diversity and inclusivity throughout the program. These videos were scripted, including only minor edits from the original Australian content.

Although much of the content of the cancer survivor testimonial videos was applicable to a UK-based cohort, we produced a new set of videos with cancer survivors from the United Kingdom to maximize the extent to which our participants would connect and affiliate with the stories and experiences shared. Using our existing networks, advocacy groups, and advertisements placed on social media, we recruited nine cancer survivors from across North Wales and the North West of

England (Table 1) and undertook individual video-recorded interviews with each, between August and September 2020. Survivors were selected to maximize the diversity of interviews, both demographically and with regard to cancer experiences. Video interviews were unscripted but followed a standard question schedule (Textbox 1) that had been used in the development of the original Australian website and that was provided to interviewees in advance for preparation purposes. Videos were reviewed by three team members to select clips that were edited into thematically linked videos for each module.

Table 1. Characteristics of the cancer survivors who participated in video interviews for the Finding My Way UK website.

Name[a]	Gender	Age (years)	Cancer type	Time from diagnosis (years)
Janet	Female	64	Bowel	3
Martin	Male	66	Prostate	>10
Sue M	Female	56	Breast	6
Dylan	Male	47	Bladder	2
Terry	Male	74	Lung	>10
Sue H	Female	61	Breast	4
Bernadette	Female	52	Breast	1
Sophie	Female	24	Burkitt lymphoma	4
Babz	Male	31	Non-Hodgkin lymphoma	>10

[a]Participants were given the choice to use their actual names or pseudonyms.

Textbox 1. Question schedule for video interviews with cancer survivors to create the Finding My Way UK intervention content.

Question schedule

1. What issues came up for you after diagnosis (and during treatment) in terms of making decisions about treatment, or when discussing things with your medical treatment team?
2. During treatment, what was your most pressing physical need/concern?
3. During treatment, what was your most pressing emotional need/concern?
4. Some people find that many of their roles change during treatment, and that they aren't able to do the tasks and activities they usually do, which then affects the way they feel about themselves. During treatment, how did your roles change and how did this affect you?
5. During treatment, what was your most pressing social need? What surprised you?
6. What things were challenging for you with your family life?
7. If you could give one piece of advice to another person with cancer, what would it be?
8. Over the process of treatment, what was the most confusing issue for you?
9. What did you do to mark the end of your treatment?
10. What advice would you give to other cancer survivors about staying healthy?
11. Some people say that having cancer gave them an opportunity to learn something new about life or themselves. What is the one learning experience you had that you would not have had if you did not have cancer?
12. Were there any other questions you thought we should have asked?

Video interview participants (survivors and health care professionals) were reimbursed for their time and travel expenses, as is good practice for patient and public involvement in health research [29]. All participants signed a consent form to permit the ongoing use of their video content after the trial was complete. Given that these interviews took place during the COVID-19 pandemic, a rigorous health and safety assessment was undertaken, and appropriate infection control measures were implemented. Video recordings (and later editing work) were undertaken by the research team, given the difficulties inherent in commissioning this work to an external company through the intermittent implementation of COVID-19 related social distancing in the United Kingdom during this time.

Evidence Review

Given that the Australian FMW content was last updated in 2013, we reviewed all research claims made throughout the website content and conducted literature reviews to identify which claims were still upheld by recent research. We subsequently updated the references for some evidence statements and edited claims that were no longer conclusively supported by the current evidence base. In brief, this includes the following:

- De-emphasizing the strength of claims made about the benefits of emotional expression and therapeutic writing [30,31].
- Updated references in relation to benefit finding and positive adjustment [7].
- Updated reference to support our recommendation for the benefits of mindfulness-based exercises [32].
- Inclusion of more recent references in relation to the impact of dyadic influences on adjustment between patients and their partners [33] and in relation to the benefits of information on distress levels in close others of people being treated for cancer [34].
- Reframing of claims made about the benefits of religious and spiritual beliefs to confirm that these may be helpful for those with existing beliefs, but that we are not seen as advocating a change in practices or beliefs.

Web Hosting and User Testing

We commissioned an independent web design company to adapt the original FMW web-based framework for our purposes. The website was designed using *Wordpress v.5.7.1* (WordPress Foundation) and was hosted through *Kinsta*. Videos are uploaded to *YouTube* with embedded links provided at relevant points on the website. The videos are not publicly listed to prevent access outside of the trial, and the FMW UK website is restricted to only those with a username and password provided by our team.

Once an initial test website had been created, we recruited a panel of four cancer survivors and three health care professionals to provide user feedback, each of whom was financially compensated for their input. Cancer survivors were identified from our initial advertisement for video interview participants, and health care professionals (oncology and psychology-based) were identified from existing professional networks. Additional user testing was performed by the trial steering group. Where relevant, feedback was integrated into a final website update (see the *Results* section) before recruitment commencing.

Participants

Sample Size Calculation

Calculations were based on the primary outcome of change in cancer-specific distress between the two patient groups. The original FMW RCT sample size calculation [27] used a standardized effect size of 0.35 and an SD of 4 units, which equates to an absolute change in cancer distress scores of 1.4 units. This study observed a larger than expected SD and we propose a sample size based on a conservative estimate of the residual SD of 7 units accordingly (but keeping the clinically relevant difference at the aforementioned 1.4 units). The correlation between successive measurements on the same patient is assumed to be high, and so a conservative r=0.70 was used. Sample size calculations were performed assuming a paired two-tailed t test using the derived SD of the change in the primary outcome of 5.42. Assuming a patient attrition of 20% and α of .05, 294 patients (147 per study arm) are required for a statistical power of 80% [35]. We will allow up to 30% overrecruitment to mitigate the effects of missing data and to allow for at least minimal recruitment of less common cancer types.

Recruitment and Eligibility Criteria

Participants will be recruited from multiple NHS hospital sites across North West England and North Wales using the National Institute for Health Research (NIHR) Clinical Research Network (CRN) research nurses (RNs). Patients will be eligible to take part if they meet the following inclusion criteria: (a) have been diagnosed with cancer of any type in the past six months, (b) received anticancer treatment with curative intent, (c) are aged 16 years or older, (d) are sufficiently proficient in English to provide informed consent and use the program; and (e) able to access the internet and have (or be willing to set up) an email address. Patients will be ineligible or excluded if they have a severe comorbidity considered to interfere with the individual's ability to complete the requirements of the study or to provide informed consent (eg, intellectual disability or neurological impairment). Nurses will complete fortnightly screening logs to provide anonymized information on the number of patients screened, eligible, and then provided with a trial information pack to inform later potential implementation decisions.

CRN RNs will screen regular multidisciplinary team meeting records for eligible patients and identify when their next clinical appointment will be. The CRN RN will approach each patient face-to-face to tell them about the study and provide an information pack. Where no appointment is planned within the subsequent 6 weeks, or where face-to-face introduction would be otherwise problematic (eg, lack of private space to discuss the study), our protocol permits a telephone introduction to the study. At the start of recruitment, records of existing multidisciplinary team meetings will be retrospectively searched for any patients meeting the eligibility criteria, although we anticipate that the majority of our sample will be recruited through prospective recruitment over a 12-month recruitment period.

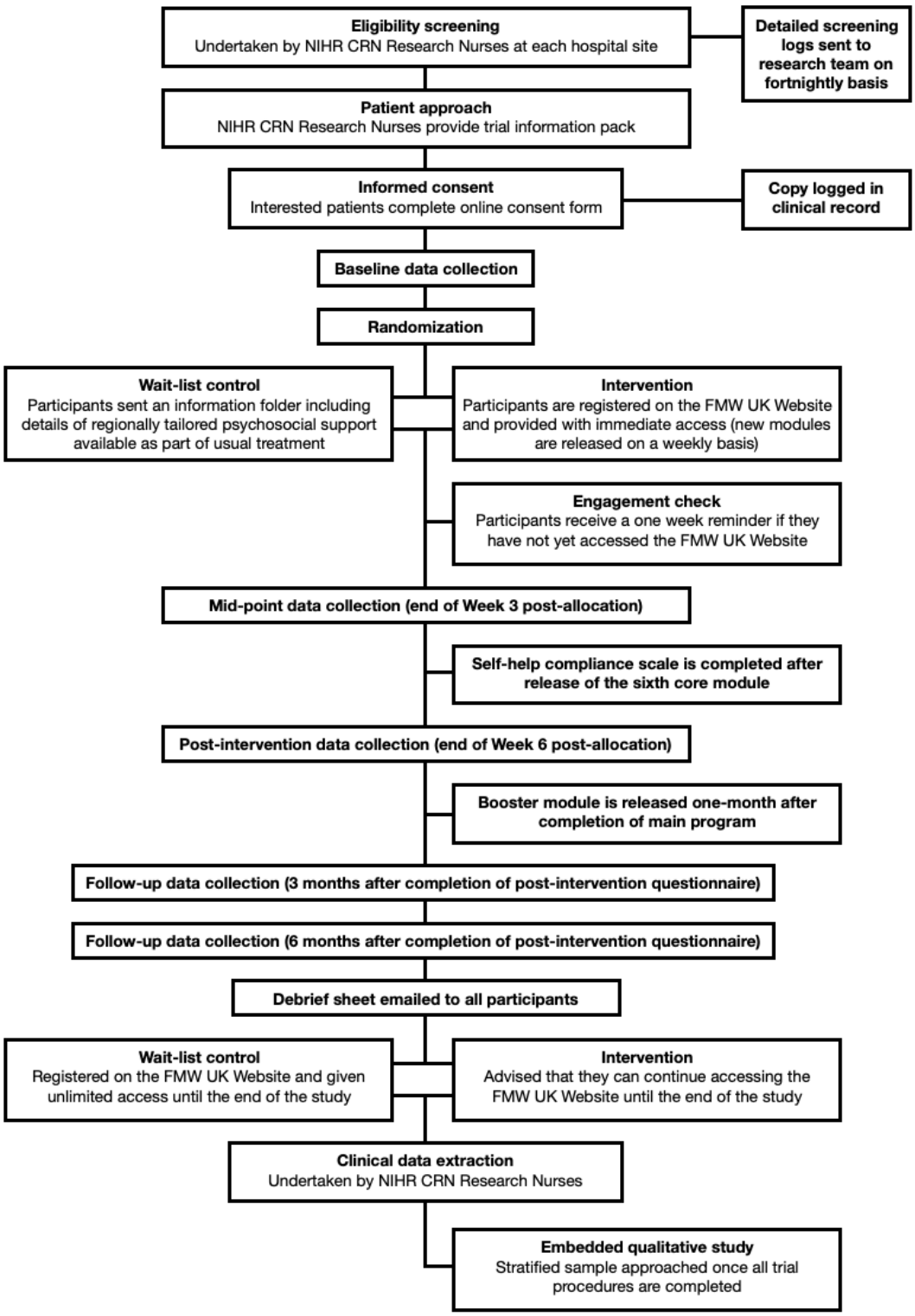
Assuming a conservative 40% consent rate [27], we estimate that 735 patients will need to be approached to reach our target sample size. We will recruit a range of cancer teams to ensure clinical diagnostic and demographic variability.

Procedure

After reading information provided by the CRN RNs, patients wishing to take part in the study can access our study recruitment website via a link in their information pack. This provides a full trial information sheet and access to a web-based consent form. Once their consent is submitted, participants are redirected immediately to the baseline survey via the *Qualtrics survey platform* (Qualtrics). Participants also will receive an automated email with a link to complete the baseline questionnaire at a later date or in a number of sittings if they prefer. Upon full completion of the baseline questionnaire, an unblinded member of the research team will complete the study arm allocation using a computerized randomization allocation system using *REDCap* software (Vanderbilt University) [36]. The randomization algorithm was set up to ensure equal numbers of participants in both the intervention and control arms, stratified by cancer diagnosis to ensure the spread of patients

across both trial arms. The randomization system was set up and is overseen by the Liverpool Clinical Trials Centre. Following allocation, participants are either emailed account details to access the FMW UK website (intervention group) or sent a PDF copy of a site-specific information pack listing existing local and national sources of psychosocial support that they can access as part of treatment as usual (control group; Figure 1). Control participants also have the option to receive a hard copy of the information pack via the post.

Figure 1. Procedure for the Finding My Way UK Clinical Trial. CRN: Clinical Research Network; FMW: Finding My Way; NIHR: National Institute for Health Research.



Those given immediate access to FMW UK are encouraged to log in within one week, study the instruction materials provided, and select the order in which they would like to receive access to the intervention modules (if no preference is given, participants receive in default numerical order). A reminder (text or phone, as preferred) is then sent if they have not logged

in during this time. Modules are then automatically released once per week; access to the booster module is also released one month after completion of the main program. Regular automated email reminders are sent as new modules are released each week.

At the point of being informed of intervention allocation, automated email reminders to complete the study questionnaires are set up through *Qualtrics*. Text messages or phone call reminders (as preferred) are sent for a period of 7 days without submission of any specific questionnaire. Questionnaires are completed at the end of the third (midintervention) and sixth (posttreatment) week, and then at 3- and 6-month follow-ups, both timed from the release of the posttreatment questionnaire. Participants are sent a debrief sheet at this point, and control arm participants are granted access to the FMW UK website. At this point, CRN RNs complete clinical data extraction from hospital records using a standard form; this includes information about the date of diagnosis, primary or recurrent diagnosis, curative or palliative treatment intent, principle treatment approach adopted (surgery, chemotherapy, radiotherapy, or watch-and-wait), date of the end of active treatment (if applicable), date of any recurrence or relapse (if applicable), date of death (if applicable), known referrals to mental health care teams since diagnosis, number of days of inpatient care since study enrollment and types of health care professionals seen during these stays, the number of outpatient visits since study enrollment and types of health care professionals seen during these visits, and any diagnostic tests conducted since study enrollment. As this study is registered on the UK NIHR CRN Portfolio, costs for most CRN RN activities (both recruitment and clinical data collection) are covered by CRN Study Support Services, with costs for additional archiving at each site reimbursed by the clinical trial research grant.

Measures

Study Outcomes

We will ask participants to self-report the following demographic characteristics: age, gender, sexuality, ethnicity, employment, education, marital status, household income, and postcode (to calculate the index of multiple deprivation). The following list of self-report questionnaires is then administered throughout the study (Table 2). We sought to use measures consistent with the original Australian FMW study to most closely replicate this previous clinical trial. Exceptions include (1) a briefer measure was identified to reduce participant burden (eg, using the Psychological Impact of Cancer Scale [37] rather than the mini-Mental Adjustment to Cancer Scale [38]); (2) an additional measure was required to assess psychological flexibility, our hypothesized mediator of the intervention effect; and (3) a UK-specific measure of health resource use was needed for context-specific health economic assessment.

Table 2. Schedule of questionnaire administration.

Variable	Baseline assessment	Midpoint assessment	Beginning of sixth module	End of Finding My Way UK	3-month follow-up	6-month follow-up
Demographic characteristics	✓[a]					
Cancer-specific distress (Post-Traumatic Stress Scale)	✓	✓		✓	✓	✓
Psychological well-being (Depression, Anxiety, and Stress Scales 21-item version)	✓	✓		✓	✓	✓
Quality of life (QLQ-C30[b])	✓	✓		✓	✓	✓
Psychological adjustment to cancer (the Psychological Impact of Cancer Scale)	✓	✓		✓	✓	✓
Health care use (the UK Cancer Costs Questionnaire)	✓	✓		✓	✓	✓
Perceived social support (the Medical Outcome Study Social Support Survey)	✓					
Emotion regulation (Difficulties in Emotion Regulation Scale)	✓					
Information-seeking preferences (the Miller Behavioral Style Scale)	✓					
Psychological flexibility (the CompACT Questionnaire)	✓	✓		✓	✓	✓
Engagement with intervention (Self-Help Compliance Scale)			✓			

[a]Assessment performed.

[b]QLQ-C30: European Organisation for Research and Treatment of Cancer Quality of Life Core Questionnaire.

Primary Outcome

The primary trial outcome variable was cancer-specific distress. For this variable, we will use the Post-Traumatic Stress Scale [39], a 17-item measure in which participants respond on a 4-point Likert scale, where responses are anchored from 0 (*not at all or only one time*) to 3 (*5 or more times per week or almost always*). The Post-Traumatic Stress Scale is associated with excellent internal consistency reliability (α=.91) [39] and has good concurrent validity, including strong positive correlations with other measures of trauma-related intrusion and avoidance, anxiety, and depression [39]. Higher scores on the Post-Traumatic Stress Scale indicate a greater severity of cancer-specific distress.

Secondary Outcomes

Psychological Well-being

The Depression, Anxiety, and Stress Scales, 21-item version [40] is a short measure of negative emotions experienced over the course of the past week for the individual. Each item is scored on a 4-point Likert scale, anchored from 0 (*did not apply to me at all*) to 3 (*applied to me very much or most of the time*). Total scores for each subscale of the Depression, Anxiety, and Stress Scales, 21-item version can be calculated, where higher scores indicate greater levels of depression, anxiety, and stress. The scale has good internal reliability (depression, α=.91; anxiety, α=.81; stress, α=.89), and concurrent validity, including strong positive correlations with other measures of depressive symptoms and anxiety [40].

Quality of Life

The European Organisation for Research and Treatment of Cancer Quality of Life Core Questionnaire (QLQ-C30) [41] is a 30-item quality of life assessment for cancer patients, which yields a global quality of life score and five functional subscale scores associated with physical, emotional, social, role, and cognitive quality of life domains. In total, 28 items are presented on a 4-point Likert scale ranging from 1 (*not at all*) to 4 (*very much*). The final two items assessing subjective assessment of overall health and quality of life are presented on a 7-point Likert scale anchored from 1 (*very poor*) to 7 (*excellent*). The global score for the QLQ-C30 is associated with good internal consistency reliability (α=.86) and has good concurrent validity, with both global quality of life and domain subscales significantly positively correlated with performance status throughout treatment [41]. A higher global score on the QLQ-C30 indicates a greater quality of life. The QLQ-C30 score can be converted into an indication of Quality-Adjusted Life Years for use in health economic analysis.

Psychological Impact of Cancer

The Psychological Impact of Cancer Scale [37] is a 12-item self-report measure of psychological adjustment to cancer. Each item is presented on a 4-point Likert scale anchored from 1 (*definitely does not apply to me*) to 4 (*definitely applied to me*). The Psychological Impact of Cancer Scale yields four subscale scores: cognitive distress, cognitive avoidance, emotional distress, and fighting spirit. Greater scores on each subscale indicate greater levels of the named construct (eg, a greater score on the Cognitive Distress subscale indicates greater levels of cognitive distress). The fighting spirit subscale will not be included because of underlying psychometric property issues [37]; the remaining three scales have reasonable internal consistency reliability (α≥.62) and good concurrent validity with longer measures of psychological adjustment to cancer [37].

The UK Cancer Costs Questionnaire

The UK Cancer Costs Questionnaire [42] is a flexible modular self-report measure of resource use by people with cancer and those with a previous diagnosis of cancer. The UK Cancer Costs Questionnaire assesses employment status, family support provided, government benefits received, and support provided by other organizations over the previous 3 months. The UK Cancer Costs Questionnaire prioritizes brevity to minimize the burden of data collection for participants. For full health care use outcome data, this self-report questionnaire is supplemented by health service resource use data extracted from clinical records and the calculation of Quality-Adjusted Life Years from the QLQ-C30.

Potential Intervention Moderator or Mediators

Rationale for Moderator and Mediator Analyses

In psychological intervention research, it is important to include measures of the hypothesized variables being acted upon to (1) verify cause-and-effect relationships on outcome improvements and (2) identify any important moderator and mediator analyses that may need to be undertaken [13]. The following measures were identified as likely moderators of the effectiveness of the intervention and have been informed in large part by a moderator analysis of the Australian FMW Trial [43].

Perceived Social Support

The Medical Outcome Study (MOS) Social Support survey [44] is a 20-item measure, with items presented as a 5-point Likert scale anchored from 1 (*none of the time*) to 5 (*all of the time*). The MOS Social Support Survey yields four subscale scores: emotional or informational support, tangible support, affectionate support, and positive social interactions. Each subscale is associated with excellent internal consistency reliability (α>.91) [44]. The MOS Social Support Survey is associated with good convergent validity with measures of family ties, family functioning, and mental health, and good divergent validity with measures of purely physical health [44]. Higher scores on individual subscales and the overall support index indicate greater social support.

Emotion Regulation

The Difficulties in Emotion Regulation Scale [45] is a 36-item self-report measure of six dimensions of emotion regulation difficulties: lack of awareness of emotional responses, lack of clarity of emotional responses, nonacceptance of emotional responses, limited access to emotion regulation strategies perceived as effective, difficulties controlling impulses when experiencing negative emotions, and difficulties engaging in goal-directed behaviors when experiencing negative emotions. Each item is scored on a 5-point Likert scale ranging from 1 (*almost never*) to 5 (*almost always*). The global difficulties in emotional regulation scale is associated with excellent internal

consistency reliability (α=.93), and each subscale is associated with good internal consistency reliability (α>.80) [45]. The Difficulties in Emotion Regulation Scale is associated with good construct validity and predictive validity [45]. Higher scores on the Difficulties in Emotion Regulation Scale indicate greater problems with emotion regulation.

Information-Seeking Preferences

The Miller Behavioral Style Scale [46] is a self-report measure of information-seeking preferences. The scale identifies individual preferences for seeking threat-related cues (monitors) versus seeking distraction to minimize exposure to threat-related cues (blunters). The scale prompts participants to imagine four stressful scenarios, each of which is followed by eight statements that describe different ways of coping with the stressor. Participants are asked to select all the statements that apply to them. The Miller Behavioral Style Scale is associated with good test-retest reliability over a 4-month period (monitoring subscale r=0.72; blunting subscale r=0.75) and high construct validity, as indicated by high correspondence with information-seeking behavior in a stress-inducing laboratory task [46]. Higher scores on the Miller Behavioral Style Scale indicate greater tendencies for monitoring information-seeking preference, rather than blunting information-seeking preference.

Self-help Compliance

The Self-Help Compliance Scale [47] is a brief measure assessing engagement with self-guided psychological interventions. The scale consists of 3 items presented on a 5-point Likert-type scale assessing the amount of information participants read (anchored from *0%* to *100%*), the number of suggestions and worksheets participants completed (anchored from *0%* to *100%*), and how much time participants spent using the program per week (anchored from *None* to *61+ minutes*). The questionnaire also includes one open question asking participants what other psychological treatment they had received during the program.

We also predict that psychological flexibility will mediate the effect of the UK-adapted FMW intervention. We operationalized psychological flexibility using CompACT [48].

Psychological Flexibility

The CompACT [48] is a 23-item self-report measure of psychological flexibility, allowing the calculation of subscale scores for (1) openness to experience, (2) behavioral awareness, and (3) valued action. Each item is presented on a 7-point Likert scale ranging from 0 (*strongly disagree*) to 6 (*strongly agree*). The CompACT has adequate internal consistency reliability (average interitem correlation, r=0.34), good convergent validity, and good discriminant validity [48]. Higher scores on CompACT indicate greater psychological flexibility.

Embedded Qualitative Interviews

We will purposively recruit 20-30 participants from the intervention group (ensuring a range of age, gender, cancer type, and website engagement) to participate in a semistructured interview 2-4 weeks after trial completion. Semistructured interviews will be used to allow flexibility in the focus of interviews for each participant [49], in-depth probing of individuals' experiences using the FMW UK website, and factors that affect acceptability and engagement. Participants willing to take part in this embedded study will be offered the option to complete the interview in person (either at the university or in their own home) or via telephone or video call, provided the chosen interview mode adheres to any government and workplace COVID-19-related social distancing rules at the time. Any travel cost will be reimbursed. Our interview topic guide will probe for participants' frequency of website use and, if applicable, reasons for low use, overall evaluation and perceived usefulness of the FMW program, and any suggestions for improvement, which are important components of acceptability and will be used to inform both refinements of the intervention materials and any planning for implementation after the trial is complete. All qualitative interviews will be audio-recorded and transcribed verbatim for later analysis.

Analysis

The analysis plan matches the Australian FMW RCT [27] as closely as possible. Members of the research team involved in the analysis will be blinded to the condition allocation until the end of the trial. First, we will conduct data cleaning to ensure that all data values are possible and plausible. Errant data entries will be deleted from the final analysis data set and missing data will be handled using either prorating or imputation methods as is (1) appropriate to the collected data and (2) congruent with the specific scoring instructions for the psychometric measure from which there is a missing response.

Descriptive statistics will be used to provide sample characteristic information and to identify any potentially prognostic demographic or clinical covariates. Inferential statistical analyses are powered to undertake mixed model repeated measures analyses to examine intervention effects on change from baseline to follow-up for each outcome, using intention-to-treat analysis. Two models will be run for each: (1) unadjusted, accounting for covariance of baseline measures of outcomes and (2) fully adjusted, controlling for all potential confounding variables assessed. Where possible and adequately powered, we will include potential confounders in our analyses and evaluate the effects of missing data using sensitivity analysis. Cohen d effect sizes reflect intervention effects, and clinically significant changes will be assessed using reliable change indices. The health care use outcome will be summarized descriptively for activity counts and cumulative costs estimated by assigning unit costs to units of activity. Cost summaries are derived from discrete payer perspectives. Generalized linear models will be used to adjust for the same confounding variables as in the efficacy analysis. All quantitative data analyses will be undertaken in R software (R Foundation for Statistical Computing) [50] where possible, with any supplementary analyses conducted in IBM SPSS as appropriate.

Qualitative data collected during the embedded qualitative interviews will be analyzed using thematic analysis [51]. In accordance with best practice guidance for thematic analysis, analysis will be undertaken by one member of the local research team with a proportion audited independently by a second researcher. A small subgroup of the trial steering group will then be convened to review the preliminary thematic structure

and provide feedback. Qualitative analysis will be performed using the NVivo software (QSR International).

Data Sharing Plan

As part of our commitment to transparent open science practices, anonymized quantitative data sets generated from the trial will be stored and made available through the Open Science Framework following the publication of trial findings. These data will include the primary and secondary outcome measures, demographic and clinical data, and any moderating or mediating variables that we ultimately include in all planned and exploratory analyses. We will not include the name of the participants' recruiting cancer centers in the interest of maintaining participant anonymity. Participants will be asked to explicitly consent for their anonymized data to be shared with other members of the research community in this way.

Given the focused nature of the qualitative interview schedule (ie, engagement with, views on, and suggestions for improving FMW UK), and the ethical risks involved in releasing qualitative data openly because of the difficulties in adequately deidentifying data, we do not currently plan to share data from this aspect of the trial. However, we will review best practice guidelines as they change over the course of the project and review this aspect of the data sharing policy at the time of project completion.

Monitoring of Adverse Events

We have risk-assessed the potential for serious adverse events from this clinical trial to be low. When a member of the research team is contacted by a participant reporting an adverse event (including elevated psychological distress), they will follow a standard protocol to assess the seriousness of the situation. In the case of disclosure of suicidality and immediate safety concerns, the researcher will contact emergency services and remain on the telephone with the participant until they arrive. In all other cases, the researcher will provide signposting to additional psychological support available as part of standard care, including to the general practitioner and clinical team. All adverse events will be reported to the principal investigator who will assess the severity of the event and report it to the study sponsor (and NHS Research Ethics Committee in the case of a serious adverse event). Provided that participants have provided consent for us to do so, we will also report the adverse event to the clinical team so that a member of the relevant care team can contact the participant to ensure that appropriate support is put into place.

Ethical Approval and Trial Registration

Ethical review was sought from the University of Chester Department of Psychology Ethics Committee to trigger agreement from the university to act as study sponsor. Full approval was obtained from the NHS Research Ethics Committee (reference: 21/WA/0029), leading to the approval of the Health Research Authority, followed by site-specific research governance approvals at each site. As one of our sites is in Wales, professional Welsh translations of study information are being provided for use at that site, in accordance with the Welsh Language Act (1993) [52]. The trial was registered on the ISRCTN (International Standard Randomized Controlled Trial Number; reference: ISRCTN14317248; date registered 08/04/2021). We have established a trial profile on the Open Science Framework (DOI 10.17605/OSF.IO/ZSHBQ; date registered: May 18, 2021) to facilitate the later sharing of data. The trial was designed in accordance with the principles for medical research involving human subjects, as laid down in the World Medical Association Declaration of Helsinki.

Results

The grant for this trial was awarded by the North West Cancer Research in September 2019. The project commenced in April 2020, but the initial progress was slower than expected because of the impact of the COVID-19 pandemic on health research in the United Kingdom [53].

User Testing of the Adapted FMW Program

All intervention adaptation work was completed by January 2021. User feedback from our panel of three health care professionals and four cancer survivor volunteers was then collated. The overall response was positive, with health care professionals noting that the program was helpful and supportive and that they would recommend it to their patients. The cancer survivors also praised the program, stating that they wished they had had access to something similar during treatment. Some minor changes were recommended, as summarized below.

First, a number of technical issues were highlighted and corrected, including the following:

- The website tutorial and resources tab were made to be more prominently visible through altered placement and graphical appearance on the webpage.
- Some navigational issues were also highlighted, with some links not working and others navigating to the wrong page.
- The embedded YouTube videos were set up as playlists, which means that each one, on completion, linked to the next video in the playlist, giving a preview to what was to come in other modules. YouTube has the option to easily disable this feature.
- The linked content was reprogrammed to launch in a new tab to prevent users from becoming lost in the underlying web architecture.

Second, user feedback highlighted some areas where content could be more inclusive. For example, some occurrences of gendered language were replaced with more inclusive language (they or them), and the skin tone of some cartoon images was varied to represent the population diversity of our target recruitment area. Minor changes were made to correct a perceived bias toward breast cancer and to be more inclusive of those without a faith belief or religion.

Third, some aspects of terminology were perceived as outdated (eg, *taking the telephone off the hook*) and were thus replaced (eg, *turning your mobile off*). Similarly, recommendations for meeting new people and maintaining social support were updated to reflect the drive toward social media over traditional media. Some minor changes were made to the language used to refer to different types of health care professionals used in the UK health care system.

Finally, changes were recommended to the flow of the *Improving Communication* page and a greater range of linked or recommended charities and support organizations were added to the support pages. One participant recommended changes to the *Sexuality and Intimacy* section related to safe sex practices during cancer treatment, which were then researched and rewritten by our team to align with current NHS guidance [54].

Clinical Trial Progress

We launched recruitment for the clinical trial in late April 2021, initially at our two largest hospital centers. The remaining sites will begin recruiting from the summer of 2021. We plan to complete recruitment by February 2022, with all follow-up quantitative data collection completed by October 2022 and all qualitative interviews completed by December 2022. Data analysis will then take place. We aim to report on the findings from the trial from spring 2023.

Discussion

Trial Status

The FMW program of psychological support has yielded promising results among recently diagnosed adult cancer survivors in Australia [25-27]. However, the adaptation work described in this protocol was necessary to make this program suitable for implementation in the United Kingdom. Including equipment, web design, videography, and patient and public reimbursement, our adaptation work has costed in the region of £25,000 (US $34,593; excluding staffing costs), taking approximately 10 months to complete. This was a considerable undertaking but still represents a very substantial cost saving compared with developing a new intervention from scratch [55,56]. These efforts were important and justified, given the positive feedback reported by our user testing group. Importantly, our approach to adaptation of the website content allowed us to adopt some elements of co-design with patient experts [57], as recommended by the UK NIHR [58]. This approach to close—and *active*—partnership work with our broader expert stakeholders will not only increase the acceptability of our adaptation [59] but will also enhance the possibility for later implementation and impact [60] across the United Kingdom, should this trial demonstrate efficacy.

The FMW UK clinical trial, which is now underway, will test the efficacy of this program in reducing cancer-specific distress, improving well-being, and reducing the need for broader health care use. As much as possible, we retained (or improved) features of the original Australian RCT to ensure that our work can act as a replication trial. Replication studies are an important aspect of the scientific process [61] and have an important place in psychological [62], broader health sciences [63], and clinical trials [64] literature. Our mixed methods design is important to the integrity of our trial and offers not only efficacy and cost-effectiveness information but also information on the sociocultural context and lived experiences of participants engaged in the intervention [65].

If our UK-based trial does indeed replicate the Australian findings, then this research study will have identified a novel and cost-effective method of psychosocial care delivery for cancer survivors in the NHS. This will of course be limited to those particular sites from which we are recruiting (ie, in North West England and North Wales), and so some additional work may need to be undertaken to explore potential barriers and appropriate pathways for rapid implementation and evaluation across other parts of the United Kingdom.

Dissemination Plans

To contribute to the transparency of our clinical trial, a full and detailed trial protocol is available as an open resource through the Open Science Framework (DOI 10.17605/OSF.IO/ZSHBQ).

Our primary scientific dissemination will be through high-quality peer-reviewed journal articles and relevant national and international conferences. We will prioritize journals and conferences that maximize dissemination to cancer care clinicians as well as psychosocial oncology researchers. Our study is registered on the NIHR CRN Cancer Portfolio, and we will work with the NIHR, NHS sites involved in recruitment, and with our existing network of charity partners to maximize dissemination opportunities. We will ensure dissemination to the public through regular newsletters to trial participants and an annual public lecture event. Our cancer survivor coinvestigator will be part of the authorship team for all of our dissemination activities, and we aim to include our additional patient, caregiver, and health care stakeholders on the trial steering group in contributing to lay summaries and public dissemination activities.

On completion of the FMW UK trial, our dedicated *YouTube* channel containing both health care professionals and edited cancer survivor videos will be publicly listed to ensure maximized societal benefit.

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Authors' Contributions

NJHW and LB conceived the idea for the study and worked with LHW and BK on leading the application for trial funding. NJHW, LHW, LB, BK, EKW, PSH, LA, NSC, RJ, and SM contributed to and were listed as coapplicants for successful grant application. NJHW is the principal investigator for the trial, with ML providing day-to-day study coordination. All authors contributed to the study design, with RJ and LHW leading the statistical analysis plan, and PSH advising on the health care use data analysis plan. EKW and LA provided additional input for the design and analysis plan for the embedded qualitative study. The manuscript was drafted by NJHW and ML. All authors commented on and approved the final manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Peer-reviewer report from North West Cancer Research (UK).
[PDF File (Adobe PDF File), 981 KB - resprot_v10i9e31976_app1.pdf]

References

1. Cancer Statistics for the UK. Cancer Research UK. 2015. URL: https://www.cancerresearchuk.org/health-professional/cancer-statistics-for-the-uk [accessed 2020-11-26]
2. Patterson P, D'Agostino NM, McDonald FE, Church TD, Costa DS, Rae CS, International AYA Cancer Distress Screening Group. Screening for distress and needs: Findings from a multinational validation of the Adolescent and Young Adult Psycho-Oncology Screening Tool with newly diagnosed patients. Psychooncology 2021 Jun 23:5757. [doi: 10.1002/pon.5757] [Medline: 34160847]
3. Carlson LE, Zelinski EL, Toivonen KI, Sundstrom L, Jobin CT, Damaskos P, et al. Prevalence of psychosocial distress in cancer patients across 55 North American cancer centers. J Psychosoc Oncol 2019;37(1):5-21. [doi: 10.1080/07347332.2018.1521490] [Medline: 30592249]
4. Hulbert-Williams N, Neal R, Morrison V, Hood K, Wilkinson C. Anxiety, depression and quality of life after cancer diagnosis: what psychosocial variables best predict how patients adjust? Psychooncology 2012 Aug;21(8):857-867. [doi: 10.1002/pon.1980] [Medline: 21695744]
5. Cimprich B. Pretreatment symptom distress in women newly diagnosed with breast cancer. Cancer Nurs 1999 Jun;22(3):185-195. [doi: 10.1097/00002820-199906000-00001] [Medline: 10376379]
6. Batty GD, Russ TC, Stamatakis E, Kivimäki M. Psychological distress in relation to site specific cancer mortality: pooling of unpublished data from 16 prospective cohort studies. Br Med J 2017 Jan 25;356:j108 [FREE Full text] [doi: 10.1136/bmj.j108] [Medline: 28122812]
7. Hulbert-Williams NJ, Storey L. Psychological flexibility correlates with patient-reported outcomes independent of clinical or sociodemographic characteristics. Support Care Cancer 2016 Jun;24(6):2513-2521. [doi: 10.1007/s00520-015-3050-9] [Medline: 26676239]
8. Morrison V, Henderson BJ, Zinovieff F, Davies G, Cartmell R, Hall A, et al. Common, important, and unmet needs of cancer outpatients. Eur J Oncol Nurs 2012 Apr;16(2):115-123. [doi: 10.1016/j.ejon.2011.04.004] [Medline: 21555246]
9. Watson E, Shinkins B, Frith E, Neal D, Hamdy F, Walter F, et al. Symptoms, unmet needs, psychological well-being and health status in survivors of prostate cancer: implications for redesigning follow-up. BJU Int 2016 Jun;117(6B):10-19. [doi: 10.1111/bju.13122] [Medline: 25818406]
10. Swash B, Bramwell R, Hulbert-Williams NJ. Unmet psychosocial supportive care needs and psychological distress in haematological cancer survivors: The moderating role of psychological flexibility. J Context Behav Sci 2017 Apr;6(2):187-194. [doi: 10.1016/j.jcbs.2017.02.005]
11. Vu JV, Matusko N, Hendren S, Regenbogen SE, Hardiman KM. Patient-reported unmet needs in colorectal cancer survivors after treatment for curative intent. Dis Colon Rectum 2019 Jul;62(7):815-822 [FREE Full text] [doi: 10.1097/DCR.0000000000001326] [Medline: 31188182]
12. Sutton PA, Bourdon-Pierre R, Smith C, Appleton N, Lightfoot T, Gabriel C, et al. Evaluating unmet needs in patients undergoing surgery for colorectal cancer: a patient reported outcome measures study. Colorectal Dis 2019 Jul;21(7):797-804. [doi: 10.1111/codi.14599] [Medline: 30828949]
13. Hulbert-Williams NJ, Beatty L, Dhillon HM. Psychological support for patients with cancer: evidence review and suggestions for future directions. Curr Opin Support Palliat Care 2018 Sep;12(3):276-292. [doi: 10.1097/SPC.0000000000000360] [Medline: 30074924]
14. Open Science Collaboration. PSYCHOLOGY. Estimating the reproducibility of psychological science. Science 2015 Aug 28;349(6251):aac4716 [FREE Full text] [doi: 10.1126/science.aac4716] [Medline: 26315443]
15. Dilworth S, Higgins I, Parker V, Kelly B, Turner J. Patient and health professional's perceived barriers to the delivery of psychosocial care to adults with cancer: a systematic review. Psychooncology 2014 Jun;23(6):601-612. [doi: 10.1002/pon.3474] [Medline: 24519814]

16. Bártolo A, Pacheco E, Rodrigues F, Pereira A, Monteiro S, Santos IM. Effectiveness of psycho-educational interventions with telecommunication technologies on emotional distress and quality of life of adult cancer patients: a systematic review. Disabil Rehabil 2019 Apr;41(8):870-878. [doi: 10.1080/09638288.2017.1411534] [Medline: 29219027]
17. Griffiths KM, Farrer L, Christensen H. The efficacy of internet interventions for depression and anxiety disorders: a review of randomised controlled trials. Med J Aust 2010 Jun 07;192(S11):4-11. [doi: 10.5694/j.1326-5377.2010.tb03685.x] [Medline: 20528707]
18. Beatty L, Binnion C. A systematic review of predictors of, and reasons for, adherence to online psychological interventions. Int J Behav Med 2016 Dec;23(6):776-794. [doi: 10.1007/s12529-016-9556-9] [Medline: 26957109]
19. Beatty L, Koczwara B, Wade T. 'Cancer Coping Online': A pilot trial of a self-guided CBT internet intervention for cancer-related distress. E-J Appl Psychol 2011 Dec 20;7(2):17-25 [FREE Full text]
20. Online Nation. Ofcom. 2020. URL: https://www.ofcom.org.uk/__data/assets/pdf_file/0027/196407/online-nation-2020-report.pdf [accessed 2021-08-10]
21. Hughes MC, Gorman JM, Ren Y, Khalid S, Clayton C. Increasing access to rural mental health care using hybrid care that includes telepsychiatry. J Rur Ment Health 2019 Jan;43(1):30-37. [doi: 10.1037/rmh0000110]
22. Wallin E, Maathz P, Parling T, Hursti T. Self-stigma and the intention to seek psychological help online compared to face-to-face. J Clin Psychol 2018 Jul;74(7):1207-1218. [doi: 10.1002/jclp.22583] [Medline: 29315545]
23. Fisk M, Livingstone A, Pit SW. Telehealth in the Context of COVID-19: Changing perspectives in Australia, the United Kingdom, and the United States. J Med Internet Res 2020 Jun 09;22(6):e19264 [FREE Full text] [doi: 10.2196/19264] [Medline: 32463377]
24. Andersson G, Titov N. Advantages and limitations of Internet-based interventions for common mental disorders. World Psychiatry 2014 Feb;13(1):4-11 [FREE Full text] [doi: 10.1002/wps.20083] [Medline: 24497236]
25. Beatty L, Kemp E, Wade T, Koczwara B, Finding My Way study investigators. Finding My Way: protocol of a randomised controlled trial evaluating an internet self-help program for cancer-related distress. BMC Cancer 2015 Apr 30;15:328 [FREE Full text] [doi: 10.1186/s12885-015-1322-x] [Medline: 25924674]
26. Beatty L, Kemp E, Binnion C, Turner J, Milne D, Butow P, et al. Uptake and adherence to an online intervention for cancer-related distress: older age is not a barrier to adherence but may be a barrier to uptake. Support Care Cancer 2017 Jun;25(6):1905-1914. [doi: 10.1007/s00520-017-3591-1] [Medline: 28155018]
27. Beatty L, Kemp E, Coll JR, Turner J, Butow P, Milne D, et al. Finding My Way: results of a multicentre RCT evaluating a web-based self-guided psychosocial intervention for newly diagnosed cancer survivors. Support Care Cancer 2019 Jul;27(7):2533-2544. [doi: 10.1007/s00520-018-4526-1] [Medline: 30411239]
28. Beatty L, Koczwara B, Butow P, Turner J, Girgis A, Schofield P, et al. Development and usability testing of a web-based psychosocial intervention for women living with metastatic breast cancer: Finding My Way-Advanced. J Cancer Surviv 2021 Jun;15(3):403-409. [doi: 10.1007/s11764-021-01019-5] [Medline: 33723741]
29. Bortoli S. Reaching Out: A practical guide to being inclusive in public involvement in health research - Lessons learnt from the Reaching Out programme. NIHR resource for public involvement. 2021. URL: https://tinyurl.com/ydxzs3ws [accessed 2021-08-10]
30. Merz EL, Fox RS, Malcarne VL. Expressive writing interventions in cancer patients: a systematic review. Health Psychol Rev 2014;8(3):339-361. [doi: 10.1080/17437199.2014.882007] [Medline: 25053218]
31. Zachariae R, O'Toole MS. The effect of expressive writing intervention on psychological and physical health outcomes in cancer patients--a systematic review and meta-analysis. Psychooncology 2015 Nov;24(11):1349-1359 [FREE Full text] [doi: 10.1002/pon.3802] [Medline: 25871981]
32. Piet J, Würtzen H, Zachariae R. The effect of mindfulness-based therapy on symptoms of anxiety and depression in adult cancer patients and survivors: a systematic review and meta-analysis. J Consult Clin Psychol 2012 Dec;80(6):1007-1020. [doi: 10.1037/a0028329] [Medline: 22563637]
33. Wadhwa D, Burman D, Swami N, Rodin G, Lo C, Zimmermann C. Quality of life and mental health in caregivers of outpatients with advanced cancer. Psychooncology 2013 Feb;22(2):403-410. [doi: 10.1002/pon.2104] [Medline: 22135229]
34. Lambert SD, Hulbert-Williams N, Belzile E, Ciampi A, Girgis A. Beyond using composite measures to analyze the effect of unmet supportive care needs on caregivers' anxiety and depression. Psychooncology 2018 Jun;27(6):1572-1579. [doi: 10.1002/pon.4696] [Medline: 29508503]
35. Borm GF, Fransen J, Lemmens WA. A simple sample size formula for analysis of covariance in randomized clinical trials. J Clin Epidemiol 2007 Dec;60(12):1234-1238. [doi: 10.1016/j.jclinepi.2007.02.006] [Medline: 17998077]
36. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009 Apr;42(2):377-381 [FREE Full text] [doi: 10.1016/j.jbi.2008.08.010] [Medline: 18929686]
37. Hulbert-Williams N, Hulbert-Williams L, Whelen L, Mulcare H. The Psychological Impact of Cancer (PIC) Scale: development and comparative psychometric testing against the Mini-MAC Scale in UK and Australian cancer survivors. J Psychosoc Oncol Res Pract 2019;1(2):e8. [doi: 10.1097/OR9.0000000000000008]
38. Watson M, Law M, Santos MD, Greer S, Baruch J, Bliss J. Mini-mental adjustment to cancer scale. J Psychosoc Oncol 1994;12(3):33-46. [doi: 10.1037/t29737-000]

39. Foa EB, Riggs DS, Dancu CV, Rothbaum BO. Reliability and validity of a brief instrument for assessing post-traumatic stress disorder. J Trauma Stress 1993 Oct;6(4):459-473. [doi: 10.1007/bf00974317]
40. Lovibond PF, Lovibond SH. The structure of negative emotional states: comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. Behav Res Ther 1995 Mar;33(3):335-343. [doi: 10.1016/0005-7967(94)00075-u] [Medline: 7726811]
41. Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst 1993 Mar 3;85(5):365-376. [Medline: 8433390]
42. UK Cancer Costs Questionnaire. The University of Edinburgh. 2021. URL: https://blogs.ed.ac.uk/ukcc/ [accessed 2020-05-12]
43. Beatty L, Kemp E, Turner J, Butow P, Milne D, Yates P, et al. Moderators of intervention efficacy for Finding My Way: A web-based psychosocial intervention for cancer-related distress. Support Care Cancer 2021 Jun 17:06291. [doi: 10.1007/s00520-021-06291-w] [Medline: 34142280]
44. Sherbourne CD, Stewart AL. The MOS social support survey. Soc Sci Med 1991;32(6):705-714. [doi: 10.1016/0277-9536(91)90150-b] [Medline: 2035047]
45. Gratz K, Roemer L. Multidimensional assessment of emotion regulation and dysregulation: development, factor structure, and initial validation of the difficulties in emotion regulation scale. J Psychopathol Behav Assess 2008 Oct 17;30(4):315 [FREE Full text] [doi: 10.1007/s10862-008-9102-4]
46. Miller SM. Monitoring and blunting: validation of a questionnaire to assess styles of information seeking under threat. J Pers Soc Psychol 1987 Feb;52(2):345-353. [doi: 10.1037//0022-3514.52.2.345] [Medline: 3559895]
47. Thiels C, Schmidt U, Troop N, Treasure J, Garthe R. Compliance with a self-care manual in guided self-change for bulimia nervosa. Eur Eat Disorders Rev 2001 Jul;9(4):255-262. [doi: 10.1002/erv.395]
48. Francis AW, Dawson DL, Golijani-Moghaddam N. The development and validation of the Comprehensive assessment of Acceptance and Commitment Therapy processes (CompACT). J Context Behav Sci 2016 Jul;5(3):134-145. [doi: 10.1016/j.jcbs.2016.05.003]
49. Howitt D. Introduction to Qualitative Research Methods in Psychology (3rd Ed). London UK: Pearson; 2016:1-600.
50. R Development Core Team. R: A language and environment for statistical computing. The R Foundation, Vienna, Austria. URL: https://www.r-project.org/ [accessed 2021-08-10]
51. Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol 2006 Jan;3(2):77-101. [doi: 10.1191/1478088706qp063oa]
52. Chapter 38. Welsh Language Act 1993. URL: https://www.legislation.gov.uk/ukpga/1993/38/pdfs/ukpga_19930038_en.pdf [accessed 2021-07-08]
53. Thornton J. Clinical trials suspended in UK to prioritise Covid-19 studies and free up staff. Br Med J 2020 Mar 23;368:m1172. [doi: 10.1136/bmj.m1172] [Medline: 32205354]
54. What happens during chemotherapy. National Health Service. URL: https://www.nhs.uk/conditions/chemotherapy/what-happens/ [accessed 2021-05-12]
55. Lewis BA, Williams DM, Neighbors CJ, Jakicic JM, Marcus BH. Cost analysis of internet vs. Print interventions for physical activity promotion. Psychol Sport Exerc 2010 May 1;11(3):246-249 [FREE Full text] [doi: 10.1016/j.psychsport.2009.10.002] [Medline: 20401164]
56. Ruby A, Marko-Holguin M, Fogel J, Van Voorhees BW. Economic analysis of an internet-based depression prevention intervention. J Ment Health Policy Econ 2013 Sep;16(3):121-130 [FREE Full text] [Medline: 24327482]
57. Bate P, Robert G. Experience-based design: from redesigning the system around the patient to co-designing services with the patient. Qual Saf Health Care 2006 Oct;15(5):307-310 [FREE Full text] [doi: 10.1136/qshc.2005.016527] [Medline: 17074863]
58. Going the extra mile: Improving the nation's health and wellbeing through public involvement in research. NIHR Open Res. URL: https://www.nihr.ac.uk/documents/about-us/our-contribution-to-research/how-we-involve-patients-carers-and-the-public/Going-the-Extra-Mile.pdf [accessed 2021-08-10]
59. Movsisyan A, Arnold L, Evans R, Hallingberg B, Moore G, O'Cathain A, et al. Adapting evidence-informed complex population health interventions for new contexts: a systematic review of guidance. Implement Sci 2019 Dec 17;14(1):105 [FREE Full text] [doi: 10.1186/s13012-019-0956-5] [Medline: 31847920]
60. Greenhalgh T, Jackson C, Shaw S, Janamian T. Achieving research impact through co-creation in community-based health services: literature review and case study. Milbank Q 2016 Jun;94(2):392-429 [FREE Full text] [doi: 10.1111/1468-0009.12197] [Medline: 27265562]
61. Lamal P. On the importance of replication. J Soc Behav Personal 1990;5(4):35 [FREE Full text]
62. Simons DJ. The value of direct replication. Perspect Psychol Sci 2014 Jan;9(1):76-80. [doi: 10.1177/1745691613514755] [Medline: 26173243]
63. Collins FS, Tabak LA. Policy: NIH plans to enhance reproducibility. Nature 2014 Jan 30;505(7485):612-613 [FREE Full text] [doi: 10.1038/505612a] [Medline: 24482835]
64. Shao J, Chow S. Reproducibility probability in clinical trials. Stat Med 2002 Jun 30;21(12):1727-1742. [doi: 10.1002/sim.1177] [Medline: 12111908]

65. Shaw RL, Larkin M, Flowers P. Expanding the evidence within evidence-based healthcare: thinking about the context, acceptability and feasibility of interventions. Evid Based Med 2014 Dec;19(6):201-203. [doi: 10.1136/eb-2014-101791] [Medline: 24799447]

Abbreviations

CRN: Clinical Research Network
FMW: Finding My Way
ISRCTN: International Standard Randomized Controlled Trial Number
MOS: Medical Outcome Study
NHS: National Health Service
NIHR: National Institute for Health Research
QLQ-C30: European Organisation for Research and Treatment of Cancer Quality of Life Core Questionnaire
RCT: randomized controlled trial
RN: research nurse

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Protocol

A Culturally Sensitive Social Support Intervention for Chinese American Breast Cancer Survivors (Joy Luck Academy): Protocol for a Randomized Controlled Trial

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Abstract

Background: Breast cancer is the most prevalent type of cancer among Asian American women. Chinese American immigrant breast cancer survivors face unique challenges because of cultural and socioecological factors. They report emotional distress and the need for social, emotional, and spiritual support. However, culturally and linguistically appropriate information for managing survivorship health care is often unavailable.

Objective: To improve the health outcomes for this underserved and understudied population, we developed, designed, and launched a randomized controlled trial to test the health benefits of a culturally sensitive social support intervention (Joy Luck Academy). In this paper, we describe the research protocol.

Methods: This randomized controlled trial will enroll Chinese-speaking, stage 0 to 3 breast cancer survivors who have completed treatment within the previous 36 months using a community-based participatory research approach. We will randomly assign 168 participants to the intervention or control group. The intervention arm will attend 7 weekly 3.5-hour peer mentor and educational sessions. The control group will receive the educational information. We will assess health outcomes at baseline, immediately after the Joy Luck Academy, and at 1- and 4-month follow-ups. The primary outcome is quality of life, as measured by the Functional Assessment of Cancer Therapy scale. Secondary outcomes include depressive symptoms, positive affect, fatigue, and perceived stress. We will also explore how the intervention influences cortisol levels. To identify how and to whom the program is effective, we will measure social and personal resources and theorized mechanisms and perform qualitative interviews with a subsample of participants to enhance the interpretation of quantitative data.

Results: Recruitment began in February 2015, and data collection was completed in February 2019. We expect to complete data management by August 2021 and publish results in 2022.

Conclusions: If the Joy Luck Academy is demonstrated to be effective, it may be easily disseminated as an intervention for other groups of Asian American immigrant breast cancer survivors. Furthermore, similar programs could be integrated into other diverse communities.

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KEYWORDS

social support; peer mentor support; randomized controlled trial; Chinese cancer survivors; breast cancer

Introduction

Background

Breast cancer is the most prevalent type of cancer among Asian American women, and its incidence is increasing [1,2]. Higher survival rates have led to a greater focus on improving cancer survivors' quality of life [3,4]. Asian American immigrant breast cancer survivors continue to face unique challenges because of cultural and socioecological factors [5,6]. Although they commonly report emotional distress and express the need for social, emotional, and spiritual support [7], they are less likely to seek support from family, friends, or mental health professionals than White Americans [8]. Asian American breast cancer survivors report cultural stigma toward cancer, gender role socialization as *caregivers*, and fear of burdening family as barriers to seeking support [6-9]. In addition, they lack culturally and linguistically appropriate information to manage their survivorship health care [7,10]. Limited English proficiency also limits survivors' ability to communicate with health care providers, understand health-related information, and make decisions about survivorship care [7]. Thus, Asian American breast cancer survivors have various informational and psychosocial needs that are not addressed by existing evidence-based interventions.

Psychosocial interventions delivered after the completion of primary oncologic treatment have improved the quality of life of breast cancer survivors [11,12]. A systematic review and meta-analysis of different psychosocial interventions showed improvement in emotional distress, anxiety, depression, and quality of life after treatment [12]. For example, women undergoing educational and nutritional interventions showed fewer depressive symptoms and improved physical functioning at follow-up [13]. Psychosocial interventions (supportive, expressive discussion groups) reduced loneliness, promoted hope, and enhanced the quality of life in women with breast cancer [14]. In addition, women who lacked personal resources (eg, self-esteem) or social support were more likely than those with these resources to show physical health improvements after participating in a psychosocial intervention [15].

Most previous interventions on breast cancer survivorship have been conducted among English-speaking, highly educated White women. Sociocultural differences between White and Asian American immigrant women may limit the applicability of existing interventions to Asian American breast cancer survivors. For example, 50% of Asian Americans do not speak fluent English [16]; however, existing interventions do not address language barriers in communication between patients and health care providers. Moreover, existing interventions do not target cultural factors that affect the quality of life, service use, or support-seeking attitudes among Asian American cancer survivors. Hence, although psychosocial interventions confer significant benefits to health and well-being, existing interventions may not address the specific needs of Asian American breast cancer survivors.

The Joy Luck Academy program was developed for Chinese-speaking breast cancer survivors [17], using a community-based participatory research (CBPR) approach (ClinicalTrials.gov NCT02946697) [18-21]. The Joy Luck Academy includes two components: education and peer mentor support. Each component was chosen based on the needs of this group, including lack of knowledge about breast cancer and survivorship management, feelings of loneliness, lack of emotional support, communication difficulties, and body image concern [22].

The results of a pilot study suggested that Joy Luck Academy has the potential to improve well-being among Chinese American breast cancer survivors [17,23]. Furthermore, qualitative data revealed that Joy Luck Academy reduced perceived stigma and loneliness and increased a sense of belonging by providing a forum for participants to share their experiences with women of similar cultural backgrounds [17]. The pilot study results confirmed that the intervention was feasible and valued by Chinese American breast cancer populations and that the CBPR approach improved the cultural sensitivity of the intervention.

Objectives

We planned a randomized controlled trial (RCT) to test the health benefits of Joy Luck Academy and identify how and to whom the Joy Luck Academy is effective using a CBPR approach and mixed methods. This study is the first RCT to test a culturally and linguistically sensitive intervention designed to address the informational and emotional needs of Chinese American breast cancer survivors.

The primary aim of this study is to test the health benefits of a culturally sensitive social support program for Chinese American breast cancer survivors (aim 1). We hypothesize that the program will confer health benefits, as indicated by improvements in outcomes. The primary outcome is quality of life; the secondary outcomes are depressive symptoms, fatigue, positive affect, and perceived stress. We also expect that the intervention will normalize diurnal cortisol levels, an exploratory outcome. Secondary objectives include identifying the characteristics of individuals who benefit from the Joy Luck Academy (aim 2) and understanding the underlying mechanisms (aim 3). On the basis of the literature and our pilot study [15,17], we hypothesize that Joy Luck Academy will be more effective for women who lack psychosocial resources, specifically, those with low levels of social support, optimism, and perceived control over illness. We hypothesize that the Joy Luck Academy will increase relatedness need satisfaction and coping self-efficacy and decrease cancer-related perceived stigma,

leading to health benefits (ie, mediators of the intervention effect).

Methods

Overview

We will conduct an RCT in Chinese American breast cancer survivors who have completed primary treatment. Participants will be randomly assigned to the Joy Luck Academy intervention or control group. Health outcomes will be assessed at baseline and immediately after the intervention (7 weeks after baseline) and at 1 and 4 months after completing the Joy Luck Academy. All study materials will be in Chinese.

Participants

We will recruit 168 Chinese American breast cancer survivors, as determined by a sample size calculation (described below in *Power Analysis* section). Experienced researchers and community staff who speak fluent Chinese (Cantonese or Mandarin) will introduce potential participants to the study, screen them for eligibility, and invite them to participate; if they decline to participate, their reasons for declining will be documented. Upon completion of the study, each participant will be given prorated US $180 in gift cards as compensation.

Eligibility Criteria

The inclusion criteria were (1) self-identifying as being comfortable speaking Mandarin or Cantonese, (2) women having stage 0 to 3 breast cancer, and (3) having completed primary treatment (surgery, chemotherapy, or radiotherapy) within the previous 36 months.

Recruitment

Participants will be recruited from the Greater Los Angeles area in Southern California. We will identify and recruit potential participants via a community organization (Herald Cancer Association [HCA]) and local advertising. The HCA provides many community services, including providing Chinese-language cancer information brochures. The HCA maintains a large database of primarily Chinese immigrant breast cancer survivors, who registered with the HCA to obtain educational and informational resources. The HCA will contact individuals on their client list, advertise the study in their monthly newsletters, ask for referrals from participants, and promote the study at cancer survivor events. Targeted announcements will be used in the Chinese American community to reach women who are not in the HCA database. The San Gabriel Valley region of Los Angeles County has the largest concentration of Chinese American communities in the United States [24]. Announcements will be distributed to local clinics, doctors' offices, and other patient services.

Consent

We will obtain approval from the human subjects protection committees of the University of Houston (Houston, Texas), the University of Texas MD Anderson Cancer Center (Houston, Texas), and the California Cancer Registry (Sacramento, California) to conduct this RCT. Written informed consent will be required before participation from each participant and will be obtained by the HCA.

Power Analysis

Power analysis was based on the primary aim of this trial. Specifically, we calculated the sample size required to detect the effect of Joy Luck Academy on the primary outcome (quality of life at the 4-month follow-up assessment). In our primary analyses, we will use maximum likelihood-type (eg, restricted maximum likelihood) estimation procedures based on all observed data, assuming a missing-at-random mechanism [25]. The pilot study revealed that the Joy Luck Academy had an intermediate or higher effect on improving participants' quality of life (Cohen d=0.47), depressive symptoms (Cohen d=0.55), and positive affect (Cohen d=0.62). On the basis of a targeted medium effect size of Cohen d=0.47, we estimated that a total sample size of 146 women at the 4-month follow-up would yield 80% power to detect this treatment effect at α=.05 (nQuery Advisor Version 7.0, Statistical Solutions Ltd). Assuming an attrition rate of 10%-20%, the final recruitment goal will range between 162 and 183 at the baseline.

Randomization

Participants who consent to participate will be randomly assigned to the Joy Luck Academy or control group at an approximate 1:1 ratio. Using minimization—a covariate adaptive randomization approach [26]—we will assign a participant to the intervention or control group by applying a randomization algorithm that will take into account participants' age, stage of cancer, and time since completing treatment. This covariate information will be obtained by the HCA staff during the participant screening process. Randomization will start 4 weeks before the orientation scheduled start date and continue until the recruitment goal is reached or until 1 week before the start of each cohort study. Only the researcher conducting random assignments and the person who informs participants of their group allocation will be aware of the condition assignment.

Intervention Group

Each Joy Luck Academy intervention program will enroll a maximum of 24 participants. We plan to deliver seven Joy Luck Academy programs during the project period. The Joy Luck Academy programs will have the same instructors, lectures, and support materials to ensure the fidelity of programs delivered at different times.

Joy Luck Academy participants will meet for 3.5 hours once a week for 7 consecutive weeks. Each session will begin with a 30-minute breakfast to allow for informal conversations among participants (mentees) and mentors. The meal is followed by a lecture given by the instructors on cancer-related topics and a question-answer session. After the lecture, 15 minutes of physical exercise will be engaged, followed by a 15-minute break. After the break, participants will join class activities and group sharing in the format of a large group sharing led by a Joy Luck Academy program facilitator, a small group sharing led by peer mentors, or a combination of both. The lecture, question-answer, class activities, and group sharing take about 2.5 hours in total.

Joy Luck Academy lecture topics include recognizing the side effects of treatment and differentiating them from the symptoms of cancer recurrence, physical therapy and complementary treatments, stress management, recognizing depression and managing emotional problems, communication with family members, and body image. The Joy Luck Academy instructors are professionals who are experienced in breast cancer treatment and support, including a breast surgeon, a clinical psychologist, a physical therapist, a dietitian, and a beautician. They will give lectures in their areas of expertise and answer the Joy Luck Academy participants' questions. Some sessions will be audio recorded to determine fidelity to the protocol, lecture plan, and activity objectives.

Each peer mentor will work with 3 to 5 mentees. Peer mentors will lead small group discussions on that week's topic and share their own experiences with mentees. This setup will encourage and allow mentees to share personal feelings in a relaxed and comfortable setting and receive support and advice. Mentors will also contact mentees once a week during the 7-week program to provide guidance and address remaining concerns. Each participant will be assigned to a volunteer peer mentor who is a breast cancer survivor and speaks a similar Chinese dialect. Mentors will be recruited from graduates of Joy Luck Academy pilot programs. Each potential mentor will be evaluated by the program facilitator based on the potential mentor's engagement in the program and support of other participants during the program. Mentors will complete a 3-hour training program to gain mentoring skills. The training will be conducted by HCA staff using a standardized manual that was jointly developed by the academic and community teams. The training program focuses on skills in establishing rapport, demonstrating understanding, listening empathically, discussing participants' concerns, and promoting the sharing of information and feelings. The training also involves lectures, case study presentations, discussions, and role-play activities.

We will use a procedure to maximize attendance and retention recommended by a previous study [27]. Participants will be asked to notify the program facilitator or their assigned mentor in advance if they will be absent. They will be told that, with their permission, the group members will be informed of the reason for their absence to reduce worries and concerns. The mentor will keep copies of the handouts for missing participants and call them within 5 days to briefly discuss the week's topic and tell them that they can pick up the handouts when they return to class. This should make participants feel that they are cared for by others and that they can catch up and will make them more likely to continue the program. Participants will also be informed that the lectures, recorded in DVD format, will be available for them to view at home so that they will not miss information in the lecture.

Control Group

Control group participants will undergo usual care and receive information booklets in Chinese that were developed by the American Cancer Society [28]. The booklets cover common issues related to breast cancer, various treatments, and life after treatment, which are similar to the topics covered in the Joy Luck Academy. Control group participants will be informed that they are in the self-study group to read the information booklets on their own to reduce potential anticipation bias and they will have the opportunity to join an in-person study group (Joy Luck Academy) after the assessment at the 4-month follow-up.

Data Management and Confidentiality

All participants' identification records will be kept confidential and stored in a secure file with password protection. Each participant will be assigned an identification number that will be used on all documents and data files. All protected health information will be removed from the data when it is exported for analyses.

Data Collection

Overview

After consenting, participants will complete the baseline questionnaires during an orientation session. These measures will be used to assess participants' demographic and treatment information and psychosocial variables of interest. Participants' demographic information (age, income, education level, and length of time living in the United States) and acculturation level [29] will be self-reported. Cancer and treatment information (cancer stage, treatments, and time since diagnosis) will be self-reported and confirmed through medical records, with participants' consent.

Self-reported health outcomes and mediators will be measured via questionnaires at baseline, immediately after Joy Luck Academy completion and 1 month and 4 months after the intervention. The hypothesized moderating variables will only be measured at the baseline. The questionnaires, along with preaddressed, postage-paid envelopes, will be mailed to all participants. Participants will be asked to complete the questionnaires at home within 7 days and return them by mail. They will be reminded by phone to complete the questionnaires.

Primary Outcome

Quality of life during the previous week will be measured using the Chinese version [30] of the Functional Assessment of Cancer Therapy-Breast (FACT-B) [31]. FACT-B comprises four Functional Assessment of Cancer Therapy-General (FACT-G) subscales (physical, social, emotional, and functional well-being) and an additional subscale pertinent to breast cancer. Each item is rated on a 5-point scale (0=not at all, 1=a little bit, 2=somewhat, 3=quite a bit, and 4=very much). To improve the comparison between this and other trials, the FACT-G total score (the sum of all the items in the first four subscales) will be used as the primary outcome. The breast cancer concern subscale will be used as an exploratory outcome measure. Higher FACT-G scores indicate a better quality of life.

Secondary Outcomes

Depressive symptoms will be measured with the Chinese short-form version [32] of the Center for Epidemiologic Studies Depression (CES-D) scale [33]. Two additional items ("I don't want to have contact with people, socialize, or go out at all" and "I have thought about hurting myself") from the Chinese American Depression Scale, which was specifically developed for Chinese Americans [34] to capture depressive symptoms

that are not assessed in the CES-D, will be used as an exploratory outcome measure. Participants will indicate on a 4-point scale how often they felt or behaved in a given way during the previous week (0=rarely or none of the time [less than a day], 1=some or a little of the time [1-2 days], 2=occasionally or a moderate amount of the time [3-4 days], and 3=most of the time [5-7 days]). Higher total scores indicate more depressive symptoms.

Positive affect will be assessed using the 10 positive affect items (eg, *cheerful*) of the Positive and Negative Affect Scale [35]. Participants will indicate to what extent they have generally felt an emotion (very slightly or not at all, a little, moderately, quite a bit, or extremely) during the previous week on a 5-point scale, which is summed. Higher scores indicate a more positive affect.

Fatigue will be assessed using 6 items of the Functional Assessment of Chronic Illness Therapy-Fatigue scale [36]. The items were selected based on our pilot studies. Participants will indicate how true each statement (eg, "I feel tired") had been for them during the previous week on a 5-point scale (0=not at all, 1=a little bit, 2=somewhat, 3=quite a bit, and 4=very much). Higher scores on the summed 6 items indicate greater fatigue.

Perceived stress will be measured using a 4-item short version of the Perceived Stress Scale [37]. Participants will be asked how often they experienced particular feelings and thoughts during the previous week (eg, "I was unable to control important things in my life") on a 5-point scale (0=not at all, 1=a little bit, 2=somewhat, 3=quite a bit, 4=very much). The four items are summed, with higher scores indicating greater perceived stress.

Exploratory Outcomes

Salivary cortisol levels will be assessed at baseline and immediately after the intervention. Participants will collect saliva 20 minutes after awakening and at 12 PM, 5 PM and 9 PM hours on 2 consecutive days so that both the mean level and slopes can be calculated [38]. Normal diurnal rhythms are expected to consistently demonstrate peak cortisol concentrations during awakening and decline thereafter [39]. Following established procedures [39,40], participants will be given detailed instructions on collecting saliva at home. Participants will be asked not to eat or drink anything, brush or floss their teeth, use mouthwash or lipstick, or smoke 30 minutes before collection. They will complete questions on comorbid conditions (such as autoimmune disorders) and medications (such as prednisone, dexamethasone, and other steroids), alcohol and caffeine intake, exercise level, and sleep quality, which influence cortisol levels. They will be given salivettes and then asked to chew a small cotton pad and spit it back into the tube of the salivette. Participants will be asked to mail their samples to the HCA office within 3 days after collection (salivary cortisol is stable at ambient temperature for 2-4 weeks) [40]. The samples will be stored in a freezer at −20°C until they are delivered in batches to a well-established independent laboratory for analysis; these procedures are routinely used [40].

Mediating Variables

Relatedness need satisfaction will be assessed using the eight-item relatedness subscale of the General Need Satisfaction Scale [41]. Participants will be asked to think about how each item (eg, "People in my life care about me") relates to their life and indicate how true it has been for them in the previous week on a scale from 1 (not true at all) to 7 (very true). The eight summed items indicate the extent to which relatedness needs are satisfied. Higher scores indicate higher needs satisfaction for relatedness.

Perceived stigma will be measured using the modified nine-item Self-Stigma Scale-Short Form [42]. The scale was originally developed for minorities and was modified for breast cancer in this study. Participants will rate how each item (eg, "I fear that others would know that I am a breast cancer survivor") is related to their thoughts and feelings about being a breast cancer survivor on a 4-point scale (1=strongly disagree, 2=disagree, 3=agree, and 4=strongly agree). Higher summed scores indicate greater perceived self-stigma.

Coping self-efficacy will be assessed using 19 items selected from the Cancer Behavior Inventory [43], a measure of self-efficacy for coping with cancer or cancer treatment. Participants will rate their confidence in accomplishing a behavior (eg, "sharing feelings of concerns") on a scale from 1 (not confident at all) to 9 (totally confident). Higher scores on the summed 19-item scale indicate greater self-efficacy.

Moderating Variables

Social support will be measured using two subscales (positive interactions and emotional and informational support) of the Medical Outcomes Study Social Support Survey [44], a multidimensional instrument that is valid in Chinese-speaking patients [45]. Each item is rated on a 5-point scale (1=none of the time, 2=a little of the time, 3=some of the time, 4=most of the time, 5=all of the time). The summed subscale scores include eight items for emotional and informational support and four items for positive interactions. The overall scale score is the sum of the two subscales, with higher scores indicating greater social support.

Dispositional optimism will be assessed using the Chinese Revised Life Orientation Test [46], which comprises three positively worded (eg, "I am always optimistic about my future") and three negatively worded (eg, "I hardly ever expect things to go my way") phrases. Each item is rated on a 4-point scale (1=disagree, 2=neutral, 3=agree, and 4=strongly agree). Higher summed scores indicate higher optimism.

Perceived control of illness will be measured using three items previously used in a psychosocial intervention with breast cancer survivors [15]. These items assess perceived control of the future course of illness, day-to-day symptoms, and emotions related to illness, with each rated on a 4-point scale (0=none, 1=a little bit, 2=somewhat, and 3=a lot). Higher scores on the summed items indicate greater perceived control.

The FACT-B, CES-D, Self-Stigma Scale, Chinese Revised Life Orientation Test, Perceived Stress Scale, and Medical Outcomes Study Social Support Survey have been validated in Chinese populations, and the other scales have been or will be translated into Chinese and back-translated into English by bilingual researchers through an iterative process to ensure conceptual and linguistic equivalence. Most of the Chinese versions have been used in previous studies [47] and have demonstrated good

psychometric properties and psychometric equivalence to the original English versions (Cronbach α=.83-.98).

Qualitative Data

A subsample of patients (n=77) will participate in focus groups or individual semistructured interviews. Seven focus group interviews (n=35) will be conducted among the Joy Luck Academy participants to identify common themes surrounding their Joy Luck Academy experience. Approximately 4 to 6 respondents from each Joy Luck Academy cohort will be approached by the program facilitator to participate in the focus groups [48]. The focus groups will be conducted within 1 week of completion of the intervention. The community research coordinator, who has been trained in qualitative interviewing, will conduct the focus group interviews at the HCA.

Individual interviews will be conducted after the last follow-up assessment to explore the culturally specific mechanisms that may explain the potential intervention effect. In-depth semistructured individual interviews will be conducted with 42 participants (half from the control group and half from those in the intervention group who have not participated in the focus groups). Approximately 6 women from each Joy Luck Academy cohort will participate in individual interviews to reach data saturation [49]. Each interview will last 60 to 90 minutes. These interviews were designed to explore participants' breast cancer experience, cancer management, supporting resources, concerns, and the effect of cancer on their lives and social networks. Each topic area will be evaluated to identify additional information and specific examples. Joy Luck Academy participants will also be asked about their experiences in the Joy Luck Academy and the changes they had experienced as a result of the Joy Luck Academy. The inductively and deductively designed interview topic guide was finalized through discussion with the HCA. Permission to audio record the individual interviews and focus groups will be obtained from the participants. Participants will receive an additional US $30 compensation for the interviews.

Data Analysis

Deductive Data Analysis Plan

Descriptive statistics and correlations among the major variables will be computed. The internal consistency of the questionnaires' reliability at baseline will be assessed using Stata 16.0 software (StataCorp LLC). The construct validity of the questionnaires will be assessed using confirmatory factor analysis with Stata 16.0. Appropriate techniques (eg, exploratory factor analysis) will be used to improve reliability and validity, when necessary.

The primary analytic strategy will be multilevel analyses, also referred to as hierarchical linear modeling or linear mixed-effects modeling. Specifically, for each outcome variable, the primary independent variables of interest will include the intervention condition (experimental vs control), time (postintervention and 1- and 4-month follow-ups), and the interaction between the intervention condition and time. Random subject or Joy Luck Academy cohort effects, as applicable, will be used to model the correlations between repeated measurements within subjects and between observations from subjects within Joy Luck Academy cohorts. The selection of the random-effect covariance and serial correlation structure (eg, autoregressive correlation), as appropriate, will be based on the Bayesian information criterion. Each hierarchical linear modeling for assessing aim 1 will use quality of life as the primary outcome and other specified variables as secondary outcomes, controlling for the baseline outcome. In addition, results will be reported by controlling for important covariates used in the randomization (eg, age at baseline, cancer stage, and time since treatment) [50]. We will analyze the impact of the intervention on cortisol by testing the change in diurnal profile from pre- to postintervention using linear mixed-effects modeling. Cortisol outcomes will be indicated by raw cortisol values, initial levels, slopes, and areas under the curve, following previous methods [51-54].

Moderation effects (aim 2) will be assessed by adding potential moderators and testing their interactions with the intervention condition and time, one moderator at a time, and testing the significance of the interaction effect between the moderator and the intervention (and time, as appropriate). Mediation effects (aim 3) will be assessed by examining bootstrapped 95% CI of the indirect effect of the intervention on the primary and secondary outcomes via each hypothesized mediator [55,56]. In the presence of more than one significant single mediator, we will fit multiple mediator models to evaluate the joint mediation effects of multiple mediators [55,57]. All statistical tests will be conducted at a two-sided significance level of P=.05. Except for the primary analysis for the quality-of-life outcome, the findings based on other analyses will be interpreted with caution because of a lack of control over the overall type 1 error rate across multiple tests. Effect sizes with 95% CIs will also be calculated for models to help characterize the magnitude and potential replicability of the findings.

Missing Data

Our proposed primary analysis approaches are likelihood-based, which are valid under the missing-at-random mechanism; that is, the probability that an outcome is missing depends only on the observed variables included in the model. In such cases, no imputation of missing data will be necessary. However, we may conduct a sensitivity analysis to determine the sensitivity of our primary findings to key patterns of missing data, particularly patterns that are consistent with the missing-not-at-random mechanism, using pattern-mixture models [25]. Additional approaches such as multiple imputations will be used, as necessary. Similar results from the sensitivity analyses would strengthen our study findings, whereas different results would suggest that caution should be taken when interpreting our findings.

Qualitative Data Analysis

The interviews will be transcribed and analyzed in Chinese to preserve the linguistic meanings and enhance the trustworthiness of the data. In the thematic analyses, we will code responses, extract broad themes, and identify subthemes [58].

Results

Recruitment began in February 2015, and all data collection was completed by February 2019. We expect to complete data

management by August 2021 and submit the study results for publication by 2022.

Discussion

Few evidence-based psychosocial interventions designed for diverse ethnic groups of cancer survivors are available. This study is the first RCT to test a culturally sensitive social support intervention in Asian American (specifically, Chinese immigrant) breast cancer survivors. In this trial, we will determine the health benefits of a 7-week education and peer mentorship intervention on quality of life, depressive symptoms, positive affect, and other outcomes in Chinese American breast cancer survivors immediately after the intervention and at 1- and 4-month follow-up assessments. These individuals may benefit from interventions tailored to their needs for survivorship health care information [10] and social support [7]. This program has the potential to be adapted for other Asian American immigrant breast cancer survivors and eliminate unnecessary emotional and physical health disparities in cancer care.

The design of this study has both strengths and limitations. The intervention is innovative, as it is culturally relevant to an ethnic group and uses a theoretically grounded CBPR approach. As this study targets breast cancer survivors who have completed treatment, cancer patients undergoing active treatment will not be enrolled in the study, which limits its generalizability. The Joy Luck Academy is specifically designed to meet the needs of Chinese American breast cancer survivors and, therefore, may not be directly applicable to survivors of other ethnic groups. Future studies are needed to test this type of intervention in other minority groups.

If the Joy Luck Academy is demonstrated to improve the well-being of Chinese American breast cancer survivors, it may be disseminated to this population across the country.

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Notes: KW is now at Centre for Research in Public Health and Community Care, University of Hertfordshire, Hatfield, UK. CSW is now at Department of Psychology, Oberlin College, Oberlin, OH, USA. LC is now at School of Education, Shanghai Jiao Tong University, Shanghai, China. QC is now at School of Public Health, Shanghai Jiao Tong University School of Medicine, Shanghai, China.

Authors' Contributions

QL conceived and designed the study and drafted and edited the manuscript. KW and CSW drafted and edited the manuscript. LC edited the manuscript. QC reviewed the manuscript. YL conducted the power analysis and drafted the power analysis and data analysis plan. MWG was involved in power analysis. MKS and ALS provided feedback on the manuscript. LY and AL were involved in protocol development and program design. All authors read and approved the final manuscript and confirmed with the streamlined description of the contribution.

Conflicts of Interest

None declared.

References

1. Gomez SL, Noone A, Lichtensztajn DY, Scoppa S, Gibson JT, Liu L, et al. Cancer incidence trends among Asian American populations in the United States, 1990-2008. J Natl Cancer Inst 2013 Aug 07;105(15):1096-1110 [FREE Full text] [doi: 10.1093/jnci/djt157] [Medline: 23878350]
2. Thompson CA, Gomez SL, Hastings KG, Kapphahn K, Yu P, Shariff-Marco S, et al. The Burden of Cancer in Asian Americans: A report of national mortality trends by Asian ethnicity. Cancer Epidemiol Biomarkers Prev 2016 Oct 02;25(10):1371-1382. [doi: 10.1158/1055-9965.epi-16-0167]
3. Stanton AL. Psychosocial concerns and interventions for cancer survivors. J Clin Oncol 2006 Nov 10;24(32):5132-5137. [doi: 10.1200/jco.2006.06.8775]
4. Ganz PA, Coscarelli A, Fred C, Kahn B, Polinsky ML, Petersen L. Breast cancer survivors: Psychosocial concerns and quality of life. Breast Cancer Res Tr 1996 Jun;38(2):183-199. [doi: 10.1007/bf01806673]
5. Ashing-Giwa KT. The contextual model of HRQoL: a paradigm for expanding the HRQoL framework. Qual Life Res 2005 Mar;14(2):297-307. [doi: 10.1007/s11136-004-0729-7] [Medline: 15892421]
6. Warmoth K, Cheung B, You J, Yeung NC, Lu Q. Exploring the social needs and challenges of Chinese American immigrant breast cancer survivors: a qualitative study using an expressive writing approach. Int J Behav Med 2017 Dec 5;24(6):827-835. [doi: 10.1007/s12529-017-9661-4] [Medline: 28585073]

7. Leng J, Lee T, Sarpel U, Lau J, Li Y, Cheng C, et al. Identifying the informational and psychosocial needs of Chinese immigrant cancer patients: a focus group study. Support Care Cancer 2012 Dec 25;20(12):3221-3229 [FREE Full text] [doi: 10.1007/s00520-012-1464-1] [Medline: 22531877]
8. Wen K, Fang CY, Ma GX. Breast cancer experience and survivorship among Asian Americans: a systematic review. J Cancer Surviv 2014 Mar 9;8(1):94-107 [FREE Full text] [doi: 10.1007/s11764-013-0320-8] [Medline: 24214498]
9. Lee S, Chen L, Ma GX, Fang CY, Oh Y, Scully L. Challenges and needs of Chinese and Korean American breast cancer survivors: in-depth interviews. N Am J Med Sci (Boston) 2013 Feb 02;6(1):1-8 [FREE Full text] [doi: 10.7156/najms.2013.0601001] [Medline: 24019995]
10. Wen K, Hu A, Ma G, Fang C, Daly M. Information and communication needs of Chinese American breast cancer patients: perspectives on survivorship care planning. J Community Support Oncol 2014 Dec;12(12):439-445 [FREE Full text] [doi: 10.12788/jcso.0095] [Medline: 25811036]
11. Stanton AL, Rowland JH, Ganz PA. Life after diagnosis and treatment of cancer in adulthood: contributions from psychosocial oncology research. Am Psychol 2015 Feb;70(2):159-174. [doi: 10.1037/a0037875] [Medline: 25730722]
12. Faller H, Schuler M, Richard M, Heckl U, Weis J, Küffner R. Effects of psycho-oncologic interventions on emotional distress and quality of life in adult patients with cancer: systematic review and meta-analysis. J Clin Oncol 2013 Feb 20;31(6):782-793. [doi: 10.1200/JCO.2011.40.8922] [Medline: 23319686]
13. Scheier MF, Helgeson VS, Schulz R, Colvin S, Berga S, Bridges MW, et al. Interventions to enhance physical and psychological functioning among younger women who are ending nonhormonal adjuvant treatment for early-stage breast cancer. J Clin Oncol 2005 Jul 01;23(19):4298-4211. [doi: 10.1200/jco.2005.05.362]
14. Tabrizi FM, Radfar M, Taei Z. Effects of supportive-expressive discussion groups on loneliness, hope and quality of life in breast cancer survivors: a randomized control trial. Psychooncology 2016 Sep 15;25(9):1057-1063. [doi: 10.1002/pon.4169] [Medline: 27302306]
15. Helgeson VS, Cohen S, Schulz R, Yasko J. Group support interventions for women with breast cancer: Who benefits from what? Health Psychol 2000;19(2):107-114. [doi: 10.1037/0278-6133.19.2.107]
16. Shin H, Kominski R. Language use in the United States: 2007. American Community Survey Reports (ACS-12), U.S. Census Bureau. 2010. URL: https://www2.census.gov/library/publications/2010/acs/acs-12/acs-12.pdf [accessed 2021-08-03]
17. Lu Q, You J, Man J, Loh A, Young L. Evaluating a culturally tailored peer-mentoring and education pilot intervention among chinese breast cancer survivors using a mixed-methods approach. Oncol Nurs Forum 2014 Oct 29;41(6):629-637. [doi: 10.1188/14.onf.629-637]
18. Kagawa-Singer M. Improving the validity and generalizability of studies with underserved U.S. Populations expanding the research paradigm. Ann Epidemiol 2000 Nov;10(8):92-103. [doi: 10.1016/s1047-2797(00)00192-7]
19. Minkler M, Wallerstein N. Community-Based Participatory Research for Health: From Process to Outcomes 2nd Edition. San Francisco, CA: John Wiley & Sons; 2008:1-544.
20. Tanjasiri SP, Kagawa-Singer M, Nguyen T, Foo MA. Collaborative research as an essential component for addressing cancer disparities among Southeast Asian and Pacific Islander women. Health Promot Pract 2002 Apr 01;3(2):144-154. [doi: 10.1177/152483990200300210]
21. Viswanathan M, Ammerman A, Eng E, Garlehner G, Lohr KN, Griffith D, et al. Community-based participatory research: assessing the evidence. Evid Rep Technol Assess (Summ) 2004 Aug(99):1-8. [Medline: 15460504]
22. Lu Q, Yeung NC, You J, Dai J. Using expressive writing to explore thoughts and beliefs about cancer and treatment among Chinese American immigrant breast cancer survivors. Psychooncology 2016 Nov 25;25(11):1371-1374 [FREE Full text] [doi: 10.1002/pon.3991] [Medline: 26403647]
23. Warmoth K, Yeung NC, Xie J, Feng H, Loh A, Young L, et al. Benefits of a psychosocial intervention on positive affect and posttraumatic growth for Chinese American breast cancer survivors: a pilot study. Behav Med 2020 Jan 18;46(1):34-42 [FREE Full text] [doi: 10.1080/08964289.2018.1541862] [Medline: 30657442]
24. Zhou M. Contemporary Chinese America: Immigration, Ethnicity, and Community Transformation. Philadelphia, Pennsylvania, United States: Temple University Press; 2009:1-328.
25. Little R, Rubin D. Statistical Analysis With Missing Data, 2nd Edition - Wiley Series in Probability and Statistics. Hoboken, New Jersey, United States: John Wiley & Sons; 2002:1-408.
26. Pocock SJ, Simon R. Sequential treatment assignment with balancing for prognostic factors in the controlled clinical trial. Biometrics 1975 Mar;31(1):103. [doi: 10.2307/2529712]
27. Andersen BL, Golden-Kreutz DM, Emery CF, Thiel DL. Biobehavioral Intervention for Cancer Stress: Conceptualization, Components, and Intervention Strategies. Cognit Behav Pract 2009 Aug;16(3):253-265. [doi: 10.1016/j.cbpra.2008.11.002]
28. Cancer information in other languages. American Cancer Society. URL: http://www.cancer.org/asianlanguagematerials/index [accessed 2021-08-03]
29. Stephenson M. Development and validation of the Stephenson Multigroup Acculturation Scale (SMAS). Psychol Assess 2000;12(1):77-88. [doi: 10.1037/1040-3590.12.1.77]
30. Wan C, Zhang D, Yang Z, Tu X, Tang W, Feng C, et al. Validation of the simplified Chinese version of the FACT-B for measuring quality of life for patients with breast cancer. Breast Cancer Res Treat 2007 Dec 22;106(3):413-418. [doi: 10.1007/s10549-007-9511-1] [Medline: 17377841]

31. Brady MJ, Cella DF, Mo F, Bonomi AE, Tulsky DS, Lloyd SR, et al. Reliability and validity of the Functional Assessment of Cancer Therapy-Breast quality-of-life instrument. J Clin Oncol 1997 Mar;15(3):974-986. [doi: 10.1200/jco.1997.15.3.974]
32. Boey KW. Cross-validation of a short form of the CES-D in Chinese elderly. Int J Geriat Psychiatry 1999 Aug;14(8):608-617. [doi: 10.1002/(sici)1099-1166(199908)14:8<608::aid-gps991>3.0.co;2-z]
33. Radloff LS. The CES-D Scale. Appl Psychol Meas 1977 Jun 01;1(3):385-401. [doi: 10.1177/014662167700100306]
34. Wong R, Wu R, Guo C, Lam JK, Snowden LR. Culturally sensitive depression assessment for Chinese American Immigrants: Development of a comprehensive measure and a screening scale using an item response approach. Asian Am J Psychol 2012 Dec;3(4):230-253 [FREE Full text] [doi: 10.1037/a0025628] [Medline: 23504503]
35. Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect: The PANAS scales. J Personal Soc Psychol 1988;54(6):1063-1070. [doi: 10.1037/0022-3514.54.6.1063]
36. Chandran V, Bhella S, Schentag C, Gladman DD. Functional assessment of chronic illness therapy-fatigue scale is valid in patients with psoriatic arthritis. Ann Rheum Dis 2007 Jul 02;66(7):936-939 [FREE Full text] [doi: 10.1136/ard.2006.065763] [Medline: 17324972]
37. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. J Health Soc Behav 1983 Dec;24(4):385. [doi: 10.2307/2136404]
38. Sephton S, Sapolsky RM, Kraemer HC, Spiegel D. Diurnal cortisol rhythm as a predictor of breast cancer survival. J Natl Cancer Inst 2000 Jun 21;92(12):994-1000. [doi: 10.1093/jnci/92.12.994] [Medline: 10861311]
39. Smyth JM, Ockenfels MC, Gorin AA, Catley D, Porter LS, Kirschbaum C, et al. Individual differences in the diurnal cycle of cortisol. Psychoneuroendocrinology 1997 Feb;22(2):89-105. [doi: 10.1016/s0306-4530(96)00039-x]
40. Kirschbaum C, Hellhammer DH. Salivary cortisol in psychoneuroendocrine research: Recent developments and applications. Psychoneuroendocrinology 1994 Jan;19(4):313-333. [doi: 10.1016/0306-4530(94)90013-2]
41. Gagné M. The role of autonomy support and autonomy orientation in prosocial behavior engagement. Motiv Emot 2003;27(3):199-223. [doi: 10.1023/A:1025007614869]
42. Mak WW, Cheung RY. Self-stigma among concealable minorities in Hong Kong: conceptualization and unified measurement. Am J Orthopsychiatry 2010 Apr;80(2):267-281. [doi: 10.1111/j.1939-0025.2010.01030.x] [Medline: 20553520]
43. Merluzzi TV, Nairn RC, Hegde K, Martinez Sanchez MA, Dunn L. Self-efficacy for coping with cancer: Revision of the Cancer Behavior Inventory (version 2.0). Psychooncology 2001 May;10(3):206-217 [FREE Full text] [doi: 10.1002/pon.511] [Medline: 11351373]
44. Sherbourne CD, Stewart AL. The MOS social support survey. Soc Sci Med 1991 Jan;32(6):705-714. [doi: 10.1016/0277-9536(91)90150-B]
45. Yu DS, Lee DT, Woo J. Psychometric testing of the Chinese version of the medical outcomes study social support survey (MOS-SSS-C). Res Nurs Health 2004 Apr;27(2):135-143. [doi: 10.1002/nur.20008] [Medline: 15042639]
46. Lai JC, Cheung H, Lee W, Yu H. The utility of the revised life orientation test to measure optimism among Hong Kong Chinese. Int J Psychol 1998 Feb;33(1):45-56. [doi: 10.1080/002075998400600]
47. Lu Q, Zheng D, Young L, Kagawa-Singer M, Loh A. A pilot study of expressive writing intervention among Chinese-speaking breast cancer survivors. Health Psychol 2012 Sep;31(5):548-551 [FREE Full text] [doi: 10.1037/a0026834] [Medline: 22229930]
48. Krueger RA. Focus Groups: A Practical Guide for Applied Research. 2nd edition. Thousand Oaks, California, United States: Sage Publications Inc; 1994:1-272.
49. Guest G, Bunce A, Johnson L. How many interviews are enough? Field Methods 2006 Feb 01;18(1):59-82. [doi: 10.1177/1525822X05279903]
50. Kahan BC, Morris TP. Improper analysis of trials randomised using stratified blocks or minimisation. Stat Med 2012 Feb 20;31(4):328-340. [doi: 10.1002/sim.4431] [Medline: 22139891]
51. Miller R, Stalder T, Jarczok M, Almeida DM, Badrick E, Bartels M, et al. The CIRCORT database: Reference ranges and seasonal changes in diurnal salivary cortisol derived from a meta-dataset comprised of 15 field studies. Psychoneuroendocrinology 2016 Nov;73:16-23 [FREE Full text] [doi: 10.1016/j.psyneuen.2016.07.201] [Medline: 27448524]
52. Pruessner JC, Kirschbaum C, Meinlschmid G, Hellhammer DH. Two formulas for computation of the area under the curve represent measures of total hormone concentration versus time-dependent change. Psychoneuroendocrinology 2003 Oct;28(7):916-931. [doi: 10.1016/s0306-4530(02)00108-7]
53. Cash E, Sephton S, Chagpar A, Spiegel D, Rebholz W, Zimmaro L, et al. Circadian disruption and biomarkers of tumor progression in breast cancer patients awaiting surgery. Brain Behav Immun 2015 Aug;48:102-114. [doi: 10.1016/j.bbi.2015.02.017] [Medline: 25728235]
54. Ho RT, Fong TC, Chan CK, Chan CL. The associations between diurnal cortisol patterns, self-perceived social support, and sleep behavior in Chinese breast cancer patients. Psychoneuroendocrinology 2013 Oct;38(10):2337-2342. [doi: 10.1016/j.psyneuen.2013.05.004] [Medline: 23742786]
55. MacKinnon D. Introduction to Statistical Mediation Analysis. New York: Lawrence Erlbaum Associates; 2008.
56. Preacher KJ, Hayes AF. SPSS and SAS procedures for estimating indirect effects in simple mediation models. Behav Res Methods Instru Comput 2004 Nov;36(4):717-731. [doi: 10.3758/BF03206553]

57. Preacher KJ, Hayes AF. Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. Behav Res Methods 2008 Aug;40(3):879-891. [doi: 10.3758/BRM.40.3.879]
58. Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol 2006 Jan;3(2):77-101. [doi: 10.1191/1478088706qp063oa]

Abbreviations

CBPR: community-based participatory research
CES-D: Center for Epidemiologic Studies Depression
FACT-B: Functional Assessment of Cancer Therapy-Breast
FACT-G: Functional Assessment of Cancer Therapy-General
HCA: Herald Cancer Association
RCT: randomized controlled trial

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Protocol

The Safety and Efficacy of Microbial Ecosystem Therapeutic-2 in People With Major Depression: Protocol for a Phase 2, Double-Blind, Placebo-Controlled Study

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Abstract

Background: The gut-brain axis is a bidirectional signaling pathway between the gastrointestinal tract and the brain; it is being studied because of its potential influence in mediating mood, anxiety, and other neuropsychiatric symptoms. Previous research examining the effects of gut microbiota on neuropsychiatric disorders suggests that gut repopulation treatments such as probiotics, microbe therapy, and fecal microbiota transplantation show promising results in treating symptoms of anxiety and depression. This study explores the use of an alternative gut repopulation treatment to fecal microbiota transplantation, known as Microbial Ecosystem Therapeutic (MET)-2, as an intervention against symptoms of depression. MET-2 is a daily, orally administered capsule containing 40 bacterial strains purified from a single healthy donor.

Objective: The primary aim of this study is to assess changes in mood in people with major depression that occur pre-, post-, and during the administration of MET-2. The secondary aims are to assess changes in anxiety symptoms, blood biomarker concentrations, and the level of repopulation of healthy gut bacteria as a response to treatment.

Methods: In this study, we will recruit 60 adults aged between 18 and 45 years old with major depression and randomly assign them to treatment or placebo groups. Patients in the treatment group will receive MET-2 once a day for 6 weeks, whereas patients in the placebo group will receive a matching placebo for 6 weeks. Participants will complete biweekly visits during the treatment period and a follow-up visit at 2 weeks post treatment. As a primary outcome measure, participants' mood will be assessed using the Montgomery-Asberg Depression Rating Scale. Secondary outcome measures include changes in mood, anxiety, early stress, gastrointestinal symptoms, and tolerability of MET-2 treatment using a series of clinical scales and changes in blood markers, particularly immunoglobulins (Igs; IgA, IgG, and IgM) and inflammatory markers (C-reactive protein, tumor necrosis factor-α, transforming growth factor-β, interleukin-6, and interleukin-10). Changes in the relative abundance, diversity, and level of engraftment in fecal samples will be assessed using 16S rRNA sequencing. All data will be integrated to identify biomarkers that could indicate disease state or predict improvement in depressive symptoms in response to MET-2 treatment.

Results: Given the association between the gut microbiome and depression, we hypothesized that participants receiving MET-2 would experience greater improvement in depressive symptoms than those receiving placebo owing to the recolonization of the gut microbiome with healthy bacteria modulating the gut-brain axis connection.

Conclusions: This study is the first of its kind to evaluate the safety and efficacy of a microbial therapy such as MET-2 in comparison with placebo for major depressive disorder. We hope that this study will also reveal the potential capabilities of microbial therapies to treat other psychiatric illnesses and mood disorders.

Trial Registration: ClinicalTrials.gov NCT04602715; https://clinicaltrials.gov/ct2/show/NCT04602715

International Registered Report Identifier (IRRID): DERR1-10.2196/31439

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KEYWORDS

gut-brain axis; depression; microbiome; probiotics; fecal transplant; MET-2

Introduction

Background

Research efforts to identify the pathophysiology and underlying mechanisms of psychiatric illnesses, such as major depressive disorder (MDD), are on the rise owing to the staggering economic burden and prevalence of mental illness. In Canada, mental illness affects approximately 20% of people and costs the Canadian economy more than Can $51 (US $39.48) billion a year, of which MDD is a major contributor [1,2]. MDD is a highly prevalent and debilitating psychiatric disorder characterized by a persistent depressed mood and loss of interest or pleasure in the surroundings. Common symptoms of MDD can include but are not limited to depressed mood, anhedonia, changes in appetite, trouble sleeping, reduced energy and fatigue, feelings of worthlessness, guilt, hopelessness, and thoughts of death or suicide [3].

Although there are a variety of psychological, pharmacological, and neurostimulation treatment methods available for people with MDD, such as cognitive behavioral therapy, antidepressant medications, and electroconvulsive therapy for treatment-resistant cases [4-6], finding the optimal treatment method can be challenging owing to a high level of individual variability among patients. Variables such as environmental influences, stress, and genetics play a role in determining the severity and course of symptoms and the response to treatment [7-9]. Furthermore, emerging treatment options addressing individual variability in patients with MDD have demonstrated the potential for creating a more precise and personalized approach to treatment, specifically within psychiatry [10].

Rationale for the Study

Composition of the Gut Microbiome

The colonization of bacteria in the gut begins at birth and significantly influences gut health throughout the lifespan [11]. In adults, the gut microbiome comprises more than 100 trillion commensal bacteria essential for the normal development and regulation of the immune system, central nervous system circuitry, and gastrointestinal (GI) functioning [12]. Under certain circumstances, environmental risk factors such as diet, lifestyle, stress, medications, and genetics can alter microbiota composition and deviate the homeostatic balance within the microbiome [13].

Previous studies have demonstrated that these alterations in microbiota composition owing to external factors may be mediated by the gut-brain axis (GBA). The GBA is a bidirectional, biochemical, and neural signaling pathway between the GI tract and the brain [14]. Although it has been long established that there is communication between the brain and the gut, only recently has there been a surge of interest in the GBA for its potential influence on depression and other symptoms of psychiatric illnesses [12]. Owing to the interaction between the gut and environmental risk factors of anxiety and depression, some interventions target the gut microbiome to aid in alleviating symptoms of anxiety and depression [15].

Gut Microbiota and Psychiatric Symptoms

Although alterations of gut microbiota may play a role in the etiology of psychiatric illnesses, the pathophysiology of MDD and how the GBA directly affects mood is complex. One of the most well-known hypotheses for the pathophysiology of depression is the monoamine hypothesis. It predicts that a deficiency in the levels of dopamine, serotonin, and norepinephrine in the central nervous system may be a key factor in the underlying mechanisms of depression [16]. Other central mechanisms that are also hypothesized to be involved in the pathophysiology of MDD include inflammation of the immune system and microbial imbalance [7].

Several studies have documented that patients diagnosed with MDD often present with elevated levels of proinflammatory cytokines, such as interleukin-6, and decreased levels of anti-inflammatory cytokines, such as interleukin-10 [7,17,18]. This proinflammatory state observed in patients with depression reaffirms the neuroinflammation hypothesis, which suggests that an increase in systemic inflammation is likely to be involved in the pathophysiology of depression by decreasing the synthesis and production of monoamines such as serotonin, resulting in a reduction of serotonin and an increase in depressive behavior [19].

Recent literature documenting the relationship between gut microbiota and symptoms of psychiatric illness has uncovered interesting findings. Microbial balance in the gut is an integral part of gut health; however, when one experiences an imbalance, the integrity of the protective epithelial and mucosal gut barrier can be compromised. This compromise might result in increased intestinal permeability of the GI tract, referred to as *leaky gut*. Leaky gut has been associated with various conditions, such as irritable bowel syndrome, autoimmune disorders, and multiple psychiatric illnesses [15]. Maes et al [20] demonstrated that bacterial translocation from the gut, also known as leaky gut, could activate immune cells to evoke specific IgA and IgM responses. Interestingly, patients diagnosed with depression often exhibit the same elevated levels of IgA and IgM responses,

which may be owing to the progressive amplification of the immune pathways and overall increased systematic inflammation [20].

Despite these relevant advances in recent literature, a complete understanding of microbial changes in the gut and their associated outcomes is still required. Previous studies have demonstrated that patients diagnosed with depression often display altered gut microbiota composition compared with healthy controls [12,21,22], which may result from the decreased abundance and lack of diversity among healthy gut microbiota [21]. In an attempt to address this problem, related research has turned to fecal microbiota transplantation (FMT) as a potential treatment option to improve symptoms of depression. FMT is a therapeutic approach that aims to repopulate the gut of an individual with fecal bacteria from a healthy donor via colonoscopy, nasogastric tube, or oral administration [23,24]. A potential advantage of discovering this link between symptoms of depression and microbiota in the gut is the greater accessibility and modifiability of microbiota compared with the human genome, giving microbial therapies a greater opportunity for aiding in the personalization of treatments for psychiatric illnesses [25]. Furthermore, given the adaptable nature of the microbiome, it may be a good representation of the individual's history and could better explain the differences in the risk of illness, disease course, and response to treatment.

Microbial Ecosystem Therapeutics

Microbial Ecosystem Therapeutic (MET)-2 is an oral, daily administered, novel treatment approach designed to repopulate the gut with microbiota from a healthy donor. MET-2 is a defined microbial community comprised 40 strains of lyophilized bacteria that are lab-grown and purified from a healthy 25-year-old donor's stool. MET-2 was originally developed by researchers at Queen's University and the University of Guelph to treat symptoms of early depression and help restore the normal gut flora. The original mixture contained pure cultures of intestinal bacteria, referred to as *Repoopulate* or MET-1, which was composed of 33 strains of bacteria that were chosen for their favorable safety profile [26]. This mixture was then refined, modified, and improved to 40 strains to create MET-2. Capsules were chosen instead of traditional FMT not only to increase acceptability to participants but also to allow for easier administration of the product for consecutive days rather than the use of raw fecal material administered via rectal suspension.

This study aims to evaluate the effects of MET-2 on symptoms of depression using pre- and posttreatment scores for overall depression and specific depressive symptoms. Our primary aim is to demonstrate the efficacy of MET-2 treatment, in comparison with placebo, on mood and related symptoms in participants with depression, using the Montgomery-Asberg Depression Rating Scale (MADRS) [27]. Those with at least a 50% reduction in MADRS scores will be considered successful responders to treatment. The secondary aims are to assess changes in anxiety symptoms, immune marker levels in response to MET-2 treatment, and the safety and tolerability of MET-2 treatment, and to evaluate any potential correlations between early life stress (eg, childhood emotional, physical, or sexual abuse history) and response to MET-2 treatment.

Methods

Study Design

This study is a phase 2, randomized, double-blinded, placebo-controlled clinical trial exploring the efficacy of MET-2 as a treatment for depressive symptoms in participants with MDD. We will randomize 60 participants with MDD into two arms: the treatment arm (30/60, 50%) and the placebo arm (30/60, 50%). Participants will consume either the investigational product MET-2 or a matching placebo daily for 6 weeks.

Setting

This study will occur at 3 sites: the Providence Care Hospital, Kingston, Ontario, Canada; the Centre for Addiction and Mental Health, Toronto, Ontario, Canada; and the University of Minnesota Medical School, Minneapolis, Minnesota, United States. There will be a total of 6 visits: a screening visit, a baseline visit (week 0), 3 treatment-period visits (weeks 2, 4, and 6), and a 2-week follow-up visit as outlined in the schedule of assessments (Table S1 in Multimedia Appendix 1).

Participants and Recruitment

This study will recruit 60 eligible participants aged between 18 and 45 years from the Kingston and Greater Toronto areas in Ontario, Canada, and the Minneapolis area in Minnesota, United States, using clinical referrals and web-based and paper advertisements. Web-based advertisements will be posted on social media platforms, whereas posters will be placed around university and college campuses, on community bulletin boards, clinics, and counseling centers. At the screening visit, all participants will be informed of the study, and any questions and concerns they may have will be addressed. Once consent is obtained, participants will then be thoroughly screened using inclusion and exclusion criteria (Textbox S1 in Multimedia Appendix 1) to ensure they are eligible for the study. Participants will be screened using the Mini-International Neuropsychiatric Interview to confirm the diagnosis of MDD and required a minimum MADRS score of ≥15 to be considered for inclusion in the trial.

Treatment

Study Drug

The 0.5-g MET-2 and placebo will be supplied as capsules for oral administration. Placebo capsules will be filled with cellulose and will be identical in appearance. The participants will be provided with a 4-week supply of either MET-2 or placebo capsules at the baseline visit and a 2-week supply at the week 4 visit. Loading or booster doses will be kept separate from daily maintenance doses.

The 0.5-g MET-2 capsules are produced under conditions compatible with good manufacturing practices at the University of Guelph and are shipped at room temperature and sealed under anaerobic conditions. All capsules are to be stored at room temperature.

Administration of Study Drug

Participants who meet the inclusion criteria and pass screening will be scheduled to start treatment at baseline. At the baseline visit, all participants will receive a 10-capsule orally administered loading dose of 5 g of either MET-2 or placebo on both days 1 and 2 (Table S2 in Multimedia Appendix 1). The participant will consume the initial loading dose in the clinic and receive the second loading dose to be taken at home on day 2. The participant will also remain at the clinic for 30 minutes after receiving the first loading dose to ensure there are no adverse reactions to the medication. A 3-capsule maintenance dose containing 1.5 g of MET-2 or placebo will be administered for the remainder of the 2-week interval from 3 to 14 days. At the week 2 visit, participants will be asked to take a 10-capsule booster dose on days 15 and 16. The 3-capsule maintenance dose will be administered for the remainder of the study for a total of 6 weeks of treatment.

If a participant is a nonresponder (a participant whose MADRS total score is not reduced by at least 50% from baseline by week 4 visit), an additional 10-capsule booster dose is to be administered at week 4 for 2 days (days 29 and 30) followed by a maintenance dose of 3 capsules for the remainder of the study (Table S2 in Multimedia Appendix 1). Responders (participants whose MADRS score is reduced by ≥50%) will not receive a booster dose at week 4. Participants will not take the maintenance dose during the loading or booster dose periods.

Treatment Compliance

Compliance with treatment will be assessed by reviewing the participant's personal logs and charts while documenting any missed and unused treatment material during the 6 weeks of intervention.

Efficacy Endpoints

Primary Efficacy Endpoint

At the first endpoint, we will assess changes in symptoms of depression from baseline to week 6 as measured by MADRS scores.

Secondary Endpoints

The secondary endpoints are:

1. Changes in symptoms of depression from baseline to week 8 as measured by the Clinical Global Impressions (CGI), Snaith-Hamilton pleasure scale (SHAPS), and Quick Inventory of Depressive Symptomatology (QIDS)-SR16 scores.
2. Changes in symptoms of anxiety from baseline to week 8 as measured by the generalized anxiety disorder (GAD)-7 and Hamilton anxiety rating scale (HAM-A) scores.
3. Changes in immune marker concentrations from screening to week 4 and week 8.
4. Changes in symptoms of depression and anxiety from baseline to week 2, week 4, week 6, and the 2-week follow-up measured using the MADRS, HAM-A, and GAD-7 scores.
5. Changes in relative abundance, diversity, and level of engraftment in stool samples, as measured by 16S rRNA sequencing.

Assessments of Safety and Efficacy

Primary Clinical Measures

Mood will primarily be assessed using the MADRS, a 10-item clinician-rated questionnaire used to evaluate the severity of depression.

Secondary Clinical Measures

Anxiety will primarily be assessed using the HAM-A, a clinician-rated questionnaire that measures the severity of anxiety symptoms. The GAD-7, a 7-item questionnaire, will be used to measure self-reported anxiety symptoms and severity. The CGI scale is a 2-item clinician-rated scale that will be used to assess the severity of illness and improvement of symptomology over time. The SHAPS is a 14-item self-rated instrument used to assess the presence of anhedonia. The QIDS-SR16 is a 16-item questionnaire that measures self-reported depressive symptom severity. The Pittsburgh Sleep Quality Index is a 19-item self-report questionnaire used to assess sleep quality and disturbances. Early life stress will be assessed using the Childhood Experience of Care and Abuse questionnaire to determine the effects of maltreatment and upbringing on treatment response and MDD biomarkers.

Participants will also use a personal log to track any newly emerging GI symptoms since the beginning of treatment to assess their tolerability to treatment and keep track of their mood symptoms and sleep. Tolerability and GI effects will be assessed using the Toronto Side Effects Scale and the GI Symptom Rating Scale during all treatment-related visits.

Molecular Analysis

Stool samples will be collected and analyzed using 16S ribosomal RNA sequencing at the University of Guelph. These data will be used to assess the relative abundance of microbial species, level of engraftment of MET-2 species, and α and β diversity of the gut microbiome. Urine samples will be collected to analyze soluble metabolites at the University of Guelph, whereas blood samples will be collected for clinical chemistry, hematology, and additional biomarker testing for safety and discovery purposes at Life Labs and Queen's University, respectively. Statistical analyses will be performed to assess the relationship between immune biomarkers and clinical symptom improvement. Additional safety blood samples may be required in the event of abnormal values or analysis failure. The blood samples collected for safety laboratory analysis will be destroyed after the analyses have been completed.

The specific parameters being assessed are presented in Table S3 in Multimedia Appendix 1, whereas collection time points can be found in Table S1 in Multimedia Appendix 1.

Safety Assessments

The primary safety analysis for this study will include the total number of treatment-emergent adverse events (TEAEs) while also categorizing TEAEs by causality, severity, and seriousness assessments made by the investigator by comparing study drug exposure to placebo.

Trends in safety will also be evaluated for the following assessments: physical examinations, vital signs, laboratory

results (hematology, lipid levels, and serum chemistry), pregnancy tests, and discontinuations because of adverse events (AEs).

Demographic Data and Medical History

At the screening visit, a complete medical history will be compiled for each participant. This history will include the use of antidepressant therapies, GI-related disorders and surgeries, depressive episodes, medical history, baseline signs, and symptoms.

Vital Signs

Vital signs, including temperature, blood pressure (systolic and diastolic), pulse, and body weight (using a calibrated weight scale), will be measured at screening, baseline, week 4, and week 8. Blood pressure will be measured with a cuff size appropriate to the participant after the participant has been sitting for 5 minutes.

Physical Examination

A complete physical examination will be conducted at the baseline visit. The physical examination will include general appearance, skin, head, ears, eyes, nose, throat, lungs, cardiovascular, abdomen, musculoskeletal and extremities, lymph nodes, and neurological. Other body and organ systems may be examined if clinically relevant.

Pregnancy Test

A pregnancy test will be performed at baseline. If pregnancy is discovered in a female participant enrolled in the study before the end of dosing, the study drug will be permanently discontinued, and an end-of-treatment visit will be scheduled. If the pregnancy is discovered in a female participant enrolled in the study after the end of dosing, the participant will continue in the study per protocol. If pregnancy occurs in a male participant's partner at any time during the study, the pregnancy is to also be reported and followed.

Adverse Events

Overview

An AE is any untoward medical occurrence in a participant administered an investigational treatment, which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign or symptom temporally associated with the use of the investigational treatment, regardless of whether it is related to the treatment. Each participant will be carefully monitored for the development of AEs during the safety reporting period. Both the frequency and severity of AEs will be collected at the time of consent throughout the study until the 2-week follow-up. AEs will be assessed and recorded at all in-hospital visits or through the phone using questionnaires and probing via discussion; these AEs will be categorized by frequency, severity, and causality [7]. Any clinically relevant abnormalities will be noted by the investigator during the follow-up interviews. All AEs will be recorded in an AE log for each participant. Any instances that lead to serious AEs (SAEs) and any untoward medical occurrences at any dose will be reported to the research ethics board (REB).

A TEAE is an AE that begins during the treatment or worsens a pre-existing medical condition (eg, worsening diarrhea). The treatment period is the period during which a participant receives the investigational treatment.

Serious Adverse Events

An SAE is a life-threatening adverse medical event that results in death, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability or incapacity, and results in a congenital anomaly or congenital disability [7]. The study site will document all SAEs that occur (whether related to the study drug) and report them to the sponsor within 24 hours of the site's first knowledge of the event. The collection period for all SAEs will begin after informed consent is obtained and will end after the procedures for the final study visit have been completed.

All SAEs will be followed until resolution. SAEs that remain ongoing past the participant's last protocol-specified follow-up visit will be evaluated by the principal investigator and NuBiyota LLC. If both parties agree that the participant's condition is unlikely to resolve, the principal investigator will determine the follow-up requirement.

Reporting of Expedited Safety Reports

A suspected unexpected serious adverse reaction (SUSAR) is an SAE that occurs in a participant, the nature or severity of which is not expected per the applicable product information (ie, the investigator's brochure).

The sponsor and investigator will report any SUSARs concerning the drug that has occurred in the study to regulatory authorities:

- If it is neither fatal nor life-threatening, within 15 days after becoming aware of the information.
- If it is fatal or life-threatening, within 7 days after becoming aware of the information. The sponsor and investigator shall, within 8 days after having informed the REB and Health Canada of a fatal or life-threatening SUSAR, submit a complete follow-up report in respect of that information that includes an assessment of the importance and implication of any findings made.

Statistics

Sample Size Determination

The sample size for this clinical investigation was calculated based on the results from the pilot study and the change from baseline to week 8 of the first 13 participants for the MADRS (primary endpoint) and GAD-7 scores (first secondary endpoint). The change from baseline to week 8 was used for the two endpoints, mirroring the time frame for the evaluation of the primary and first secondary endpoints for this clinical investigation. Two series of estimates were generated: change from baseline for the participants with scores at baseline and week 8, and a second imputed data set for participants who did not have a week 8 value using the last observation carried forward. Although the final analysis from this study will use multiple imputation to address missing data, using the last recorded observation results in a higher SD and is considered

a reasonable approach to derive a range of estimates. Estimates from the pilot investigation are presented in Table S4 in Multimedia Appendix 1.

For estimation purposes, it is assumed that the placebo participants will have a response that is 50% of the active treatment group, and the SD will be the same between the two treatment groups. The randomization will be in a 1:1 ratio (active:placebo), and the type 1 error rate will be 5%. The resulting sample sizes for 80%, 85%, and 90% power are presented in Table S5 in Multimedia Appendix 1.

If the true mean difference between the active and placebo groups is the midpoint between the observed and imputed results, a minimum target sample size of 50 participants will be required for the primary endpoint (MADRS: change at 8 weeks) and 79 participants (GAD-7: change at 8 weeks) for the other endpoints. On the basis of these estimates, the maximum number of participants to be enrolled in this clinical investigation is 80, and the target sample size is 60 participants. An interim assessment will be performed after 30 participants have completed the 8-week evaluation or withdrawn prematurely.

Populations for Analyses

Intent-to-Treat Population

This population includes all participants who consent to participate, meet the inclusion criteria, and are randomized. All baseline characteristics will be summarized based on intent-to-treat (ITT). Participants in the ITT population will be analyzed according to the original treatment assignment, regardless of the actual treatment received. All baseline tables will be based on the ITT population. The ITT population will be the primary population for efficacy endpoints.

Per-Protocol Population

The per-protocol population is a subset of the safety population. It includes all participants who meet all of the following criteria:

- No major deviations from protocol eligibility criteria;
- ≥85% of compliance with the treatment schedule; and
- ≥85% of compliance with all study visits where the samples will be obtained and the testing will be performed.

The per-protocol population will be used for the sensitivity analyses of the efficacy endpoints.

Safety Population

The safety analysis population will contain all participants who receive at least one dose of study medication (active or placebo). All safety tables will be based on the safety population.

Statistical Analysis

The statistical analysis plan will be finalized before database lock and will include a more technical and detailed description of the statistical analyses described in this section. This section summarizes the planned endpoints and statistical analyses. Participants who return after the initial treatment but later withdraw from the study will have their final scores for primary outcomes projected to week 8. If data are missing, the data from the last time point will be projected forward.

Changes from baseline to endpoint in scores on the MADRS, HAM-A, CGI, SHAPS, QIDS-SR16, GAD-7, and Pittsburgh Sleep Quality Index will be analyzed using two-tailed *t* tests or analysis of variance between and within the placebo and active arms. All statistical tests will be performed using the statistical program IBM SPSS with a significance level of .05. Similarly, stool samples will be analyzed for their diversity scores using a paired *t* test and repeated measures analysis of variance. Any changes in diversity scores will then be compared with the clinical scores to determine any correlations.

Direct Access to Source Data or Documents

The investigator or institution shall provide direct access to source data or documents for study-related monitoring, audits, REB review, and regulatory inspection.

Quality Control and Quality Assurance

Study Conduct

This study will be conducted in compliance with the current International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) guidelines. The sponsor shall ensure that all sites have the necessary standard operating procedures to ensure that the study is conducted and data are generated, documented, and reported in compliance with the protocol, ICH GCP, and applicable regulatory requirements. The investigator may not deviate from the protocol without a formal protocol amendment being established and approved by an appropriate competent authority and REB, except when necessary, to eliminate immediate hazards to the participant or when the changes involve only logistical or administrative aspects of the study. Any deviations may result in the participant being withdrawn from the study and render the participant nonevaluable. The sponsor is responsible for the distribution of protocol amendments to the principal investigators and those concerned with the conduct of the study. The principal investigator is responsible for the distribution of all amendments to the REB and all the staff concerned at their center.

Study Monitoring

All monitoring visits will be conducted by PhaseAdvance, a contract research organization appointed by NuBiyota LLC, to ensure compliance with the ICH guidelines for GCP (E6). The study monitors will conduct an initiation site visit to the institution to review the protocol and its requirements with the investigators, inspect the drug storage area, and fully inform the investigator of their responsibilities and the procedures for assuring adequate and correct documentation. During the study, the monitor will make regular site visits to review protocol compliance and individual participants' medical records and ensure that the study is being conducted according to pertinent regulatory requirements. The review of medical records will be conducted in a manner that ensures confidentiality is maintained. No information in these records regarding the identity of the participants will leave the study center. Sponsor monitoring standards require full verification of the presence of the signed informed consent form (ICF), adherence to the inclusion and exclusion criteria, documentation of SAEs, and recording primary efficacy and safety variables. The clinical research

associate will review source data compared with the case report forms (CRFs) and verify source data according to the study-specific monitoring plan. The study design, frequency of participant visits, and site enrollment rate will determine the frequency of monitoring visits. Upon study completion, the clinical research associate will visit the site to conduct a study termination visit, which will include the collection of any outstanding documentation.

Ethics

Written Informed Consent

To obtain and document informed consent, the investigator will comply with the applicable regulatory requirements and adhere to ICH GCP and the ethical principles that have their origin in the Declaration of Helsinki.

Informed consent shall be documented using a written consent form approved by the REB. The ICF must be signed and dated by the participant and investigator (or designated research professional) before protocol-specific procedures (screening or treatment) are performed. A consent form template will be provided by the sponsor and adapted by the investigator to meet the center, state, and country ethical guidelines, as appropriate.

Participants will be given a copy of the fully executed consent form, and the original will be maintained with the participant's records.

Research Ethics Board

This study will not commence until review and approval of the study protocol within each site and ICF has been obtained by local REBs. Any amendments to the study will be submitted concurrently to all REBs for review and approval unless they are required to eliminate immediate hazards to study participants.

Data Handling and Record Keeping

Data Collection

Clinical data will be collected by the study coordinator as a source document and transcribed into REDCap (Research Electronic Data Capture), a web-based data collection software. REDCap will only contain the participant's ID but no personal data.

Retention of Records

Essential documents, as defined by ICH GCP, include the signed protocol and any amendments, copies of the completed CRFs (for site archiving, digital versions of e-CRF data for specific participants will be provided), signed ICFs, hospital records and other source documents, REB approvals and all related correspondence including approved documents, drug accountability records, study correspondence, and a list of participants' names and addresses. Essential documents should be retained for at least 5 years.

Results

This study was approved by the Queen's University Health Sciences and Affiliated Teaching Hospitals REB on September 2, 2020. Owing to COVID-19–related delays, participant recruitment did not start until March 2021. Given the association between the GBA and symptoms of depression, it is expected that participants who receive MET-2 will have a significant reduction in depressive symptoms as determined by the MADRS compared with participants who received the placebo. This will be assessed by comparing pre- and posttreatment scores.

Discussion

Optimal Treatment Methods

With MDD affecting 3.7 million Canadians throughout their lifetime [28], there is a pressing need to find optimal treatment methods for these individuals. Although there are numerous psychological, pharmacological, and neurostimulation treatment options available for people experiencing MDD, it is challenging to find personalized treatments. With high individual variability in factors affecting the illness and presentation of symptoms, an effective treatment may not be effective for another [12]. Given these circumstances, novel treatment methods are being developed and evaluated for their ability to alleviate the symptoms of depression. One of these novel treatment approaches involves assessing individuals' gut health and targeting the gut microbiome through the GBA [7,12].

The gut plays a critical role in modulating physiological processes of the body, such as the immune system and GI functioning, while also playing a role in regulating aspects of brain development [13,29]. Although there has been a growing recognition of the GBA in the last few years, further research is warranted to fully elucidate the underlying mechanisms affecting mood and gut health. Fortunately, if MET-2 can alleviate symptoms of depression and produce a lasting effect on mood both during and after treatment, it may provide promising results for microbe therapy as a treatment method and may help explain how the GBA relates to mood. Similarly, given the adaptable nature of microbiota and how it can be influenced by external factors, the microbiome may indicate each individual's predicted response to treatment, severity, and course of MDD.

Limitations

Limitations to the many studies examining the efficacy of GBA treatments include small sample sizes and thus less generalizable results. Hence, in this trial, we have addressed these concerns by designing a multisite, double-blind, randomized controlled trial. We also hope to enroll 60 participants to determine any significant trends between changes in mood and MET-2 treatment. To our knowledge, assessing the effects of a daily, orally administered microbial therapeutic product such as MET-2 on mood, at this level of scale, has never been performed before. This study would not only be the first of its kind to highlight the potential capabilities of microbe therapy in treating symptoms of depression but also to expand the scope of pre-existing literature surrounding the GBA and how it mediates mood and behavior.

Acknowledgments

This trial was funded by NuBiyota LLC and MITACS Canada. A statistician from NuBiyota LLC helped with the power calculations and statistical plans for this trial. The funders did not have any role in the study design or interpretation of the results. This study was approved by Health Canada and Queen's University Health Sciences and Affiliated Teaching Hospitals REB.

Authors' Contributions

ACM and RM developed the original protocol for an open-label trial before this study. All authors helped to finalize and update this version of the protocol. All authors have read and approved this manuscript.

Conflicts of Interest

RM has received consulting and speaking honoraria from Allergan, Janssen, KYE, Lundbeck, Otsuka, Pfizer, and Sunovion. He has also received research grants from the Canadian Biomarker Integration Network for Depression, Canadian Institutes of Health Research, Janssen, Lallemand, Lundbeck, NuBiyota, Ontario Brain Institute, Ontario Mental Health Foundation, and Pfizer. ACM declares no conflicts of interest. CS declares no conflicts of interest. DJB has received consulting honoraria from Alkermes PLC and research grants from the National Institute for Drug Abuse, the University of Minnesota Department of Psychiatry and Behavioral Sciences, and the University of Minnesota Foundation. GV has received consulting and speaking honoraria from Abbvie, Allergan, Janssen, Otsuka/Lundbeck, and Sunovion and research grants from Queen's University Department of Psychiatry and Medical School and Providence Care. DJM's research projects are funded by the Canadian Institutes of Health Research, NuBiyota, the Academic Health Science Centre Alternate Funding Plan, and the Centre for Addiction and Mental Health Foundation, including the Joanne Murphy professorship.

Multimedia Appendix 1
Supplementary tables and textboxes.
[PDF File (Adobe PDF File), 262 KB - resprot_v10i9e31439_app1.pdf]

Multimedia Appendix 2
Peer-review report.
[PDF File (Adobe PDF File), 289 KB - resprot_v10i9e31439_app2.pdf]

References

1. Smetanin P, Stiff D, Briante C, Adair C, Khan M. The life and economic impact of major mental illnesses in Canada: 2011 to 2041. RiskAnalytica. 2011. URL: https://www.mentalhealthcommission.ca/sites/default/files/MHCC_Report_Base_Case_FINAL_ENG_0_0.pdf [accessed 2021-04-16]
2. Lim K, Jacobs P, Ohinmaa A, Schopflocher D, Dewa C. A new population-based measure of the economic burden of mental illness in Canada. Chronic Dis Can 2008;28(3):92-98 [FREE Full text] [Medline: 18341763]
3. What is depression? American Psychiatric Association. 2020. URL: https://www.psychiatry.org/patients-families/depression/what-is-depression [accessed 2021-04-14]
4. Lam RW, Kennedy SH, Parikh SV, MacQueen GM, Milev RV, Ravindran AV, CANMAT Depression Work Group. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 clinical guidelines for the management of adults with major depressive disorder: introduction and methods. Can J Psychiatry 2016 Sep;61(9):506-509 [FREE Full text] [doi: 10.1177/0706743716659061] [Medline: 27486152]
5. Milev RV, Giacobbe P, Kennedy SH, Blumberger DM, Daskalakis ZJ, Downar J, CANMAT Depression Work Group. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 clinical guidelines for the management of adults with major depressive disorder: section 4. neurostimulation treatments. Can J Psychiatry 2016 Sep;61(9):561-575 [FREE Full text] [doi: 10.1177/0706743716660033] [Medline: 27486154]
6. Parikh SV, Quilty LC, Ravitz P, Rosenbluth M, Pavlova B, Grigoriadis S, CANMAT Depression Work Group. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2016 clinical guidelines for the management of adults with major depressive disorder: section 2. psychological treatments. Can J Psychiatry 2016 Sep;61(9):524-539 [FREE Full text] [doi: 10.1177/0706743716659418] [Medline: 27486150]
7. Meyyappan A, Milev R. The safety, efficacy, and tolerability of microbial ecosystem therapeutic-2 in people with major depression and/or generalized anxiety disorder: protocol for a phase 1, open-label study. JMIR Res Protoc 2020 Jun 04;9(6):e17223 [FREE Full text] [doi: 10.2196/17223] [Medline: 32495743]
8. Maller JJ, Broadhouse K, Rush AJ, Gordon E, Koslow S, Grieve SM. Increased hippocampal tail volume predicts depression status and remission to anti-depressant medications in major depression. Mol Psychiatry 2018 Aug;23(8):1737-1744. [doi: 10.1038/mp.2017.224] [Medline: 29133948]

9. Papiol S, Arias B, Gastó C, Gutiérrez B, Catalán R, Fañanás L. Genetic variability at HPA axis in major depression and clinical response to antidepressant treatment. J Affect Disord 2007 Dec;104(1-3):83-90. [doi: 10.1016/j.jad.2007.02.017] [Medline: 17467808]
10. Plöderl M, Hengartner MP. What are the chances for personalised treatment with antidepressants? Detection of patient-by-treatment interaction with a variance ratio meta-analysis. BMJ Open 2019 Dec 23;9(12):e034816 [FREE Full text] [doi: 10.1136/bmjopen-2019-034816] [Medline: 31874900]
11. Martin R, Makino H, Yavuz A, Ben-Amor K, Roelofs M, Ishikawa E, et al. Early-life events, including mode of delivery and type of feeding, siblings and gender, shape the developing gut microbiota. PLoS One 2016 Jun 30;11(6):e0158498 [FREE Full text] [doi: 10.1371/journal.pone.0158498] [Medline: 27362264]
12. Foster JA, Neufeld KM. Gut-brain axis: how the microbiome influences anxiety and depression. Trends Neurosci 2013 May;36(5):305-312. [doi: 10.1016/j.tins.2013.01.005] [Medline: 23384445]
13. O'Hara AM, Shanahan F. The gut flora as a forgotten organ. EMBO Rep 2006 Jul;7(7):688-693 [FREE Full text] [doi: 10.1038/sj.embor.7400731] [Medline: 16819463]
14. Meyyappan AC, Forth E, Wallace CJ, Milev R. Effect of fecal microbiota transplant on symptoms of psychiatric disorders: a systematic review. BMC Psychiatry 2020 Jun 15;20(1):299 [FREE Full text] [doi: 10.1186/s12888-020-02654-5] [Medline: 32539741]
15. Dash S, Clarke G, Berk M, Jacka F. The gut microbiome and diet in psychiatry: focus on depression. Curr Opin Psychiatry 2015 Jan;28(1):1-6. [doi: 10.1097/YCO.0000000000000117] [Medline: 25415497]
16. Delgado PL. Depression: the case for a monoamine deficiency. J Clin Psychiatry 2000;61 Suppl 6:7-11. [Medline: 10775018]
17. Miller AH, Maletic V, Raison CL. Inflammation and its discontents: the role of cytokines in the pathophysiology of major depression. Biol Psychiatry 2009 May 01;65(9):732-741 [FREE Full text] [doi: 10.1016/j.biopsych.2008.11.029] [Medline: 19150053]
18. Verduijn J, Milaneschi Y, Schoevers RA, van Hemert AM, Beekman AT, Penninx BW. Pathophysiology of major depressive disorder: mechanisms involved in etiology are not associated with clinical progression. Transl Psychiatry 2015 Sep 29;5(9):e649 [FREE Full text] [doi: 10.1038/tp.2015.137] [Medline: 26418277]
19. Moylan S, Maes M, Wray NR, Berk M. The neuroprogressive nature of major depressive disorder: pathways to disease evolution and resistance, and therapeutic implications. Mol Psychiatry 2013 May;18(5):595-606. [doi: 10.1038/mp.2012.33] [Medline: 22525486]
20. Maes M, Kubera M, Leunis J, Berk M. Increased IgA and IgM responses against gut commensals in chronic depression: further evidence for increased bacterial translocation or leaky gut. J Affect Disord 2012 Dec 01;141(1):55-62. [doi: 10.1016/j.jad.2012.02.023] [Medline: 22410503]
21. Appleton J. The gut-brain axis: influence of microbiota on mood and mental health. Integr Med (Encinitas) 2018 Aug;17(4):28-32 [FREE Full text] [Medline: 31043907]
22. Huang HL, Chen HT, Luo QL, Xu HM, He J, Li YQ, et al. Relief of irritable bowel syndrome by fecal microbiota transplantation is associated with changes in diversity and composition of the gut microbiota. J Dig Dis 2019 Aug;20(8):401-408. [doi: 10.1111/1751-2980.12756] [Medline: 31070838]
23. Kurokawa S, Kishimoto T, Mizuno S, Masaoka T, Naganuma M, Liang K, et al. The effect of fecal microbiota transplantation on psychiatric symptoms among patients with irritable bowel syndrome, functional diarrhea and functional constipation: an open-label observational study. J Affect Disord 2018 Aug 01;235:506-512. [doi: 10.1016/j.jad.2018.04.038] [Medline: 29684865]
24. Pakyz AL, Moczygemba LR, VanderWielen LM, Edmond MB. Fecal microbiota transplantation for recurrent Clostridium difficile infection: the patient experience. Am J Infect Control 2016 May 01;44(5):554-559. [doi: 10.1016/j.ajic.2016.01.018] [Medline: 26944009]
25. Cenit MC, Sanz Y, Codoñer-Franch P. Influence of gut microbiota on neuropsychiatric disorders. World J Gastroenterol 2017 Aug 14;23(30):5486-5498 [FREE Full text] [doi: 10.3748/wjg.v23.i30.5486] [Medline: 28852308]
26. Petrof EO, Khoruts A. From stool transplants to next-generation microbiota therapeutics. Gastroenterology 2014 May;146(6):1573-1582 [FREE Full text] [doi: 10.1053/j.gastro.2014.01.004] [Medline: 24412527]
27. Montgomery SA, Asberg M. A new depression scale designed to be sensitive to change. Br J Psychiatry 1979 Apr;134:382-389. [doi: 10.1192/bjp.134.4.382] [Medline: 444788]
28. Lépine JP, Briley M. The increasing burden of depression. Neuropsychiatr Dis Treat 2011;7(Suppl 1):3-7 [FREE Full text] [doi: 10.2147/NDT.S19617] [Medline: 21750622]
29. Stilling RM, Dinan TG, Cryan JF. Microbial genes, brain and behaviour - epigenetic regulation of the gut-brain axis. Genes Brain Behav 2014 Jan;13(1):69-86 [FREE Full text] [doi: 10.1111/gbb.12109] [Medline: 24286462]

Abbreviations

AE: adverse event
CGI: Clinical Global Impressions
CRF: case report form

FMT: fecal microbiota transplantation
GAD: generalized anxiety disorder
GBA: gut-brain axis
GCP: Good Clinical Practice
GI: gastrointestinal
HAM-A: Hamilton anxiety rating scale
ICF: informed consent form
ICH: International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use
Ig: immunoglobulin
ITT: intent-to-treat
MADRS: Montgomery-Asberg Depression Rating Scale
MDD: major depressive disorder
MET: Microbial Ecosystem Therapeutic
QIDS: quick inventory of depressive symptomatology
REB: research ethics board
REDCap: Research Electronic Data Capture
SAE: serious adverse effect
SHAPS: Snaith-Hamilton pleasure scale
SUSAR: suspected unexpected serious adverse reaction
TEAE: treatment-emergent adverse event

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Protocol

Risk Factors for Surgical Site Infection After Lower Limb Revascularization Surgery in Adults With Peripheral Artery Disease: Protocol for a Systematic Review and Meta-analysis

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Abstract

Background: Surgical site infections (SSIs) are common, costly, and associated with increased morbidity and potential mortality after lower limb revascularization surgery (ie, arterial bypass, endarterectomy, and patch angioplasty). Identifying evidence-informed risk factors for SSI in patients undergoing these surgeries is therefore important.

Objective: The aim of this study is to conduct a systematic review and meta-analysis of prognostic studies to identify, synthesize, and determine the certainty in the cumulative evidence associated with reported risk factors for early and delayed SSI after lower limb revascularization surgery in adults with peripheral artery disease.

Methods: We will search MEDLINE, Embase, the seven databases in Evidence-Based Medicine Reviews, review articles identified during the search, and included article bibliographies. We will include studies of adults (aged ≥18 years) with peripheral artery disease that report odds ratios, risk ratios, or hazard ratios adjusted for the presence of other risk factors or confounding variables and relating the potential risk factor of interest to the development of SSI after lower limb revascularization surgery. We will exclude studies that did not adjust for confounding, exclusively examined certain high-risk patient cohorts, or included >20% of patients who underwent surgery for indications other than peripheral artery disease. The primary outcomes will be early (in-hospital or ≤30 days) SSI and Szilagyi grade I (cellulitis involving the wound), grade II (infection involving subcutaneous tissue), and grade III (infection involving the vascular graft) SSI. Two investigators will independently extract data and evaluate the study risk of bias using the Quality in Prognosis Studies tool. Adjusted risk factor estimates with similar definitions will be pooled using DerSimonian and Laird random-effects models. Heterogeneity will be explored using stratified meta-analyses and meta-regression. Finally, we will use the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach to determine certainty in the estimates of association between reported risk factors and the development of SSI.

Results: The protocol was registered in PROSPERO (International Prospective Register of Systematic Reviews). We will execute the peer-reviewed search strategy on June 30, 2021, and then complete the review of titles and abstracts and full-text articles by July 30, 2021, and September 15, 2021, respectively. We will complete the full-text study data extraction and risk of

bias assessment by November 15, 2021. We anticipate that we will be able to submit the manuscript for peer review by January 30, 2022.

Conclusions: This study will identify, synthesize, and determine the certainty in the cumulative evidence associated with risk factors for early and delayed SSI after lower limb revascularization surgery in patients with peripheral artery disease. The results will be used to inform practice, clinical practice statements and guidelines, and subsequent research.

Trial Registration: PROSPERO International Prospective Register of Systematic Reviews CRD42021242557; https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=242557

International Registered Report Identifier (IRRID): PRR1-10.2196/28759

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KEYWORDS

lower limb revascularization surgery; peripheral artery disease; risk factors; surgical site infection; systematic review

Introduction

Background

Lower limb revascularization surgeries (ie, arterial bypass, endarterectomy, and patch angioplasty) are costly, high-risk procedures commonly performed in North America and internationally [1-5]. Indications for these procedures include chronic limb-threatening ischemia (ie, peripheral artery disease manifested by ischemic rest pain confirmed by vascular hemodynamic studies, lower limb ulceration, or gangrene) or, less commonly, disabling intermittent vasculogenic claudication that has failed medical management [6]. Although endovascular therapies are increasingly being used to treat patients with these indications, they are not as durable or suited for all patients' anatomical pattern of peripheral artery disease [7-10]. Therefore, in the United States, approximately 15,000-20,000 lower limb revascularization surgeries are performed each year, and the estimated cost per procedure can exceed US $120,000 [1,2].

Surgical site infections (SSIs) are common and costly; they are also associated with a significantly increased risk of morbidity, limb loss, and potential mortality after lower limb revascularization surgery [11-14]. They represent the leading cause of unplanned and potentially preventable hospital readmissions after vascular surgery [15,16]. After vascular surgery, postoperative complications are commonly classified using the Szilagyi grading system, which includes Szilagyi grade I (cellulitis involving the wound), grade II (infection involving subcutaneous tissue), and grade III (infection involving the vascular graft) SSIs [17-19]. SSI has been estimated to occur in approximately 7% to 8% of patients after infrainguinal bypass surgery (and to result in graft infection in approximately 2%), nearly double the incidence of prolonged (>10 days) hospitalization, and increase the risk-adjusted costs per peripheral vascular surgery by approximately US $7300 (and likely several-fold higher after a deep SSI) [11,12,20]. SSIs involving prosthetic (and sometimes autologous) grafts also often necessitate urgent reoperation for graft excision to prevent pseudoaneurysm formation and catastrophic hemorrhage [21].

Identifying valid, evidence-informed risk factors for SSI after lower limb revascularization surgery is important to assist in deciding which patients may benefit most from interventions designed to prevent them. It may also help in determining the benefit-to-risk profile of performing open over endovascular revascularization in patients who are candidates for both. However, although many studies examining potential risk factors for SSI after lower limb revascularization surgery have been published, some are difficult to access because their titles may not indicate that they examined risk factors for SSI. They are also collectively difficult to interpret, as some have included potentially overlapping data and many are limited by between-study clinical heterogeneity. This heterogeneity includes the recruitment of patients with different indications for surgery (eg, intermittent vasculogenic claudication, chronic limb-threatening ischemia, or even aneurysms and vascular trauma [14]) and examination of different types of lower limb revascularization surgery (eg, ranging from groin-only procedures [22,23] to infrainguinal or aortofemoral bypass [24,25]) or vascular surgery in general [26]. Studies have also either not adjusted for or variably adjusted for potential confounding factors when examining associations between potential risk factors and SSI. Further, some studies have reported on risk factors for specific types of infection (eg, prosthetic graft infection [27] or that requiring reoperation [28]) or for infection or wound complications in general [29]. Finally, others measured their SSI outcomes at different time points ranging from in-hospital to 30 days or longer or defined the severity of SSIs using different classification systems.

Objectives

We aim to conduct a systematic review and meta-analysis of prognostic studies to identify, synthesize, and determine the certainty in the cumulative evidence associated with reported risk factors for early and delayed SSI after lower limb revascularization surgery in adults with peripheral artery disease. We will also determine whether the strength of association for individual risk factors varies according to different clinical or methodological study characteristics.

Methods

Protocol and Role of the Sponsor

We prespecified our methods according to the PRISMA (Preferred Reporting Items in Systematic Reviews and Meta-Analyses) statement [30] and the Meta-Analysis of Observational Studies in Epidemiology proposal [31]. It is reported according to the PRISMA-P (Preferred Reporting Items in Systematic Reviews and Meta-Analysis Protocols) statement

(and the completed PRISMA-P checklist is given in Multimedia Appendix 1) [32,33]. The study will follow guidelines for conducting systematic reviews and meta-analyses of prognostic factor studies [34,35]. The protocol is registered on PROSPERO (International Prospective Register of Systematic Reviews; CRD42021242557). The study sponsor, the University of Ottawa, played no role in the development of the protocol.

Focused Clinical Question

We formulated the study-focused clinical question using the PICOTS (Population, Index Prognostic Factor, Comparison of Prognostic Factors, Outcome, Timing, and Setting) framework for posing clinical questions for systematic reviews of prognostic factor studies [34,36]. The focused clinical question was as follows:

- P: in adults (aged ≥18 years) with peripheral artery disease who underwent lower limb revascularization surgery
- I: which factors increase the risk of SSI or Szilagyi grade I (cellulitis involving the wound), grade II (infection involving subcutaneous tissue), or grade III (infection involving the vascular graft) SSI
- C: over and above other comparator risk and confounding factors for predicting SSI
- OTS: in-hospital or within ≤30 days or longer than 30 days after lower limb revascularization surgery?

Information Sources

We will search MEDLINE; MEDLINE Epub Ahead of Print, In-Process, and Other Nonindexed Citations; Embase; and the databases contained within Evidence-Based Medicine Reviews (American College of Physicians Journal Club; the Cochrane Central Register of Controlled Trials, the Database of Systematic Reviews, and the Methodology Register Database; the Database of Abstracts of Reviews of Effects; the Health Technology Assessment Database; and the National Health Service Economic Evaluation Database) from their first available dates without restrictions. To identify additional citations, we will also use the PubMed *related articles* feature and manually search bibliographies of included studies and relevant review articles identified during the search.

Search Strategy

A vascular and endovascular surgeon and epidemiologist with a PhD training in information science and evidence synthesis methods created the initial MEDLINE search strategy, which was refined after input from a medical librarian and information specialist and by adding additional thesaurus or indexing terms when new and relevant citations were located during iterative search strategies. Using a combination of Medical Subject Heading/Emtree terms and keywords, we constructed search filters covering the themes *lower limb revascularization surgery* and *surgical site infection*. After the refined search strategy was created, we submitted it to another medical librarian or information scientist to peer review this search strategy using the Peer Review of Electronic Search Strategies guidelines [37] (our pre–peer-reviewed electronic search strategies are given in Table 1).

Table 1. Pre–Peer Review of Electronic Search Strategies database search strategies.

Search theme	Search terms			
	Ovid MEDLINE, PubMed, and Evidence-Based Medicine Reviews		Ovid Embase	
	Exploded MeSH[a] terms	Title and subject keywords	Exploded Emtree terms	Title and subject keywords
Lower extremity revascularization surgery	Arterial occlusive disease/surgery OR endarterectomy OR ischemia/surgery OR lower extremity/surgery OR peripheral arterial disease/surgery OR peripheral vascular diseases/surgery OR vascular surgical procedures	((iliofemoral OR femoral OR femoral artery*) adj3 (endarterectom* OR patch* OR repair*)) OR ((aortofemoral OR aortobifemoral OR femoral-distal OR femoral distal OR femoral-popliteal OR femoral popliteal OR femoral-tibial OR femoral tibial OR infrageniculate OR suprageniculate OR infrainguinal OR lower extremity OR lower limb OR peripheral vascular) adj3 (arterial surg* OR arterial bypass* OR bypass* OR bypass graft* OR bypass surg* OR graft* OR intervention* OR revascularization* OR revascularization procedure* OR vascular bypass* OR vascular bypass surg* OR vascular graft* OR vein graft* OR prosthetic graft*))	Artery bypass OR blood vessel graft OR bypass surgery OR critical limb ischemia/surgery OR endarterectomy OR limb ischemia/surgery OR peripheral artery occlusive disease/surgery OR prosthetic vascular graft OR vascular surgery	((iliofemoral OR femoral OR femoral artery*) adj3 (endarterectom* OR patch* OR repair*)) OR ((aortofemoral OR aortobifemoral OR femoral-distal OR femoral distal OR femoral-popliteal OR femoral popliteal OR femoral-tibial OR femoral tibial OR infrageniculate OR suprageniculate OR infrainguinal OR lower extremity OR lower limb OR peripheral vascular) adj3 (arterial surg* OR arterial bypass* OR bypass* OR bypass graft* OR bypass surg* OR graft* OR intervention* OR revascularization* OR revascularization procedure* OR vascular bypass* OR vascular bypass surg* OR vascular graft* OR vein graft* OR prosthetic graft*))
Infection	Infections OR surgical wound infection	infection* OR surgical site infection* OR surgical wound infection* OR wound infection*	Surgical infection OR wound infection	infection* OR surgical site infection* OR surgical wound infection* OR wound infection*

[a]MeSH: Medical Subject Heading.

Data Management and Selection Process

The titles and abstracts of citations identified during the search will be imported into EndNote X9 reference management software (Clarivate, Thomson Reuters Corporation). This software will be used to remove identical duplicate citations before exporting them into Distiller SR (Evidence Reviews). Two investigators will then independently review the titles and abstracts of the articles identified by the search and select any article deemed potentially relevant by either investigator for full-text review. Finally, 2 investigators will review the full text of all potentially relevant citations and select studies for inclusion in the systematic review. Disagreements regarding study inclusion will be resolved via consensus or arbitration by a third investigator (Textbox 1).

Peripheral artery disease will be defined as intermittent vasculogenic claudication or chronic limb-threatening ischemia (ie, ischemic rest pain confirmed by vascular hemodynamic studies, lower limb ulceration, or gangrene) [6]. Lower limb revascularization surgery will be considered to include iliofemoral or femoral endarterectomy or patch angioplasty and aortofemoral, aortobifemoral, iliofemoral, femoral-popliteal, femoral-tibial, femoral-peroneal, axillofemoral, and femoral-femoral bypass. We will exclude studies that did not adjust for confounding in their effect estimates, exclusively examined certain high-risk patient cohorts (eg, those with obesity, diabetes, or chronic renal failure requiring dialysis), or included >20% of patients who underwent surgery for indications other than peripheral artery disease (eg, aneurysm disease). There will be no restrictions regarding the publication date, setting, or language of the study.

Textbox 1. Eligibility criteria.

Inclusion criteria

- Population: The study included adults (aged ≥18 years) with peripheral artery disease who underwent lower limb revascularization surgery.
- Index and comparison prognostic factors: The study evaluated the prognostic value of a potential risk factor over and above (ie, adjusted for or independent of) other existing or comparator risk and confounding factors for predicting postoperative surgical site infection (SSI).
- Outcome, timing, and setting: The study reported odds ratios, risk ratios, or hazard ratios (and surrounding SE or 95% CIs) adjusted for the presence of other risk factors or confounding variables and relating the potential risk factors of interest to the development of SSI in patients undergoing lower limb revascularization surgery [18,19].
- Study design: Observational (ie, cohort or case-control) studies or secondary analyses of randomized controlled trial data.

Outcomes

The primary outcomes will be early (in-hospital or ≤30 days) SSI and early Szilagyi grade I (cellulitis involving the wound), grade II (infection involving subcutaneous tissue), and grade III (infection involving the vascular graft) SSI. Secondary outcomes will be longer-term (>30 days) SSI or Szilagyi grade I (cellulitis involving the wound), grade II (infection involving subcutaneous tissue), or grade III (infection involving the vascular graft) SSI [17-19]. Although we will primarily use the Szilagyi classification to classify the severity of SSIs (as it is the most commonly used system in vascular surgery [18]), alternate classification systems for the severity of SSI are permitted if used by study authors (eg, the Centers for Disease Control, the American College of Surgeons National Surgical Quality Improvement Program, or the Veterans Affairs Quality Improvement Program).

Data Items and Collection Process

Two investigators will independently extract data in duplicate using a predesigned electronic data extraction spreadsheet piloted on a representative sample of five included studies. We will extract the following data from the included studies: (1) design, data source, and setting of the study; (2) patient recruitment period; (3) patient and procedural characteristics, including the number and types of procedures performed, the proportion of patients who had a groin incision (vertical or oblique), and the indication for the procedure (ie, intermittent vasculogenic claudication or chronic limb-threatening ischemia); (4) reported potential risk factors for SSI; (5) reported adjusted associations between the reported risk factors and the development of SSI and Szilagyi grade I, grade II, and grade III SSI after lower limb revascularization surgery (or different severities of SSI defined using different classification systems); (6) other prognostic or confounding factors that were adjusted for when evaluating associations between potential risk factors and SSI (crude or unadjusted associations were not extracted); and (7) whether the authors adjusted for a minimum confounder set in their analyses. This minimum confounder set was defined based on a narrative review of published studies and will include surgical urgency, age, sex, obesity, diabetes, the presence of critical or chronic limb-threatening ischemia, and whether a groin incision was used.

Risk of Bias Assessment

Two investigators will independently evaluate the study risk of bias in duplicate using the Quality in Prognosis Studies tool [38,39]. This tool includes questions regarding study participation and attrition, potential risk factor and outcome descriptions and measurements, confounding measurement and account, and methods and reporting of statistical analyses (the operationalized list of quality domains containing the prompting items used when making risk of bias decisions is given in Multimedia Appendix 2 [40]) [38,39]. The assessment of statistical analyses will incorporate recommendations for building and appraising logistic regression models [40,41]. We will assess whether studies that used administrative data used validated coding algorithms to identify indications for revascularization (eg, intermittent vasculogenic claudication or chronic limb-threatening ischemia), SSI, and SSI severity. Disagreements regarding risk of bias assessments will be resolved by consensus.

Qualitative Data Synthesis

Before conducting quantitative data analyses, we will perform a narrative synthesis of candidate risk factors for SSI [42]. First, we will tabulate the reported risk factors along with the time of measurement of the SSI, the classification system used to determine the severity of SSI (where relevant), study data source, patient recruitment period, and study SSI outcome definition. This tabulation will be used to cluster reported risk factors into themes (eg, patient characteristics) and subthemes (eg, comorbidities) and identify potentially duplicate data. It will also allow us to identify risk factors for different severities of SSI after lower limb revascularization surgery that were classified using different severity classification systems but that have similar enough definitions to allow for meta-analysis. For example, we will combine risk factor estimates for Szilagyi grade I and grade II SSIs with those for superficial and deep incisional infections as defined by the Centers for Disease Control and American College of Surgeons National Quality Improvement Program.

Quantitative Data Synthesis and Statistical Analyses

We will use the odds ratio as the summary measure of association for pooled analyses. Adjusted risk factor estimates with similar definitions will be pooled using DerSimonian and Laird random-effects models [43]. We will limit the primary analysis to prognostic studies that controlled for the minimum set of confounders, as recommended by guidance documents on meta-analyses of prognostic studies [34]. When adjusted risk factor estimates with the same definition were calculated from the same data source (eg, the American College of Surgeons National Surgical Quality Improvement Program) across several studies, we will include the estimate derived from the largest study. As a sensitivity analysis, we will also recalculate the estimate using that derived from the other smaller studies, as studies may have variably adjusted their estimates for potentially confounding factors.

We will inspect forest plots, calculate Cochran Q homogeneity and I^2 inconsistency statistics, and conduct tests of homogeneity ($P<.10$ will be considered significant, given the low power of these tests) to assess for interstudy heterogeneity in the aforementioned estimates [44-46]. As suggested by Higgins et al [45], we will consider I^2 statistics >25%, >50%, and >75% to represent low, moderate, and high degrees of heterogeneity, respectively. In the presence of at least low interstudy heterogeneity, we will conduct subgroup meta-analyses and meta-regression using DerSimonian and Laird random-effects models, with the summary odds ratio for SSI as the dependent variable. We will use the following predictor variables in an attempt to explain heterogeneity in these stratified meta-analyses and meta-regressions: (1) a high versus low risk of bias related to study participation and attrition, potential risk factor and outcome description and measurement, or methods and reporting of statistical analyses; (2) whether the potential risk factor was adjusted for the minimum confounder set; and (3) the type of lower limb revascularization surgery (stratified by aortofemoral or bifemoral bypass, axillofemoral or bifemoral bypass, a groin-only procedure, or an infrainguinal bypass). Finally, the proportion of patients undergoing an urgent surgical procedure or with these different types of lower limb revascularization surgeries will also be included as predictor variables in meta-regressions.

We will evaluate for evidence of small study effects potentially due to publication bias for each potential risk factor–SSI association by visually inspecting produced funnel plots and using Begg and Egger tests ($P<.05$ will be considered significant) [47]. Statistical analyses will be performed by a trained meta-analyst using Stata MP version 13.1 (Stata Corporation).

Certainty in the Cumulative Evidence

We will use the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach for the assessment of evidence about prognostic factors to determine the certainty in the estimates of association between the reported risk factors and the development of SSI [48]. To do this, we will first assess the risk of bias, imprecision, inconsistency, indirectness, and publication bias associated with the evidence for the reported risk factors [49-53]. The overall certainty in these estimates will then be adjudicated as high (*further research is very unlikely to change our confidence in the estimate of effect*), moderate (*further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate*), low (*further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate*), or very low (*very uncertain about the estimate of effect*) [33].

Results

As of June 10, 2021, we have submitted the search strategy to another medical librarian or information scientist to peer review it using the Peer Review of Electronic Search Strategies guideline [37]. We will execute the peer-reviewed search strategy on June 30 and then complete the review of titles and abstracts and full-text articles by July 30, 2021, and September 15, 2021, respectively. We will complete the full-text study data extraction and risk of bias assessment by November 15, 2021. Subsequently, we will conduct the qualitative data synthesis, followed by the quantitative data synthesis and the Grading of Recommendations, Assessment, Development, and Evaluation assessment of the results by November 1, 2021 before drafting the manuscript. We anticipate that we will be able to submit the manuscript for peer review by January 30, 2022.

Discussion

Principal Findings

SSIs are one of the most important complications in vascular surgery [11]. This study will identify, synthesize, and determine the certainty in the cumulative evidence associated with reported risk factors for SSI after lower limb revascularization surgery in patients with peripheral artery disease. It will also determine whether risk factors vary by the type of procedure performed (eg, a groin-only procedure or an infrainguinal bypass) or when the SSI was measured to occur (ie, in-hospital or more delayed). Finally, it will examine whether risk factors vary by how well study investigators accounted for different study risks of bias

or other confounding or risk factors or whether the SSI involves the skin, subcutaneous tissue, or vascular graft.

Implications

Results will be used to help surgeons, patients, and authors of clinical practice statements and guidelines in deciding on the safety of open vascular surgery in patients with medically refractory intermittent claudication and in selecting between open and endovascular revascularization when patients with chronic limb-threatening ischemia are candidates for both. It will also assist clinicians and policy makers in deciding which patients may benefit most from interventions designed to prevent SSIs (eg, incisional negative-pressure wound therapy [54]) and in designing future research in this area. This will include the creation of a prediction tool for identifying those at high risk for SSI after lower limb revascularization surgery and studies determining whether interventions that modify these risk factors before, during, or after surgery reduce the risk of SSI in this vulnerable population. The results may also assist in creating eligibility criteria for future randomized controlled trials designed to determine whether novel interventions or pathways are efficacious in preventing SSIs in this patient population.

Authors' Contributions

DJR conceived the study, and DJR, SKN, HTS, TB, VCM, LD, and DIM developed the study. DJR designed the search strategy and the qualitative and quantitative data synthesis plan, which was refined by SKN, HTS, TB, VCM, LD, and DIM. DJR wrote the draft of the protocol, which was critically revised by SKN, HTS, TB, VCM, LD, and DIM. DJR submitted the protocol to PROSPERO. All authors read and approved the final version of the protocol.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Completed PRISMA-P (Preferred Reporting Items in Systematic Reviews and Meta-Analyses-Protocols) checklist.
[DOCX File , 39 KB - resprot_v10i9e28759_app1.docx]

Multimedia Appendix 2
Operationalized list of quality domains containing the prompting items used when making risk of bias decisions.
[DOCX File , 107 KB - resprot_v10i9e28759_app2.docx]

References

1. Mustapha JA, Katzen BT, Neville RF, Lookstein RA, Zeller T, Miller LE, et al. Determinants of long-term outcomes and costs in the management of critical limb ischemia: a population-based cohort study. J Am Heart Assoc 2018 Aug 21;7(16):e009724 [FREE Full text] [doi: 10.1161/JAHA.118.009724] [Medline: 30369325]
2. Nejim BJ, Wang S, Arhuidese I, Obeid T, Alshaikh HN, Aridi HD, et al. Regional variation in the cost of infrainguinal lower extremity bypass surgery in the United States. J Vasc Surg 2018 Apr;67(4):1170-1180 [FREE Full text] [doi: 10.1016/j.jvs.2017.08.055] [Medline: 29074114]
3. Goodney PP, Travis LL, Brooke BS, DeMartino RR, Goodman DC, Fisher ES, et al. Relationship between regional spending on vascular care and amputation rate. JAMA Surg 2014 Jan;149(1):34-42 [FREE Full text] [doi: 10.1001/jamasurg.2013.4277] [Medline: 24258010]
4. Antoniou GA, Georgiadis GS, Antoniou SA, Makar RR, Smout JD, Torella F. Bypass surgery for chronic lower limb ischaemia. Cochrane Database Syst Rev 2017 Apr 03;4:CD002000 [FREE Full text] [doi: 10.1002/14651858.CD002000.pub3] [Medline: 28368090]
5. LaMuraglia GM, Conrad MF, Chung T, Hutter M, Watkins MT, Cambria RP. Significant perioperative morbidity accompanies contemporary infrainguinal bypass surgery: an NSQIP report. J Vasc Surg 2009 Aug;50(2):299-304 [FREE Full text] [doi: 10.1016/j.jvs.2009.01.043] [Medline: 19631864]
6. Conte MS, Bradbury AW, Kolh P, White JV, Dick F, Fitridge R, GVG Writing Group for the Joint Guidelines of the Society for Vascular Surgery (SVS), European Society for Vascular Surgery (ESVS),World Federation of Vascular Societies (WFVS). Global vascular guidelines on the management of chronic limb-threatening ischemia. Eur J Vasc Endovasc Surg 2019 Jul;58(1S):1-109. [doi: 10.1016/j.ejvs.2019.05.006] [Medline: 31182334]
7. Adam DJ, Beard JD, Cleveland T, Bell J, Bradbury AW, Forbes JF, BASIL trial participants. Bypass versus angioplasty in severe ischaemia of the leg (BASIL): multicentre, randomised controlled trial. Lancet 2005 Dec 03;366(9501):1925-1934. [doi: 10.1016/S0140-6736(05)67704-5] [Medline: 16325694]
8. Bradbury AW, Adam DJ, Bell J, Forbes JF, Fowkes FG, Gillespie I, BASIL trial Participants. Bypass versus Angioplasty in Severe Ischaemia of the Leg (BASIL) trial: an intention-to-treat analysis of amputation-free and overall survival in patients randomized to a bypass surgery-first or a balloon angioplasty-first revascularization strategy. J Vasc Surg 2010 May;51(5 Suppl):5-17 [FREE Full text] [doi: 10.1016/j.jvs.2010.01.073] [Medline: 20435258]

9. Menard MT, Farber A, Assmann SF, Choudhry NK, Conte MS, Creager MA, et al. Design and rationale of the best endovascular versus best surgical therapy for patients with critical limb ischemia (BEST-CLI) trial. J Am Heart Assoc 2016 Jul 08;5(7):e003219 [FREE Full text] [doi: 10.1161/JAHA.116.003219] [Medline: 27402237]
10. Popplewell MA, Davies H, Jarrett H, Bate G, Grant M, Patel S, BASIL-2 Trial Investigators. Bypass versus angio plasty in severe ischaemia of the leg - 2 (BASIL-2) trial: study protocol for a randomised controlled trial. Trials 2016 Jan 06;17:11 [FREE Full text] [doi: 10.1186/s13063-015-1114-2] [Medline: 26739146]
11. Bennett KM, Kent KC, Schumacher J, Greenberg CC, Scarborough JE. Targeting the most important complications in vascular surgery. J Vasc Surg 2017 Mar;65(3):793-803 [FREE Full text] [doi: 10.1016/j.jvs.2016.08.107] [Medline: 28236921]
12. Schweizer ML, Cullen JJ, Perencevich EN, Sarrazin MS. Costs associated with surgical site infections in veterans affairs hospitals. JAMA Surg 2014 Jun;149(6):575-581 [FREE Full text] [doi: 10.1001/jamasurg.2013.4663] [Medline: 24848779]
13. Greenblatt DY, Rajamanickam V, Mell MW. Predictors of surgical site infection after open lower extremity revascularization. J Vasc Surg 2011 Aug;54(2):433-439 [FREE Full text] [doi: 10.1016/j.jvs.2011.01.034] [Medline: 21458203]
14. Kuy S, Dua A, Desai S, Dua A, Patel B, Tondravi N, et al. Surgical site infections after lower extremity revascularization procedures involving groin incisions. Ann Vasc Surg 2014 Jan;28(1):53-58. [doi: 10.1016/j.avsg.2013.08.002] [Medline: 24189008]
15. Zhang JQ, Curran T, McCallum JC, Wang L, Wyers MC, Hamdan AD, et al. Risk factors for readmission after lower extremity bypass in the American College of Surgeons National Surgery Quality Improvement Program. J Vasc Surg 2014 May;59(5):1331-1339 [FREE Full text] [doi: 10.1016/j.jvs.2013.12.032] [Medline: 24491239]
16. Glebova NO, Bronsert M, Hammermeister KE, Nehler MR, Gibula DR, Malas MB, et al. Drivers of readmissions in vascular surgery patients. J Vasc Surg 2016 Jul;64(1):185-194 [FREE Full text] [doi: 10.1016/j.jvs.2016.02.024] [Medline: 27038838]
17. Surgical Site Infection Event (SSI). Centers for Disease Control and Prevention - National Healthcare Safety Network. 2017. URL: http://www.cdc.gov/nhsn/pdfs/pscmanual/9pscssicurrent.pdf [accessed 2019-03-23]
18. Inui T, Bandyk DF. Vascular surgical site infection: risk factors and preventive measures. Semin Vasc Surg 2015;28(3-4):201-207. [doi: 10.1053/j.semvascsurg.2016.02.002] [Medline: 27113288]
19. Szilagyi DE, Smith RF, Elliott JP, Vrandecic MP. Infection in arterial reconstruction with synthetic grafts. Ann Surg 1972 Sep;176(3):321-333. [doi: 10.1097/00000658-197209000-00008] [Medline: 4262892]
20. van de Weijer MA, Kruse RR, Schamp K, Zeebregts CJ, Reijnen MM. Morbidity of femoropopliteal bypass surgery. Semin Vasc Surg 2015 Jun;28(2):112-121. [doi: 10.1053/j.semvascsurg.2015.09.004] [Medline: 26655055]
21. Brothers TE, Robison JG, Elliott BM. Predictors of prosthetic graft infection after infrainguinal bypass. J Am Coll Surg 2009 Apr;208(4):557-561. [doi: 10.1016/j.jamcollsurg.2009.01.001] [Medline: 19476790]
22. Nguyen B, Amdur RL, Abugideiri M, Rahbar R, Neville RF, Sidawy AN. Postoperative complications after common femoral endarterectomy. J Vasc Surg 2015 Jun;61(6):1489-1494 [FREE Full text] [doi: 10.1016/j.jvs.2015.01.024] [Medline: 25702917]
23. Derksen WJ, Verhoeven BA, van de Mortel RH, Moll FL, de Vries JP. Risk factors for surgical-site infection following common femoral artery endarterectomy. Vasc Endovascular Surg 2009;43(1):69-75. [doi: 10.1177/1538574408323502] [Medline: 18829586]
24. Tan T, Kalish JA, Hamburg NM, Rybin D, Doros G, Eberhardt RT, et al. Shorter duration of femoral-popliteal bypass is associated with decreased surgical site infection and shorter hospital length of stay. J Am Coll Surg 2012 Oct;215(4):512-518. [doi: 10.1016/j.jamcollsurg.2012.06.007] [Medline: 22819641]
25. Lee ES, Santilli SM, Olson MM, Kuskowski MA, Lee JT. Wound infection after infrainguinal bypass operations: multivariate analysis of putative risk factors. Surg Infect (Larchmt) 2000;1(4):257-263. [doi: 10.1089/109629600750067183] [Medline: 12594881]
26. Vogel TR, Dombrovskiy VY, Carson JL, Haser PB, Lowry SF, Graham AM. Infectious complications after elective vascular surgical procedures. J Vasc Surg 2010 Jan;51(1):122-129 [FREE Full text] [doi: 10.1016/j.jvs.2009.08.006] [Medline: 19954920]
27. Antonios VS, Noel AA, Steckelberg JM, Wilson WR, Mandrekar JN, Harmsen WS, et al. Prosthetic vascular graft infection: a risk factor analysis using a case-control study. J Infect 2006 Jul;53(1):49-55. [doi: 10.1016/j.jinf.2005.10.004] [Medline: 16310254]
28. Bennett KM, Levinson H, Scarborough JE, Shortell CK. Validated prediction model for severe groin wound infection after lower extremity revascularization procedures. J Vasc Surg 2016 Feb;63(2):414-419 [FREE Full text] [doi: 10.1016/j.jvs.2015.08.094] [Medline: 26526055]
29. Kent KC, Bartek S, Kuntz KM, Anninos E, Skillman JJ. Prospective study of wound complications in continuous infrainguinal incisions after lower limb arterial reconstruction: incidence, risk factors, and cost. Surgery 1996 Apr;119(4):378-383. [doi: 10.1016/s0039-6060(96)80135-8] [Medline: 8644000]
30. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. Ann Intern Med 2009 Aug 18;151(4):65-94 [FREE Full text] [doi: 10.7326/0003-4819-151-4-200908180-00136] [Medline: 19622512]

31. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. J Am Med Assoc 2000 Apr 19;283(15):2008-2012. [doi: 10.1001/jama.283.15.2008] [Medline: 10789670]
32. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev 2015 Jan;4:1 [FREE Full text] [doi: 10.1186/2046-4053-4-1] [Medline: 25554246]
33. Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. Br Med J 2015 Jan 02;350:g7647 [FREE Full text] [doi: 10.1136/bmj.g7647] [Medline: 25555855]
34. Riley RD, Moons KG, Snell KI, Ensor J, Hooft L, Altman DG, et al. A guide to systematic review and meta-analysis of prognostic factor studies. Br Med J 2019 Jan 30;364:k4597. [doi: 10.1136/bmj.k4597] [Medline: 30700442]
35. Mueller M, D'Addario M, Egger M, Cevallos M, Dekkers O, Mugglin C, et al. Methods to systematically review and meta-analyse observational studies: a systematic scoping review of recommendations. BMC Med Res Methodol 2018 May 21;18(1):44 [FREE Full text] [doi: 10.1186/s12874-018-0495-9] [Medline: 29783954]
36. Moons KG, de Groot JA, Bouwmeester W, Vergouwe Y, Mallett S, Altman DG, et al. Critical appraisal and data extraction for systematic reviews of prediction modelling studies: the CHARMS checklist. PLoS Med 2014 Oct;11(10):e1001744 [FREE Full text] [doi: 10.1371/journal.pmed.1001744] [Medline: 25314315]
37. McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C. PRESS Peer review of electronic search strategies: 2015 guideline statement. J Clin Epidemiol 2016 Dec;75:40-46 [FREE Full text] [doi: 10.1016/j.jclinepi.2016.01.021] [Medline: 27005575]
38. Hayden JA, Côté P, Bombardier C. Evaluation of the quality of prognosis studies in systematic reviews. Ann Intern Med 2006 Mar 21;144(6):427-437. [doi: 10.7326/0003-4819-144-6-200603210-00010] [Medline: 16549855]
39. Hayden JA, van der Windt DA, Cartwright JL, Côté P, Bombardier C. Assessing bias in studies of prognostic factors. Ann Intern Med 2013 Feb 19;158(4):280-286. [doi: 10.7326/0003-4819-158-4-201302190-00009] [Medline: 23420236]
40. Bagley SC, White H, Golomb BA. Logistic regression in the medical literature: standards for use and reporting, with particular attention to one medical domain. J Clin Epidemiol 2001 Oct;54(10):979-985. [doi: 10.1016/s0895-4356(01)00372-9] [Medline: 11576808]
41. Vittinghoff E, Glidden D, Shiboski S, McCulloch C. In: Vittinghoff E, Glidden DV, Shiboski SC, McCulloch CE, editors. Regression Methods in Biostatistics: Linear, Logistic, Survival, and Repeated Measures Models, Second Edition. New York, NY: Springer Science & Business Media; 2012:395-429.
42. Popay J, Roberts H, Sowden A, Petticrew M, Arai L, Rodgers M, et al. Guidance on the conduct of narrative synthesis in systematic reviews. ESRC Methods Programme. 2006. URL: https://www.lancaster.ac.uk/media/lancaster-university/content-assets/documents/fhm/dhr/chir/NSsynthesisguidanceVersion1-April2006.pdf [accessed 2021-08-04]
43. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986 Sep;7(3):177-188. [Medline: 3802833]
44. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med 2002 Jun 15;21(11):1539-1558. [doi: 10.1002/sim.1186] [Medline: 12111919]
45. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. Br Med J 2003 Sep 6;327(7414):557-560 [FREE Full text] [doi: 10.1136/bmj.327.7414.557] [Medline: 12958120]
46. Egger M, Davey-Smith G, Altman D. Systematic Reviews in Health Care: Meta-Analysis in Context. London, U.K: BMJ Publishing Group; 2001:1-512.
47. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. Biometrics 1994 Dec;50(4):1088-1101. [Medline: 7786990]
48. Foroutan F, Guyatt G, Zuk V, Vandvik PO, Alba AC, Mustafa R, et al. GRADE Guidelines 28: Use of GRADE for the assessment of evidence about prognostic factors: rating certainty in identification of groups of patients with different absolute risks. J Clin Epidemiol 2020 May;121:62-70. [doi: 10.1016/j.jclinepi.2019.12.023] [Medline: 31982539]
49. Guyatt GH, Oxman AD, Vist G, Kunz R, Brozek J, Alonso-Coello P, et al. GRADE guidelines: 4. Rating the quality of evidence--study limitations (risk of bias). J Clin Epidemiol 2011 Apr;64(4):407-415. [doi: 10.1016/j.jclinepi.2010.07.017] [Medline: 21247734]
50. Guyatt GH, Oxman AD, Montori V, Vist G, Kunz R, Brozek J, et al. GRADE guidelines: 5. Rating the quality of evidence--publication bias. J Clin Epidemiol 2011 Dec;64(12):1277-1282. [doi: 10.1016/j.jclinepi.2011.01.011] [Medline: 21802904]
51. Guyatt GH, Oxman AD, Kunz R, Brozek J, Alonso-Coello P, Rind D, et al. GRADE guidelines 6. Rating the quality of evidence--imprecision. J Clin Epidemiol 2011 Dec;64(12):1283-1293. [doi: 10.1016/j.jclinepi.2011.01.012] [Medline: 21839614]
52. Guyatt GH, Oxman AD, Kunz R, Woodcock J, Brozek J, Helfand M, et al. GRADE guidelines: 7. Rating the quality of evidence--inconsistency. J Clin Epidemiol 2011 Dec;64(12):1294-1302. [doi: 10.1016/j.jclinepi.2011.03.017] [Medline: 21803546]

53. Guyatt GH, Oxman AD, Kunz R, Woodcock J, Brozek J, Helfand M, et al. GRADE guidelines: 8. Rating the quality of evidence--indirectness. J Clin Epidemiol 2011 Dec;64(12):1303-1310. [doi: 10.1016/j.jclinepi.2011.04.014] [Medline: 21802903]
54. Svensson-Björk R, Zarrouk M, Asciutto G, Hasselmann J, Acosta S. Meta-analysis of negative pressure wound therapy of closed groin incisions in arterial surgery. Br J Surg 2019 Mar;106(4):310-318. [doi: 10.1002/bjs.11100] [Medline: 30725478]

Abbreviations

GRADE: Grading of Recommendations, Assessment, Development, and Evaluation
PICOTS: Population, Index Prognostic Factor, Comparison of Prognostic Factors, Outcome, Timing, and Setting
PRISMA: Preferred Reporting Items in Systematic Reviews and Meta-Analyses
PRISMA-P: Preferred Reporting Items in Systematic Reviews and Meta-Analysis Protocols
PROSPERO: International Prospective Register of Systematic Reviews
SSI: surgical site infection

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Protocol

Implementation of an Internet-Based Acceptance and Commitment Therapy for Promoting Mental Health Among Migrant Live-in Caregivers in Canada: Protocol

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Abstract

Background: Psychological distress, isolation, feelings of powerlessness, and limited social support are realities faced by temporary migrant live-in caregivers in Canada. Furthermore, they experience multiple barriers in accessing mental health services due to their long work hours, limited knowledge of health resources, precarious employment, and immigration status.

Objective: The Women Empowerment - Caregiver Acceptance & Resilience E-Learning (WE2CARE) project is a pilot intervention research project that aims to promote the mental well-being and resiliency of migrant live-in caregivers. The objectives include exploring the effectiveness of this program in achieving the following: (1) reducing psychological distress (depression, anxiety, and stress); (2) promoting committed actions of self-care; and (3) building mutual support social networks. Further, participants' satisfaction with the intervention and their perceived barriers to and facilitators of practicing the self-care strategies embedded in WE2CARE will be examined.

Methods: A total of 36 live-in caregivers residing in the Greater Toronto Area will be recruited and randomly assigned to either the intervention or waitlist control group. The intervention group will receive a 6-week web-based psychosocial intervention that will be based on Acceptance and Commitment Therapy (ACT). Standardized self-reported surveys will be administered online preintervention, postintervention, and at 6 weeks postintervention to assess mental distress (Depression, Anxiety and Stress Scale), psychological flexibility (Acceptance and Action Questionnaire), mindfulness (Cognitive and Affective Mindfulness Scale – Revised), and resilience (Multi-System Model of Resilience Inventory). In addition, two focus groups will be held with a subset of participants to explore their feedback on the utility of the WE2CARE program.

Results: WE2CARE was funded in January 2019 for a year. The protocol was approved by the research ethics boards of Ryerson University (REB 2019-036) and the University of Toronto (RIS37623) in February and May 2019, respectively. Data collection started upon ethics approval and was completed by May 2020. A total of 29 caregivers completed the study and 20 participated in the focus groups. Data analyses are in progress and results will be published in 2021.

Conclusions: WE2CARE could be a promising approach to reducing stress, promoting resilience, and providing a virtual space for peer emotional support and collaborative learning among socially isolated and marginalized women. The results of this pilot study will inform the adaptation of an ACT-based psychological intervention for online delivery and determine its utility in promoting mental health among disadvantaged and vulnerable populations.

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KEYWORDS

migrant live-in caregiver; women; mental health; acceptance commitment therapy; resiliency; empowerment

Introduction

The Canadian Temporary Foreign Worker Program engages workers in sectors such as agriculture, petroleum, home caregiving, and other low-skilled occupations [1-3]. Temporary foreign workers (TFWs) are restricted to work only for the employers designated in their work permits. Most TFWs earn low wages, work long hours without any overtime compensation, live in substandard conditions, and have limited to no access to health care services or employment insurance despite paying into these programs [4-7]. The Caregiver Program, previously known as the Live-in Caregiver Program, is a stream of the Temporary Foreign Worker Program, which engages workers in in-home caregiving [1,8,9]. Despite Caregiver Program reforms in November 2014, which provided caregivers with the option of living outside of their employers' homes, most caregivers continue to live with their employer due to low wages, inability to afford to live independently, and precarious work permits [5,6,10]. Most caregivers are racialized women from lower- or middle-income countries like the Philippines [2,11]. Live-in caregivers are one of the most vulnerable TFW groups because they live and work in private households where government surveillance remains nonexistent, employees' privacy is gravely undermined, seclusion is often imposed, and unionization is unattainable [4,12]. TFWs are often the primary source of income for their families in their home country, sending back regular remittances and being compelled to tolerate substandard working and living conditions [4,6]. Although participants in this program are eligible to apply for permanent residency for themselves and their immediate families after 24 months of service, they are not allowed to bring their families to Canada until they become permanent residents, which could take 4 to 10 years [1,8]. In other words, family separation is one of the main requirements for receiving their work permit.

A limited but valuable body of literature examined the mental health of migrant live-in caregivers in Canada [13-16]. These studies reported high psychological distress among live-in caregivers, mainly related to concerns about family at home, an inability to fulfill requests for money, precarious employment and immigration, excessive work demands, lack of privacy, reproaches and abuse from employers, fear of deportation and job loss, feelings of alienation, extreme loneliness, and limited social support [14,15]. Based on caregivers' reality of high stress and limited free time, it is imperative that they be provided with psychosocial support to reduce stress and promote their resilience.

Acceptance and Commitment Therapy (ACT) is an evidence-based psychological intervention that has proven to be effective in addressing mental and physical health challenges in both clinical and nonclinical populations [17-19]. Web-based ACT has also been found to be effective in addressing health challenges such as distress related to trauma, anxiety, depression, and chronic pain [20-22]. It promotes mental wellness and psychological flexibility by helping participants face their distress while engaging in the pursuit of valued actions such as self-care and other meaningful activities. ACT uses mindfulness-based exercises and experiential exercises to decrease experiential avoidance and to enhance one's psychological flexibility through advancing six core processes: defusion (observing thoughts as thoughts), acceptance (of experiences of emotions and feelings), contact with the present moment (mindfulness), self-as-context (awareness and self-perspective), values (being clear about what matters), and committed action (based on values) [23,24].

The six ACT core processes can support migrant live-in caregivers in coping effectively with their mental health stress by enabling them to recognize their internal psychological struggles (eg, fusion with ideas and thoughts, avoidance of emotions and feelings) and apply ACT strategies like mindfulness, defusion from unworkable ideas, and engaging in committed action consistent with the value of self-care (eg, engaging in culturally syntonic activities like singing or praying and building social support networks). Given that live-in caregivers work long hours, have extremely limited free time, and lack social support, a web-based intervention offers flexible access while promoting virtual social connection.

This paper presents the study protocol of Women Empowerment - Caregiver Acceptance & Resilience E-Learning (WE2CARE), an internet-based ACT for promoting the mental well-being of migrant live-in caregivers. The study aims to reduce psychological distress (depression, anxiety, and stress) and promote committed actions of self-care. The study protocol received ethical approval from the research ethics review boards of Ryerson University (REB 2019-036) and the University of Toronto (RIS37623).

Methods

Study Design

A pilot community-based mixed methods design is used to assess the feasibility and effectiveness of the WE2CARE program. WE2CARE involves two sequential phases: a quantitative component that includes a waitlist randomized controlled trial and a qualitative component that involves focus groups. The waitlist control group will be used as an untreated comparison for the active experimental group to determine if the program had an effect.

Participants and Recruitment Strategies

A total of 36 participants will be recruited by two community champions (ie, trusted members of the caregivers' community

collaborating with community health organizations serving the TFW population) and a snowball sampling technique. The inclusion criteria will include the following: (1) female adults aged ≥18 years, (2) residing in the Greater Toronto Area, (3) working on a temporary work permit as live-in caregivers, (4) able to speak and read English, (5) have internet access, and (6) able to take part in the 6-week intervention. They will be randomized to either the intervention arm or control arm using a random number generator.

In Phase 2 of our study, we will conduct two focus groups with a subset of participants from Phase 1 who indicate interest in participating. The aim of the focus groups is to gain a deeper understanding about participants' views of the effectiveness of WE2CARE in promoting mental health, their perceived barriers and challenges in accessing this method of delivery (ie, online), and their recommendations to improve the content and method of delivery of this program.

Treatment Intervention

Overview

The WE2CARE intervention consist of six e-learning modules that cover the ACT processes. Each week, participants are invited to complete an online, self-directed, interactive experiential session on ACT strategies (approximately one hour to complete) and to attend a 90-minute live online videoconference during which group discussions and question-and-answer sessions are facilitated by our research team members to support participants' ACT practice.

Module 1: Reflecting on the Present Journey

This module provides the following: (1) an introductory overview of the course, (2) a guided interactive exercise for participants to reflect on their identity and experience as live-in caregivers, including their current distress and challenges, and the factors that motivate them to continue with their jobs (ie, both the immediate tangible rewards and internal values, such as caring for their families back home), and (3) an introduction to mindfulness as an approach toward all experiences, including psychological suffering.

Module 2: Developing Adaptive ACT Strategies to Deal With Distressing Experiences

This module supports participants to achieve the following: (1) recognize all thoughts as thought processes rather than being trapped by their literal content; for example, rather than worrying or arguing back with a thought about one's uncertain future ("I am going to lose my job soon," "my life will always be hopeless," etc), one can mindfully recognize and accept them as thoughts and not reality, and focus on experiencing the here and now (defusion, acceptance, present moment); (2) overcome the tyranny of unhelpful rules or stories that constrict adaptive or valued behaviors (eg, "showing emotions is a weakness," "I am no longer worthy," "my needs are not important") (defusion, acceptance); and (3) cultivate appreciation and gratitude, enabling them to connect to any positive aspects of their experience, however small, that may have been neglected due to fusion with the everyday challenges caused by difficult work conditions (eg, enjoying the sunrise, a cup of tea, a warm bath, fresh air; acceptance, present moment).

Module 3: Experiencing the Transcendent Self

This module engages participants in experiential exercises that support them to do the following: (1) reconnect with their former sense of self and identities before becoming a migrant caregiver, including their personal and cultural strengths; (2) defuse from any rigid conceptualized self (ie, being just an objectified migrant caregiver) and become aware through the "observer self" that they are not defined by their memories, their experiences, or labels imposed on them (rather, they are the holders of their lived experiences that continue to change throughout life); and (3) rediscover their strengths, passion, interests, and aspirations, and recognize their capacity to make choices based their values (eg, singing in a choir, attending a community event, choosing a new style of clothing; self-as-context, acceptance, present moment, values).

Module 4: Getting in Touch With Values and Meaning

This module engages participants to do the following: (1) explore their values in all domains in their life (self-care, family, friends, career, community, spirituality, etc); (2) evaluate whether their actions are moving toward or away from their values and supporting them to achieve balanced living; and (3) commit to self-care and other actions based on their values (values, committed action, acceptance).

Module 5: Building a Supportive Network

This module support participants to accomplish the following: (1) negotiate barriers to self-care by drawing from learned ACT strategies; (2) identify personal and community resources and reconnect with existing supports (eg, church, community associations); and (3) build new supports, such as mutual virtual support networks (values, defusion, acceptance, present moment, committed action).

Module 6: Committing to Valued Action

This module supports participants to consolidate their commitment to self-care by doing the following: (1) developing concrete short, intermediate, and long-term plans for self-care and (2) anticipating future barriers and formulating mitigating ACT strategies to sustain a commitment to self-care (committed action, values, present moment).

One of the therapeutic goals of WE2CARE is to motivate participants to engage collectively in building social support networks. The weekly videoconference, which will be cofacilitated by two trained research team members, will provide a viable venue to facilitate and model the development of a virtual community of mutual support, which may continue beyond the project.

A previous ACT intervention study conducted by our team members demonstrated that a participant-driven social support e-network (a closed group on Facebook) was effective in reducing social isolation, promoting community engagement, and strengthening mutual support.

Data Collection

Informed consent will be obtained prior to data collection. Data will be gathered using both quantitative and qualitative tools, which include self-completed questionnaires and focus groups.

Quantitative data will be captured for participants in the control and intervention groups through self-report instruments that will be administered online pre- and postintervention. The intervention group will also complete the questionnaires 6 weeks postintervention. The survey questionnaires will include the following:

1. The preintervention survey will include sociodemographic and health-related questions.

2. The standardized scales administered preintervention, postintervention, and at the 6-week follow-up will include the following:

- The Depression, Anxiety and Stress Scale (DASS-21), a set of three self-report scales (21 items) designed to measure the emotional states of depression, anxiety, and stress.
- The Acceptance and Action Questionnaire (AAQ-2), a 7-item scale specifically designed to measure the impact of ACT core processes conceptualized as psychological flexibility.
- The Cognitive and Affective Mindfulness Scale – Revised (CAMS-R), a 12-item measure designed to capture a broad conceptualization of mindfulness not specific to any particular type of meditation training.
- The Multi-System Model of Resilience Inventory (MSMR-I), which consists of three subscales: internal resilience, pursuits and coping, and external resilience. Each subscale contains 9 self-reported items and indicates where the barriers to one's resilience lie. These scales have shown good psychometric properties including internal consistency, test-retest reliability, and validity.

3. Participants' evaluation of the WE2CARE program. Participants' feedback about the program will be captured through a 12-item questionnaire that elicited their perceptions of the impact the program had on their mental and social well-being and their knowledge of how to access mental health services.

Qualitative data will be obtained through focus groups and interactive entries embedded throughout the 6 online modules, including questions on caregiving burden and factors that promote resilience in Module 1 and weekly valued action data logs on self-care in Modules 2-6.

Data Analysis Planning

Descriptive statistics will be used to summarize participants' sociodemographics, self-reported health characteristics, and practices. Both independent and dependent *t* tests will be performed to assess the mean score differences for each outcome measure across and within groups. An independent *t* test will be used to compare mean scores across the intervention and control groups. Paired *t* tests will be used to compare the following: (1) baseline and postintervention outcomes and (2) baseline and 6-week postintervention outcomes among intervention participants.

The number of intervention participants at low risk and at risk for anxiety, depression, and stress will also be compared at baseline, postintervention, and 6 weeks postintervention. The Fisher exact test will be used to determine if the number of intervention participants at risk for anxiety, depression, and stress changed across time. Risk for anxiety, depression, and stress will be assessed using the DASS-21 and AAQ-7. The DASS-21 contains three subscales that assess anxiety, depression, and stress. Those that score at a moderate severity level or above for anxiety, depression, and stress will be considered at risk. The cutoffs for a moderate severity level will be set at 9 for anxiety, 13 for depression, and 18 for stress. Based on the AAQ-7 scoring instructions, a score above 23 is associated with depression or anxiety symptoms.

Linear mixed effects models will be created for each outcome of interest from baseline to postintervention among participants in the intervention and control groups. Each model will include two fixed effects parameters and two random effects parameters, one for the intercept and one for the outcome. The intercept fixed effect represents the typical initial score of an outcome and the outcome fixed effect represents the typical increase or decrease in score from baseline to postintervention.

Participants' feedback on the 12-item questionnaire will be stratified by study arm allocation and an independent *t* test will be used to determine if there are differences in survey responses by study arm allocation.

Quantitative data will be analyzed using SPSS (version 27; IBM Corp) and R (version 1.2.5003; R Foundation for Statistical Computing) for Windows. A threshold of .05 will be used to determine the level of significance for all *P* values.

Qualitative data include transcripts of the audiotaped focus groups and interactive entries embedded throughout the 6 online modules. Both data-driven inductive and question-driven deductive approaches will be used to analyze the data [25]. Each transcript and responses to each module will be reviewed independently by at least two research team members to generate initial codes, which will be reviewed by all team members and developed into a codebook through discussion and consensus. The team will then organize the coded data into themes (common patterns) and illustrations (unique aspects of experience) for reporting [25]. Integrity of data interpretation will be maintained by following strategies of credibility (member check, peer debriefing) and auditability [26,27].

Results

The WE2CARE study protocol has been approved by the research ethics boards of Ryerson University (REB 2019-036) and the University of Toronto (RIS37623). Data collection occurred between November 2019 and May 2020. Of 18 participants in the intervention group, one did not complete the baseline questionnaire, while 6 of 18 participants in the control group withdrew from the study due to other competing life priorities. The total number of participants who completed the study was 29, with 17 in the intervention group and 12 in the control group. Our intervention group was divided into two cohorts of 9 and 8 participants, respectively. This allowed more

opportunity for participants to share their experiences, mental health stressors, and application of ACT strategies during weekly videoconferences. The control group received the intervention after the two intervention cohorts were completed. Data analysis is in progress and results will be published in 2021.

Discussion

WE2CARE is among the first studies exploring the effectiveness of ACT in addressing mental health challenges among live-in caregivers. Although there are numerous studies on web-based ACT intervention, few use group videoconferencing to promote peer connection and mutual support. One of the key goals of WE2CARE is to motivate participants to engage collectively in building social support networks. The weekly videoconferences, facilitated by trained counsellors, provide a viable vehicle to facilitate the building of a virtual community of mutual support. The results of both quantitative and qualitative data will guide the adoption of this intervention to best meet the mental health needs of migrant live-in caregivers.

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Authors' Contributions

MV (the nominated principal investigator) developed the initial protocol together with JPHW and KPLF (coprincipal investigators). MM (research coordinator) and AA (research assistant) helped with the implementation of the protocol. JJWL helped with setting up the study database and monitored data entry. MV, JPHW, and KPLF contributed to the initial draft of the manuscript while all authors reviewed, revised, and endorsed the final submission.

Conflicts of Interest

None declared.

Multimedia Appendix 1
External peer review report.
[PDF File (Adobe PDF File), 68 KB - resprot_v10i9e31211_app1.pdf]

References

1. Improving Canada's Caregiver Program. Government of Canada. 2014 Oct 31. URL: https://www.canada.ca/en/news/archive/2014/10/improving-canada-caregiver-program.html [accessed 2015-07-12]
2. Immigration, Refugees and Citizenship Canada. Facts and Figures 2016: Immigration Overview – Temporary Residents. Government of Canada. 2016. URL: https://www.cic.gc.ca/opendata-donneesouvertes/data/Facts_and_Figures_2016_TR_EN.pdf [accessed 2020-06-20]
3. Sweetman A, Casey C. Canada's Temporary Foreign Workers Programs. Canadian Issues/Thèmes Canadiens 2010(Spring):19-24.
4. Faraday F. Made in Canada: How the Law Constructs Migrant Workers' Insecurity. Metcalf Foundation. 2012. URL: https://metcalffoundation.com/publication/made-in-canada-how-the-law-constructs-migrant-workers-insecurity/ [accessed 2020-07-10]
5. Hennebry JL. Not Just a few bad apples: Vulnerability, health and temporary migration in Canada. Canadian Issues/Thèmes canadiens 2010(Spring):73-77.
6. Salami B, Meharali S, Salami A. The health of temporary foreign workers in Canada: A scoping review. Can J Public Health 2015 Nov 1;106(8):e546-e554. [doi: 10.17269/CJPH.106.5182]
7. Walia H. Transient servitude: migrant labour in Canada and the apartheid of citizenship. Race & Class 2010 Jul 05;52(1):71-84. [doi: 10.1177/0306396810371766]
8. Citizenship and Immigration Canada. Improving Canada's Caregiver Program. Government of Canada. 2014. URL: https://www.canada.ca/en/news/archive/2014/10/improving-canada-caregiver-program.html [accessed 2020-05-13]
9. Atanackovic J, Bourgeault I. The Employment and Recruitment of Immigrant Care Workers in Canada. Canadian Public Policy/Analyse De Politiques 2013;39(2):335-350 [FREE Full text] [doi: 10.3138/cpp.39.2.335]
10. Salami B, Meherali S. One of the family? Familial and professional relationships between migrant live-in caregivers and their employers. International Journal of Migration Health and Social Care (IJMHSC) 2018 Mar 26;14(2):174-185. [doi: 10.1108/ijmhsc-09-2016-0034]
11. Kelly P, Park S, de Leon C, Priest J. TIEDI Analytic Report 18. Profile of Live-in-Caregiver Immigrants to Canada 1993-2009. Toronto Immigrant Employment Data Initiative. Toronto; 2011 Mar. URL: http://www.yorku.ca/tiedi/doc/AnalyticalReport18.pdf [accessed 2020-06-05]
12. Shahvisi A. Hermeneutical injustice and outsourced domestic work. Women's Studies International Forum 2018 Jul;69:18-25. [doi: 10.1016/j.wsif.2018.04.002]

13. Carlos JK, Wilson K. Migration among temporary foreign workers: Examining health and access to health care among Filipina live-in caregivers. Soc Sci Med 2018 Jul;209:117-124. [doi: 10.1016/j.socscimed.2018.05.045] [Medline: 29859389]
14. Vahabi M, Wong JP, Lofters A. Migrant Live-in Caregivers Mental Health in Canada. Community Ment Health J 2018 Jul 12;54(5):590-599. [doi: 10.1007/s10597-017-0225-5] [Medline: 29330696]
15. Vahabi M, Wong JP. Caught between a rock and a hard place: mental health of migrant live-in caregivers in Canada. BMC Public Health 2017 May 23;17(1):498. [doi: 10.1186/s12889-017-4431-4]
16. Pratt G. Circulating sadness: witnessing Filipina mothers' stories of family separation. Gender, Place & Culture 2009 Mar 04;16(1):3-22. [doi: 10.1080/09663690802574753]
17. Graham CD, Gouick J, Krahé C, Gillanders D. A systematic review of the use of Acceptance and Commitment Therapy (ACT) in chronic disease and long-term conditions. Clinical Psychology Review 2016 Jun;46:46-58. [doi: 10.1016/j.cpr.2016.04.009]
18. Montgomery KL, Kim JS, Franklin C. Acceptance and Commitment Therapy for Psychological and Physiological Illnesses: A Systematic Review for Social Workers. Health & Social Work 2011 Aug 01;36(3):169-181. [doi: 10.1093/hsw/36.3.169]
19. Swain J, Hancock K, Hainsworth C, Bowman J. Acceptance and Commitment Therapy in the treatment of anxiety: A systematic review. Clinical Psychology Review 2013 Dec;33(8):965-978. [doi: 10.1016/j.cpr.2013.07.002]
20. Brown M, Glendenning A, Hoon AE, John A. Effectiveness of Web-Delivered Acceptance and Commitment Therapy in Relation to Mental Health and Well-Being: A Systematic Review and Meta-Analysis. J Med Internet Res 2016 Aug 24;18(8):e221 [FREE Full text] [doi: 10.2196/jmir.6200] [Medline: 27558740]
21. Kaltenbaugh D, Klem ML, Hu L, Turi E, Haines A, Hagerty Lingler J. Using Web-Based Interventions to Support Caregivers of Patients With Cancer: A Systematic Review. Oncology nursing forum (ONF) 2015 Feb 28;42(2):156-164. [doi: 10.1188/15.onf.156-164]
22. Lappalainen P, Langrial S, Oinas-Kukkonen H, Tolvanen A, Lappalainen R. Web-Based Acceptance and Commitment Therapy for Depressive Symptoms With Minimal Support. Behav Modif 2015 Aug 06;39(6):805-834. [doi: 10.1177/0145445515598142]
23. Hayes SC. Acceptance and commitment therapy, relational frame theory, and the third wave of behavioral and cognitive therapies. Behavior Therapy 2004 Oct;35(4):639-665. [doi: 10.1016/s0005-7894(04)80013-3]
24. Hayes SC, Luoma JB, Bond FW, Masuda A, Lillis J. Acceptance and Commitment Therapy: Model, processes and outcomes. Behaviour Research and Therapy 2006 Jan;44(1):1-25. [doi: 10.1016/j.brat.2005.06.006]
25. Silverman D. Interpreting qualitative data: methods for analyzing talk, text and interaction. London-Thousand Oaks-New Delhi: SAGE Publications; 2006.
26. Seale C. Quality in qualitative research. In: Seale C, Gobo G, Gubrium JF, Silverman D, editors. Qualitative research practice. London-Thousand Oaks-New Delhi: SAGE Publications; 2004:379-389.
27. Gobo G. Discourse analytic practice. In: Seale C, Gobo G, Gubrium JF, Silverman D, editors. Qualitative research practice. London-Thousand Oaks-New Delhi: SAGE Publications; 2004:405-426.

Abbreviations

AAQ-2: Acceptance and Action Questionnaire
ACT: Acceptance and Commitment Therapy
CAMS-R: Cognitive and Affective Mindfulness Scale – Revised
DASS-21: Depression, Anxiety and Stress Scale
MSMR-I: Multi-System Model of Resilience Inventory
TFW: temporary foreign worker
WE2CARE: Women Empowerment - Caregiver Acceptance & Resilience E-Learning

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Protocol

Perceived Benefits, Barriers, and Facilitators of a Digital Patient-Reported Outcomes Tool for Routine Diabetes Care: Protocol for a National, Multicenter, Mixed Methods Implementation Study

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Abstract

Background: There is growing evidence that digital patient-reported outcome (PRO) questionnaires and PRO-based decision support tools may help improve the active engagement of people with diabetes in self-care, thereby improving the quality of care. However, many barriers still exist for the real-world effectiveness and implementation of such PRO tools in routine care. Furthermore, limited research has evaluated the acceptability, feasibility, and benefits of such tools across different health care settings.

Objective: This study aims to evaluate the acceptability, feasibility, and perceived benefits of the Danish digital PRO diabetes tool in different health care settings in Denmark and to determine the factors affecting its implementation. Furthermore, the study evaluates the psychometric characteristics of the Danish PRO Diabetes Questionnaire and the validity of the scoring algorithms for dialogue support. The objective of this study is to guide the ongoing optimization of the PRO diabetes tool, its implementation, and the design of future randomized controlled effectiveness studies.

Methods: We designed a multicenter, mixed methods, single-arm acceptability-feasibility implementation study protocol to contribute to the real-world pilot test of a new digital PRO diabetes tool in routine diabetes care. The use of the tool involves two main steps. First, the people with diabetes will complete a digital PRO Diabetes Questionnaire in the days before a routine diabetes visit. Second, the health care professional (HCP) will use a digital PRO tool to review the PRO results together with the people with diabetes during the visit. The PRO diabetes tool is designed to encourage and support people to take an active role for the people with diabetes in their own care and to expedite the delivery of person-centered, collaborative, and coordinated care.

Results: A multicenter pilot study protocol and psychometrically designed digital data collection tools for evaluation were developed and deployed as part of a national evaluation of a new digital PRO diabetes intervention. A total of 598 people with diabetes and 34 HCPs completed the study protocol by April 1, 2021.

Conclusions: A large-scale, mixed methods, multicenter study for evaluating the use of the nationally developed PRO Diabetes Questionnaire in routine care across all health care sectors in Denmark by using the RE-AIM (Reach, Efficacy, Adoption, Implementation and Maintenance) model as a framework has been designed and is ongoing. This study is expected to provide new important and detailed information about the real-world acceptability, perceived relevance, and benefits of the PRO diabetes tool among a large heterogeneous population of people with diabetes in Denmark and HCPs in different care settings. The results will be used to further improve the PRO tool, design implementation facilitation support strategies, and design future controlled effectiveness studies.

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KEYWORDS

diabetes; type 1 diabetes; type 2 diabetes; multisector care; digital health; patient-reported outcomes; patient-centered care; internet-administered; feasibility; mixed-method research; mobile phone

Introduction

Background

Patient-reported outcome (PRO) questionnaires and PRO-based digital decision support tools, henceforth referred to as PRO tools, may help improve the quality of life and multiple person-centered aspects of quality of care for those with diabetes when appropriately designed for use in routine practice [1-3]. Depending on the purpose, content, and design of the tool, digital self-assessment and PRO tools have the potential to increase person-centered care in many ways [4-7].

PRO tools may facilitate the active engagement of people with diabetes in caring for themselves on their own through improved self-insight and disease insight [8-10]; better preparation (of both the person with diabetes and health care professional [HCP]) before visits, thereby benefiting the quality of the visit [11]; focus on the person with diabetes' individual needs and priorities [1]; detection of symptoms and underlying conditions requiring treatment [12-15]; assessment of symptom severity [16], prioritization of topics to discuss at the care visit [17]; monitoring of side effects [18,19] and treatment response; provision of treatment decision support [18]; and the creation of data allowing ongoing quality monitoring, benchmarking, and care improvement [20].

However, evidence shows that designing digital PRO tools that are acceptable, feasible, and effective among the majority of the population and successfully implementing them in diverse routine care settings are difficult tasks, owing to a variety of barriers to and challenges for both people with diabetes and HCPs [21-24]. The use of participatory research and the systematic involvement of patients in the design and evaluation of PRO tools has been emphasized as a means of improving the field's knowledge and understanding the barriers to and facilitators for their sustainable use [1,2,25].

A national PRO diabetes tool comprising a PRO questionnaire and a digital clinical dialogue and decision support tool was developed in 2018-2020 [1] for use in routine diabetes care across health care sectors in Denmark as part of a national strategy to implement PRO in diabetes care. Its development was undertaken using a multi-stakeholder participatory and systematic stepwise approach involving both people with diabetes and HCPs across all stages to achieve an acceptable, person-centered, and feasible solution [1,26]. A detailed real-world evaluation of how people with diabetes experience the introduction of the new digital PRO diabetes tool in their routine care at a larger scale is important to guide the continued improvement of the tool. A multidimensional evaluation framework is required to evaluate the full range of potential factors influencing the reach, implementation, and effectiveness of the PRO tool [27,28].

This study is a multicenter PRO diabetes study (M-PRODIA) conducted in the context of a national evaluation of the newly developed national PRO diabetes tool under the auspices of the Danish Health Authority and the Region of North Denmark. The Danish PRO Diabetes Tool has two primary benefits. First, the tool is intended to support people with diabetes in becoming actively engaged in their own care and experiencing a greater influence on their care. Second, the tool was designed to improve the dialogue and quality of care visits by (1) improving the focus of care on what is most important to the individual person with diabetes; (2) enabling a structured and comprehensive review of people with diabetes' biopsychosocial needs and priorities; and (3) facilitating a collaborative and coordinated approach to caring for people with diabetes.

Three broader strategic aims guiding the national value-based PRO diabetes program were to improve the delivery of coordinated, person-centered quality diabetes care for adults with type 1 and type 2 diabetes in Denmark, to allocate health services for optimal value to people with diabetes, and to collect PRO data to enable person-centered quality of diabetes care improvement and research.

The PRO diabetes tool consists of two elements: a newly developed diabetes questionnaire covering a wide range of topics relevant to people with diabetes (Multimedia Appendix 1) to be completed by people with diabetes before their routine visit [1], and a digital PRO tool that includes an interactive display of PRO results (PRO dashboard) for use by people with diabetes and HCPs together during the care visit.

In a 2019 study, we showed that in an outpatient clinic, the PRO diabetes tool was perceived as acceptable, feasible, and helpful in improving the active participation of people with diabetes and overall quality of the dialogue [29]. Further evidence involving a broader group of people with diabetes and HCPs is required to evaluate the validity, reliability, acceptability, feasibility, and effectiveness of the PRO diabetes tool and identify knowledge gaps, guide future research, and inform the planning of wider implementation. Research on the acceptance of digital PRO solutions among people with diabetes highlights that multiple possible issues may affect acceptance, including eHealth literacy, privacy concerns, emotional impact [24], and factors such as expected personal benefit, expected ease of use, perceived social acceptance, and facilitating conditions (user-centered design for use) [30]. It is hypothesized that this PRO diabetes tool, due to the use of systematic patient involvement [31,32] in the design phase to address these factors, will have a high real-world acceptance among people with diabetes. Few studies similarly highlight a range of possible barriers to the optimal adoption and use of PRO tools in diabetes care by HCP [33-35]. As a national multidisciplinary group of HCPs was involved in all stages of the development of the PRO diabetes tool with attention to these issues, it is hypothesized that there will be a high level of adoption of this tool among people with diabetes. Defining the prerequisites for effective use by HCPs, such as indicators for fidelity, skills training, and support, will be significant in guiding the implementation of the tool [33].

Furthermore, it is necessary to confirm the extent to which the PRO questionnaire meets overall quality criteria for clinical PRO tools [1], including (1) its acceptability for both people with diabetes and HCPs, (2) its usefulness and relevance across the care continuum, (3) its support for active engagement of the people with diabetes, and (4) its contribution to person-centered care outcomes (eg, care experience, care quality, care satisfaction, health-related empowerment, and health and diabetes-related quality of life outcomes) [36].

It is essential to evaluate the extent to which the PRO tool influences process indicators for person-centered diabetes care, such as the quality of communication and interpersonal relationships, collaboration, and the use of shared decision-making. The introduction of PRO may affect the quality of person-centered diabetes language and communication among people with diabetes, people with diabetes and family members of people with diabetes, among HCP within and across teams, and among health care sectors [37-39]. Furthermore, PRO may affect the quality of preventive and health-promoting activities, the quality of medical diabetes care and self-management support [1], and the consideration of the voice of people with diabetes in payer decisions on health care. It is relevant to evaluate the extent to which the PRO tool impacts individual factors such as the health competency, health-related empowerment, active engagement, and self-management behaviors of the people with diabetes; the experiences of people with diabetes with regard to care and support; and patient-relevant treatment outcomes.

Detailed empirical data, both qualitative and quantitative, are needed regarding the process of implementation in practice, identifying the key barriers to and facilitators for its effective implementation, its reach among the adult diabetes population, and the intervention requirements to fulfill the tool's purpose and exert its intended effect at the population level [40]. To our knowledge, the Danish PRO Diabetes Tool is the first digital multidimensional PRO Diabetes Questionnaire, specifically designed through a systematic multi-stakeholder participatory process to improve the quality of person-centered care across primary, secondary, and municipality care settings. This tool was designed from 2017 to 2020 through a stepwise national participatory process including 5 multi-stakeholder, multidisciplinary full-day meetings with the representation of people with diabetes, payers, patient groups, health care sectors, and geographical regions in Denmark and 7 workshops with people with diabetes and ongoing clinically anchored partnering with people with diabetes.

Therefore, there is a need to evaluate the multi-faceted potential of the PRO diabetes tool to improve care quality and benefit people with diabetes through multiple pathways. This includes but is not limited to the active involvement of people with diabetes in their care, the facilitation of health literacy and health-related empowerment [41], early detection and preventive care [42,43], dialogue and decision support, outcome monitoring, value-based person-centered care, communication, culture, and organization for patient-centricity and chronic illness care coordination.

Examining the usability, acceptability, benefits, psychometric reliability, and validity (face validity, content validity, construct validity, and discriminatory validity), sensitivity, and responsiveness of the tool in different care settings and patient subgroups is required to ensure quality and optimize scaling and planning for implementation. This involves disentangling the complex interdependencies influencing reach, adoption, efficacy, and institutionalization through the use of mixed methods research [2].

The RE-AIM (Reach, Efficacy, Adoption, Implementation and Maintenance) model has been found to be helpful in previous diabetes research to evaluate person-centered diabetes initiatives and digital health interventions [40,44,45]. We adapted this model to facilitate the integration of many factors that influence the public health potential of an intervention.

The M-PRODIA is designed to piggyback on a pilot test program in routine care, as it is not possible to establish attention-control groups. Instead, considering feasibility, at one site, substudies were designed in parallel to compare PRO visits with regular visits in relation to follow-up care and health care use parameters and examine longitudinal changes in clinical care and outcomes. These have been reported in separate protocols. The M-PRODIA aims to use both quantitative and qualitative methods to characterize the real-world experiences of using the national Danish digital PRO diabetes tool among a large heterogeneous population of people with diabetes in Denmark and HCPs in different care settings.

Study Objectives

The primary objective of this study is to evaluate the feasibility and acceptability of the PRO diabetes tool in practice and to

explore and characterize its perceived benefits, risks, and disadvantages in routine diabetes care as part of a national pilot study. The study is designed for formative research purposes [46], using both exploratory and confirmatory approaches to inform the design of future research, such as potentially stepped-wedge [47] and randomized controlled protocols for the examination of public health and cost- and clinical effectiveness [46]. Furthermore, it aims to explore the individual, HCP, and system-level factors that may significantly influence different aspects of reach, implementation, and effectiveness.

The M-PRODIA's specific research objectives are fivefold, as follows:

1. The study aims to assess and compare the perceived benefits and disadvantages related to the use of the PRO diabetes tool for dialogue and decision support in different care settings in a diverse population of people with diabetes.
2. The study aims to identify barriers to and facilitators for the optimal use of the tool from both the viewpoints of people with diabetes and HCPs.
3. The study aims to evaluate the validity, reliability, and clinical utility of the tool PRO Diabetes Questionnaire and Tool.
4. The study aims to obtain data to check for errors and optimize the PRO Diabetes Questionnaire and digital support tools.
5. The study aims to obtain the initial experience with estimation of RE-AIM indicators and guide future RE-AIM evaluation studies of the PRO diabetes tool.

Methods

Study Design

The M-PRODIA is a pragmatic, single-arm, real-world, mixed methods formative feasibility-acceptability pilot implementation study.

Involvement of People With Diabetes in the Research Design

A panel of 3 persons with type 2 diabetes and 2 persons with type 1 diabetes all with experience as advocates for the perspective of people with diabetes were involved as collaborators in the design of this study and its study materials through regular working meetings with the research team. Several participants were involved in ongoing patient association activities and contributed with personal as well as collective insights regarding the perspective of people with diabetes on study questions. Meetings continue to be held regularly to ensure input to all phases of the study including study questions, study materials and questionnaires, and interpretation and dissemination of study results in line with seven quality criteria for patient involvement [26].

People with diabetes and family members of people with diabetes were systematically involved in all stages of the collaborative development and design of the national PRO Diabetes Questionnaire and the digital PRO diabetes tool, DiaProfil [1]. A total of 7 quality criteria for guiding involvement of people with diabetes were agreed upon between the Value Based Health Care and PRO in Diabetes Project (VBHC-PRO-DIA) research team and people with diabetes from the beginning [26]. The involvement of people with diabetes in the design of the PRO tool was undertaken as part of a separate embedded research study to develop and evaluate methods for patient involvement in clinical PRO tools design. All people with diabetes partnering on the development of the PRO diabetes tool completed informed consent for this research study. Results regarding the outcomes and impacts of involvement of people with diabetes will be analyzed and disseminated separately [48].

Study Setting

The PRO diabetes tool was tested in three different health care settings, as shown in Table 1.

Table 1. Characteristics of study settings.

Settings	Target group characteristics	Primary use of PRO[a]
Hospital outpatient diabetes clinics	• Type 1 diabetes • Type 2 diabetes referred due to complexity and treatment burden	PRO data are mainly used in annual diabetes visits (30-60 minutes) with a specialized the diabetes nurse. Physicians may also use it during initial medical visits with people with diabetes (40 minutes).
Municipality rehabilitation service centers	• Type 2 diabetes referred from general practice for lifestyle, health promotion, and diabetes education	The PRO is used during initial start-up visits at municipality centers and is potentially used during 3-month follow-up evaluation visits by multidisciplinary HCPs[b] (dietitians and physiotherapists).
Primary care	• Mainly type 2 diabetes treated regularly in primary practice	The PRO tool is used in regular routine and on-demand visits in primary practice settings (physician and nurse).

[a]PRO: patient-reported outcome.

[b]HCP: health care professional.

Eligibility Criteria

Participants were eligible for this study if they were (1) adults with type 1, 2, or other type of diabetes; (2) able to read and understand Danish; and (3) scheduled for a diabetes visit during the study period. Participants were excluded if they had another severe illness that would make their participation impossible. In one hospital, people with diabetes would also be excluded if they had been diagnosed with diabetes less than 12 months ago.

Description of the PRO Diabetes Intervention

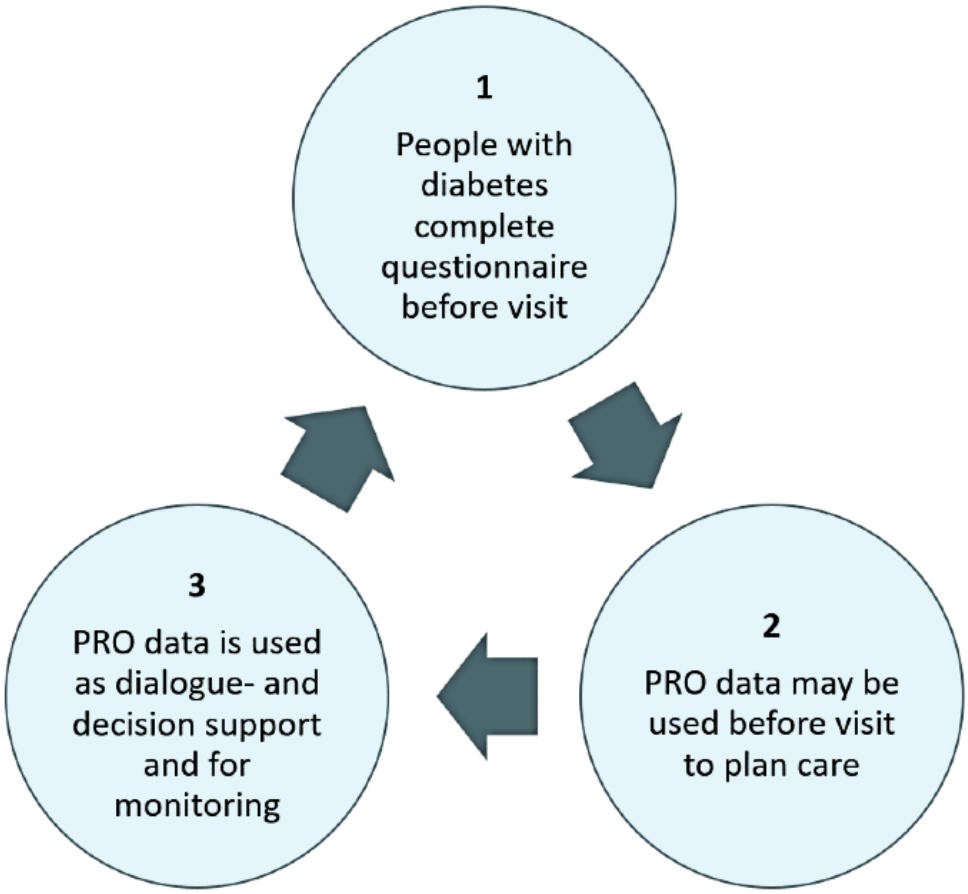
Overview

The PRO Diabetes Questionnaire and its scoring algorithms for clinical use were developed through a national participatory design process to create a psychometrically valid tool that would be feasible for use in routine care to increase the delivery of person-centered diabetes care [1,26,49].

The questionnaire design was guided by participatory cocreation processes with people with diabetes and HCPs, using qualitative research [1] and extensive literature review to take into account empirical research related to diabetes self-efficacy [50], self-determination [51], empowerment [52], social ecological and biopsychosocial care [53], behavioral and health psychological diabetes research [43], and person-centered diabetes care [1].

The core elements of the PRO diabetes intervention used across care settings are shown in Figure 1.

Figure 1. Key components of the PRO diabetes intervention used in all care settings. PRO: patient-reported outcome.



Initially, people with diabetes completed the PRO Diabetes Questionnaire at home using their smartphone, tablet, or computer preferably 2-10 days before their scheduled diabetes visit at a clinical care center or municipality diabetes center. This is intended to facilitate an optimal dialogue with an enhanced focus on the most important priorities of people with diabetes. The questionnaire measures generic and diabetes-specific topics that can only be reported directly by people with diabetes. The topics were established as important and relevant for both people with diabetes and HCPs. The HCP actively uses the PRO results during the care visit, together with the person with diabetes. A digital clinical PRO tool is used, which includes a dashboard that shows all the PRO results, to facilitate a review of issues and setting of priorities as part of a collaborative dialogue. The HCP had the technical option to access the PRO results of the people with diabetes through the HCP interface of the digital PRO tool once people with diabetes completed the questionnaire. However, upon completion of the questionnaire, it was explained to the person with diabetes that the results will be reviewed by the HCP just before the visit. If the person with diabetes needed support before the visit, they were advised to contact the HCP by phone or email.

Each PRO question answered by the people with diabetes is scored using a predefined scoring algorithm so that the results can be indicated in the digital PRO tool by green, yellow, or red colors. The scoring algorithms were defined through an iterative process involving HCPs, people with diabetes, and researchers to optimize clinical utility and validity. A green score indicates that there may be no problem for the responder on that item, a yellow score indicates the presence of concerns or issues requiring attention, and a red score indicates that there is a likely need for action and that the HCP and person with diabetes should address the topic. The digital PRO tool also provides easy access to raw data or scale scores if preferred by the people with diabetes or HCPs.

Before the study, each participating study site identified the most suitable way to fit the PRO tool into their existing care visits, which resulted in minor differences in the application of the tool while preserving the aim of delivering a common intervention.

All study sites participated in collaborative meetings to exchange experiences and approaches across the sites. An outline of the generally agreed approach to recommended person-centered use of the PRO Diabetes results is shown in Multimedia Appendix 2.

Two different digital software systems were used to provide the functionality defined by the PRO Diabetes Questionnaire and its scoring algorithms, the DiaProfil PRO diabetes tool developed by the VBHC-PRO-DIA at Aalborg University Hospital, and the health platform, EpicCare, the working tool of the hospitals in two of five Danish regions.

The Danish PRO Diabetes Questionnaire

The Danish PRO Diabetes Questionnaire includes 33-71 items and covers a range of carefully selected and defined health-related constructs.

The key content categories of the PRO Diabetes Questionnaire are shown in Textbox 1.

Textbox 1. Overview of the main content categories of the Danish Patient-Reported Outcomes Diabetes Questionnaire (2020). Constructs, short descriptions, and examples of content are presented.

General health and life situation

- Self-assessed general health, social support, and life stressors affecting diabetes management

Mental well-being

- Positive psychological well-being and depression symptoms

Symptom distress

- Distress related to pain, heart, gastrointestinal, sexual dysfunction, and sleep and foot problems or symptoms

Daily life with diabetes

- Fitting diabetes into daily life and diabetes-specific social support

Worries due to diabetes

- Worry about disease progression, that is, diabetes complications

Diabetes self-management confidence

- Confidence in managing diabetes (diet, physical activity, adjusting treatment, self-monitoring, and care seeking)

Blood sugar regulation

- Perceived quality of blood sugar regulation and burden due to hypoglycemia and the fluctuation of blood sugar levels

Medicine experience

- Efficacy, convenience, side effect distress, and satisfaction

Access to care

- Confidence in ability to get in contact with a health care professional if needed in relation to diabetes

Personal priorities for diabetes care

- Wish for support for specific aspects of self-management
- Priority topics to discuss at the diabetes visit

The questionnaire consists of a combination of previously psychometrically validated items and scales, as well as newly adapted or designed items. Adaptation or design of new items was only done if no previously validated items were available that fit the requirements of people with diabetes and HCPs. In addition, a participatory and qualitative approach was used, including literature review, desk research, and qualitative research for each construct. It uses branch logic, so each person with diabetes only receives directly relevant questions. The psychometric validity, reliability of each item, and appropriateness of the scoring algorithms and logic rules will be examined in this study.

The Digital PRO Tool: DiaProfil

DiaProfil is a stand-alone PRO diabetes digital tool, codeveloped with the inputs of people with diabetes and HCPs by Aalborg University Hospital with the support of Zitelab, specifically for augmented use of the national PRO Diabetes Questionnaire as

a tool for person-centered care delivery across care settings. An iterative, user-centered design process was undertaken involving people with diabetes and a multidisciplinary HCP team at Aalborg University Hospital to define optimal functionality and user interfaces. Previous experiences with other multidimensional PRO tools for diabetes were also considered [54].

DiaProfil allows the person with diabetes to complete the PRO questionnaire using mobile, tablet, or a PC and provides the HCP with web-based access to a multi-layered interactive PRO dashboard and an administrative system for reviewing and ordering PRO assessments. A significant new functionality in DiaProfil, resulting from the participatory design process, was the integration of actionable information for each PRO construct into the dashboard. The tool provided the HCP with information about available treatment and referral options, community services, and educational materials for each PRO construct. It required the clinical team to undertake an extensive desk-research exercise to map all resources and follow-up actions for each construct beyond its own care setting.

The DiaProfil dashboard was designed to provide an intuitive overview of the people with diabetes' overall PRO results in one screen to allow HCPs to achieve an overview almost instantly, which can be useful in daily practice. Furthermore, the tool was developed for acceptability and readability for people with diabetes to facilitate collaborative use by people with diabetes and HCPs together on equal terms during the visit.

A screenshot of the DiaProfil PRO dashboard is shown in Multimedia Appendix 3.

The dashboard presenting the results is interactive and contains multiple layers of information that are accessible with one or two mouse clicks from the main screen. For each PRO topic and output, key information is obtained with a single click, including (1) dialogue tips and tools, (2) educational materials, (3) referral options, and (4) listing of locally relevant care and support options. For instance, if a person with diabetes likely had depression, the HCP could click on the topic on the screen to directly view information about local referral options and various psychosocial support and self-help resources.

DiaProfil was used in all participating study sites, except for one hospital that used the health platform tool.

The Danish Health Care Platform: Sundhedsplatformen

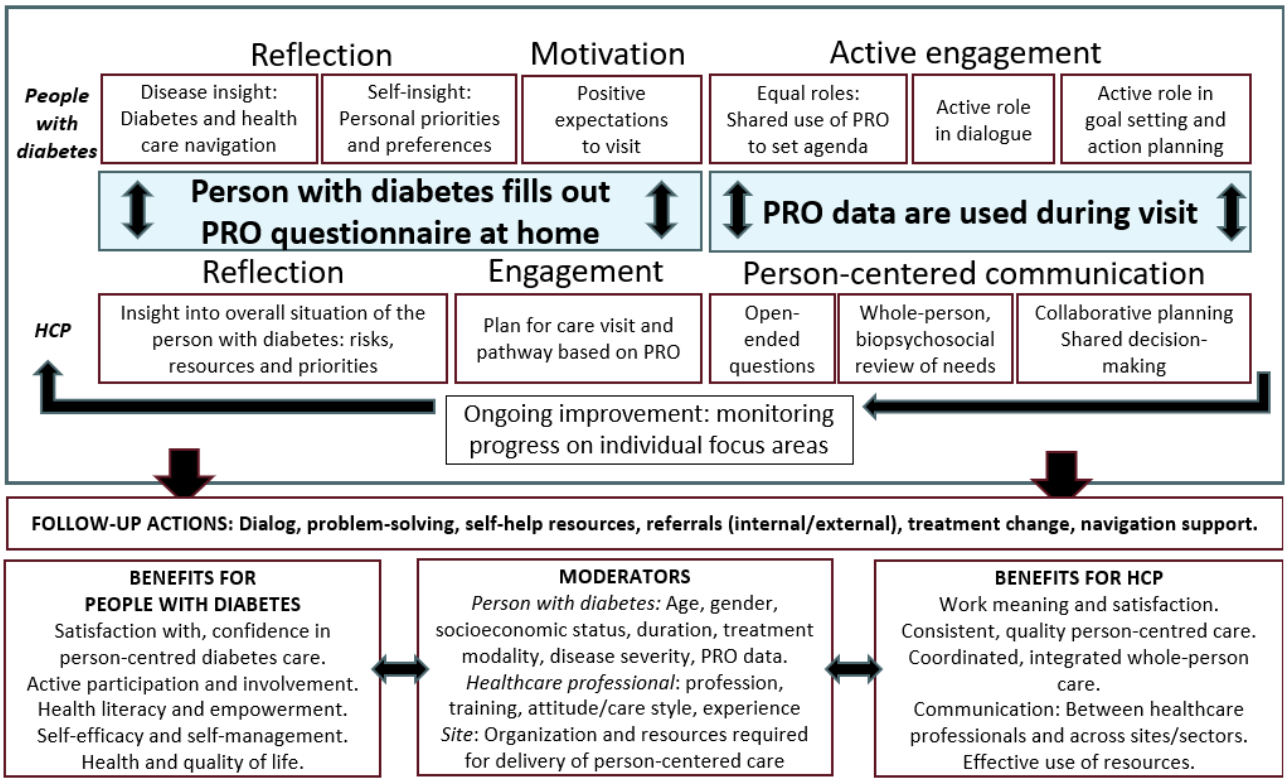
To integrate PRO data into their existing health information technology infrastructure, one hospital, Frederiksberg-Bispebjerg, used their existing generic IT health platform, EPIC, to collect and display PRO data. This platform is used by all hospitals covering 2.6 million inhabitants. In this hospital, people with diabetes completed the PRO Diabetes Questionnaire using the existing *My Health* app, which patients in the Capital Region of Denmark use to access general health care information. In this system, the HCP can view PRO results on multiple data screens that combine clinical and PRO data. Detailed methods for displaying PRO data on the clinical screen and ensuring proper placement in the patient flow were developed by the clinical diabetes care team together with the health information technology provider (Center for IT, Medico and Telephony) for optimal usability and integration into the existing workflow.

Outcomes

Working Model for the Evaluation of the Process and Outcome Indicators

A conceptual model to illustrate the key hypothesized mechanisms of action, moderators, and outcomes for the PRO diabetes intervention is shown in Figure 2. This was used to guide the design of outcomes and data collection tools. The working model reflects preliminary data from the formative evaluation process of the PRO diabetes tool [1,11] and will be continuously updated and expanded with the progress of the study.

Figure 2. A working model to illustrate hypothesized mechanisms, moderators, and impacts related to the use of the PRO diabetes tool. HCP: health care professional; PRO: patient-reported outcome.



The top part of the model illustrates that completion of PRO at home is hypothesized to impact care through mechanisms of reflection, motivation, and engagement before the visit and through mechanisms of active engagement of the people with diabetes and use of person-centered and value-based care strategies by the HCP during the visit. The use of PRO is hypothesized to lead to different follow-up actions by the health care team, which in turn is hypothesized to lead to different benefits for people with diabetes and HCPs. Both patient, health professional, and care setting factors are hypothesized to potentially moderate the extent to which use of the intervention impacts outcomes for people with diabetes and HCPs. Textbox 2 provides an overview of the main outcomes of this study.

Textbox 2. Overview of the main outcomes of the study.

Primary outcomes

- Perceptions of people with diabetes with regard to the following:
  - Acceptability, usability, and appropriateness of the patient-reported outcome (PRO) intervention (outcome 1A)
  - Impact (positive and negative) on them of using the PRO diabetes tool as part of their care (outcome 1B)
- Perceptions among health care professionals regarding:
  - Usability, feasibility, fidelity and appropriateness of the PRO intervention (outcome 2A)
  - Impacts (positive and negative) on diabetes care of using the PRO diabetes tool as part of routine care (outcome 2B)

Secondary outcomes

- Psychometric and clinical validity and reliability of the PRO questionnaire, scoring algorithms, and clinical dialogue support (outcome 3)
- Barriers and facilitators for the implementation and impact of PRO diabetes tool for people with diabetes, for health care professionals, and at the health system level (outcome 4)
- Estimation of public health impact indicators of the PRO intervention according to the RE-AIM (Reach, Efficacy, Adoption, Implementation and Maintenance) model (outcome 5)

Primary Outcomes

This study uses two primary descriptive outcomes. First, data will be gathered on the perceptions of the usability, acceptability, and appropriateness of the PRO diabetes tool of people with diabetes, along with the perceived positive and negative effects of their use of the tool. Data extracted about their disease and care are classified by type of diabetes, age, gender, treatment

modality, duration, disease complications, comorbidities, treatment setting, PRO outcomes, and general rating of visit quality (primary outcomes for people with diabetes). In addition, data will be collected on the HCP's perception of acceptability, appropriateness, and perceived positive and negative effects of the tool on care quality and experience by HCPs. Furthermore, information on years of professional experience, years of diabetes experience, training in use of person-centered communication, confidence in use of PRO in visits, treatment setting, and general rating of visit quality (primary outcome for HCP) is also obtained.

Measures and data sources for outcomes pertaining to indicators of feasibility and implementation [55,56] are detailed in Multimedia Appendix 4.

Secondary Outcomes

Characterization of the validity and reliability of the PRO questionnaire and clinical algorithms is a secondary outcome of the study (outcome 3). This outcome is assessed in three ways. First, the people with diabetes' perception of relevance, comprehensiveness, difficulty, acceptability, appropriateness, and comprehension of the questionnaire according to the type of diabetes, age, gender, treatment modality, duration of diabetes, disease complications, comorbidities, and treatment setting are measured (outcome 3A).

Next, the HCP's evaluation of the clinical and face validity of the PRO data; the clinical relevance and utility of the PRO content, including the items, scoring, outputs, algorithms, and digital dialogue; and decision support are measured (outcome 3B).

Then, the psychometric properties of the questionnaire pertaining to the extent to which it provides valid, reliable measurements of the selected constructs, can predict relevant future clinical or care needs, events, and prognoses, and can discriminate appropriately between relevant levels of symptom severity are evaluated (outcome 3C).

We also assessed the barriers and facilitators at the people with diabetes, HCP, clinic, and health care system levels for the implementation and impact of the PRO diabetes tool as a secondary outcome (outcome 4). Finally, the initial indicators of the reach, efficacy, adoption, implementation, and maintenance of the intervention in accordance with the RE-AIM model will be examined (outcome 5). The measures and data sources used to evaluate the intervention according to RE-AIM indicators are detailed in Multimedia Appendix 5.

Participant Timeline

All sites used the same core data collection and intervention procedure, as shown in Figures 3 and 4, with local modifications and adaptations, for seamless integration into routine care. Each participant was recruited approximately 14 days before their scheduled visit. People with diabetes will receive a link or electronic invitation to access and complete informed consent and the PRO Diabetes Questionnaire 2-14 days before their visit. People with diabetes will complete the PRO before their visit, unless there are specific barriers preventing this. At their scheduled visit, the HCPs use the IT PRO Dialogue Tool to review the results with the people with diabetes to support their dialogue. People with diabetes and HCPs will independently complete the evaluation forms when they are physically separated after the visit. Selected people with diabetes are invited for a 30- to 45-minute semistructured interview within 0-12 days after their diabetes visit. HCPs will participate in 4- to 5-hour multidisciplinary, structured HCP evaluation workshops halfway through and at the end of the study as well as complete individual end-of-study questionnaires.

Figure 3. Timeline for people with diabetes participating in the study. PRO: patient-reported outcome.

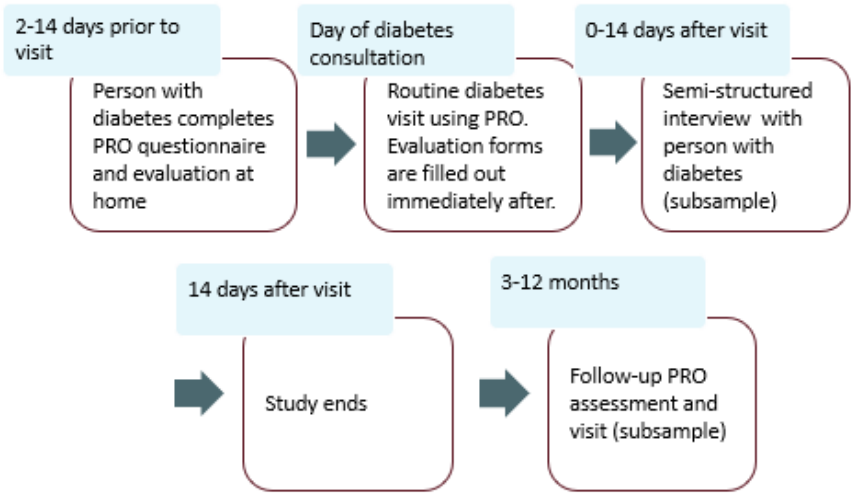
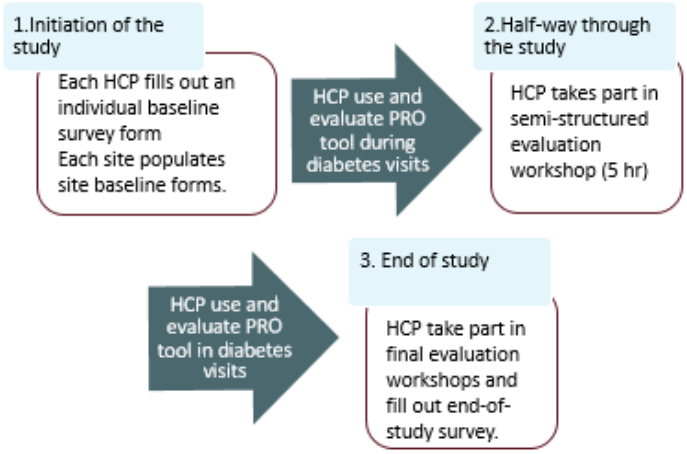


Figure 4. Timeline for HCPs participating in the study. HCP: health care professional; PRO: patient-reported outcome.



Sample Size

As the study has descriptive purposes, formal requirements for sample size estimation for the primary outcome were not applied. However, for any subgroup analysis, the minimum number of patients per group was estimated to be 64. For continuous variables, a minimal subgroup size of 64 was estimated to achieve 80% power for detecting an effect size of 0.5 at a significance level of P=.05 by using a two-sided, 2-sample, equal-variance t test. For proportions, minimal group sample sizes were estimated to be 63 to achieve 80% power for detecting an effect size of 0.5 with a significance level of .05 by using a two-sided z test in a similar manner.

The minimum target for recruitment was 125 people with type 1 diabetes and 375 people with type 2 diabetes, based on requirements for comparatively analyzing by subgroups and requirements for psychometric analyses.

According to the available data, group comparisons will be undertaken using data across all centers by age groups, treatment modality (none, tablet only, short- and long-acting insulin, insulin pump, and glucagon-like peptide-1), blood sugar measurement technology (finger prick, flash glucose monitoring, and continuous glucose monitoring), diabetes complications (neuropathy, cardiovascular disease, gastrointestinal complications, sexual dysfunction, and sleep difficulty), and comorbidities.

Power analyses for comparative analyses will be conducted based on the final number of people with diabetes by site for PRO and PRO evaluation data to determine the extent to which outcomes can be comparatively analyzed either at the site or at the care-setting level.

The expected number of HCPs to participate was 25-40, based on what was reported to be feasible by the study sites. Sites were encouraged to have several HCPs participating as a minimum and to include HCPs with a good diversity of health care discipline, age, diabetes experience, and profession.

To compare experiences across different health care settings, the aim of this study was to include sites from secondary care, municipality rehabilitation centers, and primary care. On the basis of the resources available for the pilot study, the total number of sites was estimated to be 7-10.

Recruitment

During the recruitment period from November 2019 to December 2020, each site recruited people with diabetes who met the eligibility criteria as part of their routine practice. The sites molded the recruitment procedures based on their local care flow and requirements for the use of PRO in routine diabetes care visits or rehabilitation. At every site, recruitment involves inviting eligible people with diabetes who are registered or scheduled for a diabetes care visit to try the PRO diabetes tool in conjunction with their upcoming visit. Only people with diabetes who provided written informed consent for participation in the study are included. Each site uses different methods of communication with people with diabetes for recruitment depending on their routine care pathways, including using the phone, electronic (app or email), and in-person invitations.

Data Collection

Overview

The data collection and data collection tools are listed in Textbox 3. Data for the primary outcomes are collected using Likert scales and open-ended evaluation questionnaires that are completed by people with diabetes and HCPs in connection with the use of the PRO diabetes tool in routine care and by HCPs at the end of the study. In the mixed methods analysis, qualitative data are collected from transcribed interviews, consultations, evaluations, and debriefing workshops completed during the entire study period.

Textbox 3. Data collection tools. The contents of the main data collection tools are available in the multimedia appendices.

Multicenter patient-reported outcome (PRO) diabetes study core data collection tools

- People with diabetes
  - PRO Diabetes Questionnaire (Multimedia Appendix 6)
  - PRO Evaluation Questionnaires (PRO-EVAL-P; Multimedia Appendix 7)
  - Post-Visit PRO Evaluation Questionnaire (PRO-CON-EVAL-P-SF; Multimedia Appendix 8)
  - Semistructured interview guide for people with diabetes (Multimedia Appendix 9)
  - Baseline sociodemographic data sheet for people with diabetes (Multimedia Appendix 10)
- Health care professional (HCP)
  - Baseline background data (HCP profile questionnaire; Multimedia Appendix 11)
  - Post-Visit PRO Evaluation Questionnaire (PRO-CON-EVAL-HCP-SF) and evaluation form for algorithm evaluation (Multimedia Appendix 12)
  - Semistructured guide for HCP evaluation workshops (HCP evaluation guide; Multimedia Appendix 13)
  - HCP End-of-Study Evaluation (HCP end-of-study PRO evaluation form; Multimedia Appendix 1)
- Study site
  - Diabetes Clinic Resources for Person-Centered Diabetes Care Survey (Multimedia Appendix 14 [57])
  - Site datasheet: Organization, services, population, resources for PRO follow-up

Data Collection for Primary Outcome 1: People With Diabetes' Perceptions of the PRO Diabetes Questionnaire

The perceptions of people with diabetes regarding the PRO Diabetes Questionnaire are evaluated by the people with diabetes at home immediately after completing it using a digital PRO Evaluation Questionnaire (PRO-EVAL-P). This immediate evaluation of the PRO Diabetes Questionnaire by the people with diabetes assesses the perceived relevance of the questionnaire in a realistic scenario before their routinely scheduled visit and allows for both closed and open-ended responses.

Data Collection for Primary Outcome 1: People With Diabetes' Perceptions of the Dialogue and Impact of the PRO Diabetes Questionnaire

This outcome assesses the multi-item and single-item scores from the people with diabetes evaluations using the Post-Visit PRO Tool Evaluation Questionnaire after each visit where the PRO tool was used (PRO diabetes visit). To minimize bias due to social desirability, people with diabetes are informed that their evaluation will be kept confidential, that their HCP will not see their responses, and that their answers will only be used in research after deidentification. These data provide important new information regarding the diversity and variability of individual experiences of people with diabetes when using the PRO diabetes tool in the visit and allow for an analysis of interactions among HCPs, people with diabetes, and setting factors in relation to primary outcomes. Verbatim transcripts of structured interviews conducted with a subset of a minimum of 10 randomly selected people with diabetes in each care setting after their PRO diabetes visit are coded and analyzed for mixed methods analysis.

Data Collection for Primary Outcome 2: HCP's Perceptions of the Use of the PRO Diabetes Tool in Individual Care Visits

These outcome data were obtained from the multi-item and single-item scores for each PRO visit in the study using the HCP evaluations on the Post-Visit PRO Tool Evaluation Questionnaire immediately after or within a few days of the visit. The HCPs will complete informed consent and are informed that the collected data are only used in an anonymized manner. In addition, the HCPs will complete evaluation questionnaires at the end of the study, which evaluate their overall views and attitudes regarding the use of PRO, impact of use of PRO, and requirements for use of PRO.

Data Collection for Secondary Outcomes: Predictors, Barriers, Facilitators, and Readiness Factors for the Adoption, Usage, Satisfaction, and Benefits of PRO

Sociodemographic and diabetes profile data were collected for all participating people with diabetes to analyze the known-group and discriminative validity and reliability of the PRO Diabetes Questionnaire together with primary study outcomes by people with diabetes subgroups. A core set of HCP profile data is collected for all HCPs to evaluate primary outcomes by the relevant HCP subgroups. Two comprehensive questionnaires are used—one adapted for use in Denmark for this study from the Primary Care Resources for Chronic Illness Care Questionnaire [57] (Multimedia Appendix 14) and one study-specific questionnaire. The study-specific questionnaire assesses details for each site about the local PRO setup and examines the extent to which the site has resources and services to follow-up on each PRO construct covered by the PRO Diabetes Questionnaire. These data are used to qualitatively analyze relationships between primary outcomes by contextual

factors relevant to the delivery of person-centered and psychosocial diabetes care and the RE-AIM analysis.

Likert Scale Evaluation Questionnaires of Experience of Use of PRO in Routine Care

We did not identify any previously published PRO evaluation questionnaires that had been specifically designed and validated for our intended large-scale use in routine care settings. The VBHC-PRO-DIA team therefore developed and tested a set of purpose-built Likert Scale evaluation questionnaires in collaboration with people with diabetes and HCPs as part of the PRO tool's formative evaluation [29]. A first set of long form questionnaires was developed for a hospital-based clinical study to evaluate the impact of the PRO diabetes tool on person-centered communication and autonomy support using multi-item scale scores.

For this study, HCPs from all care settings and a panel of people with diabetes were involved to identify a core set of evaluation questions that were appropriate and acceptable for use in all sites and care settings, which would allow for pooled and comparative analyses. The short-form questionnaires evaluated experiences of people with diabetes and HCPs related to the use of PRO data in their diabetes visit, such as the extent to which the data were used, impact on engagement, dialogue and person-centered care qualities of the visit, impact on self-management and on care quality, and overall satisfaction and interest in continued use. The questionnaires also briefly assess the perceptions of people with diabetes and HCPs on the general quality of the dialogue and aspects of person-centered communication [10,58].

Data Management

Each research site is responsible for data entry, security, storage, and data quality verification. Of the 10 study sites, 9 opted to use a uniform web-based research data collection system that was purpose-built for M-PRODIA data collection by Aalborg University Hospital. The web-based data collection forms for the M-PRODIA are integrated into the DiaProfil solution for seamless completion by both people with diabetes and HCPs as part of the study procedures. In the hospital study site in the Capital Region, where a separate health platform system is used for PRO data collection and dialogue support, evaluation forms are provided in paper and pencil format, and manual data entry is performed by clinical staff using formats that are comparable with the electronic forms. Double-entry is used for the sample cases. All paper forms and raw data will be stored for 5 years or as required by law.

A comprehensive codebook with operational definitions, numerical codes, and standardized formats for all variables was established for data monitoring, quality control, coding, and harmonization purposes. At multiple points during the study period, sample data are collected to assess data completeness, missing value patterns, and range checks. At the halfway point, the HCP will participate in an interim study review meeting where data quality is evaluated.

Data Analysis

Statistical Methods

Quantitative data (ie, closed-ended questionnaire data and numerical data) will be coded, and all numerical data will be prepared for descriptive analyses and main statistical analyses using IBM SPSS Statistics for Windows (IBM Cooperation). The SAS statistical software package (SAS Institute Inc) is used for multilevel hierarchical regression analyses. Descriptive statistics will be used for continuous (mean and SD) and categorical (frequency and percentage) variables to analyze and compare evaluation data by center and subgroups. The aim of this study is to analyze drop-out data, including nonparticipation, attrition, and completion rates across centers, to characterize the generalizability of findings relating to population reach and outreach to vulnerable populations, and to compare implementation drivers across participating centers. Both parametric and nonparametric statistics were used for group comparisons based on the distribution of each data variable.

Missing value analysis, including the identification of variables missing completely at random or not at random, will be conducted for all variables.

PRO results are scored and analyzed as both raw and scored data using predefined clinical scoring algorithms according to subgroups of adequate sizes for multilevel regression and multilevel logistic regression models [59]. Multi-item scores will be transformed and standardized to a score range of 0-100.

For subgroup comparisons, two-tailed *t* tests and nonparametric statistics, such as the Mann-Whitney *U* test, are used. Multivariate mediation regression analysis will be used to examine the relative contribution of the different participant, treatment, and setting characteristics. Multilevel analyses will be used as feasible and required to separate the variance by people with diabetes, HCP, and care setting. Bonferroni and associated methods will be used to adjust P values for multiple comparisons. Intraclass coefficient analysis will be used to examine the level of agreement between HCPs and people with diabetes on the primary outcomes of the visits, which were evaluated both by people with diabetes and HCPs.

Psychometric Analysis

Study variables will be evaluated for skewed or nonnormal distributions using measures of dispersion (eg, means and SDs, kurtosis, and Pearson skew coefficients). Cosmin guidelines are used as a reference framework for the characterization of psychometric reliability and validity [60,61]. Exploratory and confirmatory factor analyses will be used to examine the hypothesized multi-item scales for multi-dimensionality, convergent validity, and discriminant validity. Internal consistency of the multi-item scales will be examined using accepted methods, including Cronbach α or Kuder-Richardson reliability coefficients, as appropriate. We will use Pearson product-moment and Spearman correlation coefficients, depending on the nature of the data, to assess the construct validity between PROs and hypothesized validity variables (eg, glycemic control and use of health services). If feasible, we will estimate the responsiveness of PRO indicators to change and

minimal clinically important differences where follow-up PRO data are available.

Qualitative Analysis

Qualitative data (eg, focus groups, workshops, interview transcripts, open-ended responses from evaluation questionnaires, notes, minutes, and video, audio, and graphic outputs from evaluation and study activities) were entered and coded in NVivo 12 (QSR International).

Multiple qualitative analysis methods will be used for different purposes and, as relevant, for specific qualitative data [62-64]. Qualitative data are primarily coded and categorized using content and semantic analysis, and where appropriate, using mixed inductive-deductive analysis rooted in a phenomenological approach [65] with the involvement of multiple coders.

A code book using the taxonomy of the PRO questionnaire content (ie, items and constructs) is used across data from all informants to examine the validity, utility, and perceived benefits and enable multi-informant triangulation analysis for each individual PRO construct and item.

Qualitative data pertaining to implementation from HCP evaluation workshops and center evaluations will be analyzed with guidance from the RE-AIM framework [64].

In this way, data can be combined to evaluate indicators of the PRO questionnaire relevance, acceptability, difficulty, comprehensiveness, comprehension, clinical utility, validity, scoring validity, self-insight, utility, emotional impact, and emergent insights. To the extent feasible, coding will also cover indicators of fidelity, feasibility, appropriateness, care quality impact, engagement, benefits, disadvantages, barriers and facilitators, attitudes, sustainability, and emergent insights.

Mixed Methods Analysis

We aim to combine qualitative and quantitative data from different informants (ie, people with diabetes, HCPs, and centers) using convergent and parallel mixed methods research designs to provide increased robustness and depth of analyses [66]. An explanatory mixed methods analysis approach is completed using the coding of transcribed interviews of people with diabetes. Where feasible and appropriate, the frequency of codes will be used to supplement and corroborate the quantitative analyses of primary outcomes and to characterize any differences across subgroups [67,68].

Data Monitoring

Each participating site collects and is responsible for its own data and the delivery of these data to the centralized VBS-PRO-DIA research group at the Department of Endocrinology at Aalborg University Hospital, Aalborg, Denmark, in accordance with specified requirements for the anonymization of data, use of study-specific IDs, and secure data transfers. Furthermore, each site was responsible for ensuring that informed consent was obtained and validated for all participants. All primary analyses were single-arm and noncomparative. Data from each participating site were traceable in the analyses. A data monitoring committee was not deemed necessary because of the accessibility of the data and the nature of the study as a real-world pilot study evaluation.

Interim Analyses and Stopping Guidelines

We conducted an interim analysis at the halfway point of the study in 2020 to assess the recruitment status and analyze a sample of interim results to consider potential early termination of the study. The study is considered to carry minimal risk for the participants, as the PRO Diabetes Questionnaire had been developed with and evaluated by people with diabetes in advance.

Evaluation questionnaires used from the beginning of the study period after each diabetes visit included specific prompting questions for the people with diabetes to determine if there were any unpleasant experiences or problems related to using the PRO Diabetes Questionnaire. Specifically, we wanted to understand if, due to patient characteristics or treatment context, certain questions, such as those relating to sexual dysfunction, loneliness, or psychological well-being, would be experienced by some people with diabetes as unpleasant. Alongside the ongoing communication with HCPs involved in the use of PRO, these questionnaires ensure ongoing continuous monitoring for potential negative effects of the intervention. Interviews were conducted with approximately 5 people with diabetes from each site halfway to obtain qualitative insights regarding any positive and negative experiences associated with the study at each site.

Auditing and Independent Data Verification

The Danish National Health Data Authorities independently reviewed the transcripts of the evaluation interviews with people with diabetes, verbatim evaluation of the open-ended responses from the HCPs and people with diabetes following each visit, and the transcripts of the HCP evaluation workshops for vetting and auditing analysis.

Ethics and Dissemination

Research Ethics Approval

The M-PRODIA has been approved by the regional research approval authority and evaluated by the authority not to be in the scope of the scientific ethics committee evaluation as the study does not involve the collection of human biological materials and does not involve medical intervention.

Protocol Amendments

This is a pragmatic and formative real-world pilot study, so insights and data obtained during the study period may be used to adjust and optimize the study protocol.

Informed Consent

Each study site is responsible for obtaining informed consent from all people with diabetes and HCPs participating in the study. Consent forms are locally adjusted if necessary, in accordance with the specific data that are collected from each site. A duly signed and complete informed consent form is a prerequisite for transferring anonymized data to the M-PRODIA research team.

Confidentiality

Anonymized, deidentified data using study IDs for people with diabetes, HCPs, and evaluated visits are sent from each site using secure data transmission to the M-PRODIA research team at Aalborg University Hospital. Data are stored and processed using data protection procedures in accordance with the requirements of the Danish Data Protection Agency and the region of northern Denmark.

Dissemination Policy

Results will be disseminated to guide implementation of the PRO diabetes tool in the national health system in collaboration with the Danish National Health Data Authority and health care stakeholders. Vancouver guiding rules for authorships will be used for scientific publications [69]. Interim findings will be shared with the Danish Health Data Authority in support of the public health objectives of the national pilot study.

Results

A total of 7 study sites, 598 people with diabetes, and 34 HCPs completed the study by April 1, 2021. Data cleaning and management are ongoing. Primary results based on primary outcomes are expected to be disseminated by the end of 2021.

Discussion

Study Implications

This is the first large-scale study to evaluate the use of the national PRO diabetes tool in routine care across different health care settings using psychometrically tested PRO evaluation questionnaires for both people with diabetes and HCPs.

This study is expected to provide important new information about perceived acceptability, relevance, and benefits of the PRO diabetes tool in a large representative and heterogeneous population of adults with type 1 and 2 diabetes in Denmark and in a diverse group of HCPs representing multiple professions and different health care settings.

Although a great deal of research has focused on evaluating the psychometric characteristics of PRO diabetes questionnaires [70-72], we found very limited research examining how people with diabetes perceive the relevance and personal value of a comprehensive digital PRO questionnaire in the context of their routine diabetes care.

We believe this study generates important new insights into the experiences of using PRO in diabetes care, which can contribute to the identification of strategies for improvement of the questionnaire, its use, and implementation and provide general insights to guide future digital PRO interventions.

This study is the result of a long-standing national multidisciplinary and patient-centric collaboration to design and evaluate a nationally agreed PRO diabetes tool. It is hoped that the implementation of a shared national PRO diabetes tool, created with the involvement of all health sectors, can help facilitate a coordinated, continuous person-centered care experience for people with diabetes in Denmark over time. However, this study reflects that we are only at the beginning of a long learning curve. Long-term implementation, health and cost-effectiveness research, and collaborative quality assurance efforts are warranted to optimize and evaluate the long-term impact of implementation across the health system and communities. The introduction of this PRO tool on a larger scale may strengthen the role and influence of people with diabetes and family members of people with diabetes in the health care system in multiple ways, which may change how people with diabetes and family members of people with diabetes communicate about diabetes, how HCPs communicate within and across teams about person-centered care, and how health care sectors and communities communicate and coordinate about the provision of person-centered diabetes care.

Methodological Considerations

The main strengths of this study are that it combines qualitative and quantitative data to provide detailed insights into the perspective of people with diabetes on the real-world use of PRO and provides a wide range of insights regarding the many factors likely to influence the public health impact potential of the PRO diabetes tool in Denmark.

This pilot study has important limitations. One limitation is the lack of a randomized control group and the other is that the main outcomes are mainly process-orientated and rely solely on self-reported data, which may be subject to bias related to social desirability and recall issues.

The study is not designed to quantify the magnitude of clinical, health, and empowerment-related benefits that may be achieved by using the PRO intervention. The study also does not compare reach and effectiveness performance of different PRO tools, which will be important to determine mechanisms of action. These are important research questions that must be addressed in parallel and planned research. Separate clinical studies by the VBHC-PRO-DIA team are underway to address these issues separately and to examine the impacts of PRO use over time on clinical and health care use indicators and health cost drivers.

Study Status

The main fieldwork and recruitment of people with diabetes and HCPs for the M-PRODIA was completed in January 2021; however, due to the challenges and restrictions imposed by COVID-19, some study sites have encountered delays in data collection. Therefore, the closure of the database was expected by April 2021.

Conclusions

A detailed study protocol and newly developed psychometrically designed data collection tools are developed and implemented in 2020 to collect detailed data on how people with diabetes and HCPs experience the use of a newly designed digital PRO tool in routine diabetes care across different care settings.

Acknowledgments

The authors thank the people with diabetes and family members of people with diabetes who contributed to the design of the PRO diabetes tool, the study, and study materials and the people with diabetes who participated in the study. They also thank the Danish Diabetes Association, the Danish regions, the Region of North Denmark, the PRO Secretariat of the Danish Health Data Authority, and all the members of the National Clinical Coordination Group for PRO diabetes who took part in the development of the national PRO Diabetes Questionnaire. The North Denmark Region provided unrestricted funding (kr 5.6 million) for the VBHC-PRO-DIA project. The Danish Health Data Authority provided separate funding for the study sites to pilot test the PRO diabetes tool in routine care and report findings. Sites covered their own costs for participating in the M-PRODIA. No restrictions are imposed by sponsors regarding scientific analysis and dissemination of results. Zitelab Aps managed digital PRO and PRO evaluation data collection from the majority of centers. The M-PRODIA research committee who oversaw initial study design and initiation consisted of SES, HP, CG, DBB, NBM, and NE. Participating sites in the M-PRODIA at the present time are (1) the Department of Endocrinology, Aalborg University Hospital, Aalborg, North Denmark Region; (2) the Department of Diabetes and Endocrinology, Frederik-Bispebjerg Hospital, Copenhagen, Capital Region; (3) Copenhagen Center for Diabetes, Copenhagen, Capital Region; (4) Guldborgsund Rehabilitation Center, Guldborgsund Municipality, Zealand Region; (5) Hjoerring Municipality, Hjoerring, North Denmark Region; (6) Broenderslev Municipality, Broenderslev, North Denmark Region; and (7) primary care clinics located at Regionsklinikken, Broenderslev, North Denmark Region, and Praksis 201, Tingbjerglaegen and Groendalslaegerne in Copenhagen.

Authors' Contributions

SES conceived the original study idea; designed the study, the study materials, the data collection tools, and methods; and drafted the manuscript. SES is the scientific project lead. SES and NE are coprincipal investigators. NE is responsible for the clinical data and is the clinical project lead. AN and SK provided statistical expertise. All authors reviewed and approved the manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Health care professional guidance for the use of patient-reported outcomes in annual outpatient diabetes visits.
[DOCX File , 18 KB - resprot_v10i9e28391_app1.docx]

Multimedia Appendix 2
DiaProfil patient-reported outcomes dashboard screenshot.
[DOCX File , 151 KB - resprot_v10i9e28391_app2.docx]

Multimedia Appendix 3
Feasibility and implementation indicators and measurements.
[DOCX File , 17 KB - resprot_v10i9e28391_app3.docx]

Multimedia Appendix 4
Indicators and measurements used for the Reach, Efficacy, Adoption, Implementation and Maintenance evaluation.
[DOCX File , 18 KB - resprot_v10i9e28391_app4.docx]

Multimedia Appendix 5
Content of the Danish Patient-Reported Outcomes Diabetes Questionnaire.
[DOCX File , 19 KB - resprot_v10i9e28391_app5.docx]

Multimedia Appendix 6
Patient Evaluation of the Patient-Reported Outcomes Questionnaire (PRO-EVAL-P).
[DOCX File , 14 KB - resprot_v10i9e28391_app6.docx]

Multimedia Appendix 7
Patient evaluation of patient-reported outcomes use after the diabetes visit (PRO-CON-EVAL-P-Short Form).
[DOCX File , 15 KB - resprot_v10i9e28391_app7.docx]

Multimedia Appendix 8
Semistructured interview guide for use with people with diabetes.

[DOCX File , 17 KB - resprot_v10i9e28391_app8.docx]

Multimedia Appendix 9
Background and sociodemographic data for people with diabetes.
[DOCX File , 15 KB - resprot_v10i9e28391_app9.docx]

Multimedia Appendix 10
Health care professional Baseline Profile Questionnaire.
[DOCX File , 16 KB - resprot_v10i9e28391_app10.docx]

Multimedia Appendix 11
Health care professional evaluation of the use of patient-reported outcomes (PRO-CON-EVAL-HCP in algorithm review form).
[DOCX File , 20 KB - resprot_v10i9e28391_app11.docx]

Multimedia Appendix 12
Semistructured guide for health care professional evaluation.
[DOCX File , 15 KB - resprot_v10i9e28391_app12.docx]

Multimedia Appendix 13
Health care professional End-of-Study Patient-Reported Outcomes Evaluation Questionnaire.
[DOCX File , 17 KB - resprot_v10i9e28391_app13.docx]

Multimedia Appendix 14
Center Resource Profile for Person-Centered Diabetes Care.
[DOCX File , 17 KB - resprot_v10i9e28391_app14.docx]

References

1. Skovlund SE, Lichtenberg TH, Hessler D, Ejskjaer N. Can the routine use of patient-reported outcome measures improve the delivery of person-centered diabetes care? A review of recent developments and a case study. Curr Diab Rep 2019 Aug 16;19(9):84. [doi: 10.1007/s11892-019-1190-x] [Medline: 31420754]
2. Greenhalgh J, Dalkin S, Gooding K, Gibbons E, Wright J, Meads D, et al. Functionality and feedback: a realist synthesis of the collation, interpretation and utilisation of patient-reported outcome measures data to improve patient care. Health Serv Deliv Res 2017 Jan;5(2):1-280. [doi: 10.3310/hsdr05020] [Medline: 28121094]
3. Snyder CF, Aaronson NK, Choucair AK, Elliott TE, Greenhalgh J, Halyard MY, et al. Implementing patient-reported outcomes assessment in clinical practice: a review of the options and considerations. Qual Life Res 2012 Oct;21(8):1305-1314. [doi: 10.1007/s11136-011-0054-x] [Medline: 22048932]
4. Yu JS, Xu T, James RA, Lu W, Hoffman JE. Relationship between diabetes, stress, and self-management to inform chronic disease product development: retrospective cross-sectional study. JMIR Diabetes 2020 Dec 23;5(4):e20888 [FREE Full text] [doi: 10.2196/20888] [Medline: 33355538]
5. Weatherall J, Paprocki Y, Meyer TM, Kudel I, Witt EA. Sleep tracking and exercise in patients with type 2 diabetes mellitus (Step-D): pilot study to determine correlations between fitbit data and patient-reported outcomes. JMIR Mhealth Uhealth 2018 Jun 05;6(6):e131 [FREE Full text] [doi: 10.2196/mhealth.8122] [Medline: 29871856]
6. Jiwani R, Wang J, Berndt A, Ramaswamy P, Joseph N, Du Y, et al. Changes in patient-reported outcome measures with a technology-supported behavioral lifestyle intervention among patients with type 2 diabetes: pilot randomized controlled clinical trial. JMIR Diabetes 2020 Jul 24;5(3):e19268 [FREE Full text] [doi: 10.2196/19268] [Medline: 32706652]
7. Richter J, Nannen C, Chehab G, Acar H, Becker A, Willers R, et al. Mobile App-based documentation of patient-reported outcomes - 3-months results from a proof-of-concept study on modern rheumatology patient management. Arthritis Res Ther 2021 Apr 19;23(1):121 [FREE Full text] [doi: 10.1186/s13075-021-02500-3] [Medline: 33874994]
8. Corathers SD, Mara CA, Chundi PK, Kichler JC. Psychosocial patient-reported outcomes in pediatric and adolescent diabetes: a review and case example. Curr Diab Rep 2017 Jul 15;17(7):45. [doi: 10.1007/s11892-017-0872-5] [Medline: 28508255]
9. Gómez-Velasco DV, Almeda-Valdes P, Martagón AJ, Galán-Ramírez GA, Aguilar Salinas CA. Empowerment of patients with type 2 diabetes: current perspectives. Diabetes Metab Syndr Obes Targets Ther 2019 Aug;Volume 12:1311-1321. [doi: 10.2147/dmso.s174910]
10. Williams GC, Freedman ZR, Deci EL. Supporting autonomy to motivate patients with diabetes for glucose control. Diabetes Care 1998 Oct 01;21(10):1644-1651. [doi: 10.2337/diacare.21.10.1644] [Medline: 9773724]

11. Skovlund SE, Troelsen L, Nørgaard LM, Kjaer PH, Pietraszek A, Larsen HR, et al. 753-P: A clinical mixed-methods study of the perceived benefits of using the Danish diabetes patient reported outcome measure and dialogue support tool in routine outpatient diabetes care. Diabetes 2020 Jun 09;69(Supplement 1):753-P [FREE Full text] [doi: 10.2337/db20-753-p]
12. Worswick J, Wayne SC, Bennett R, Fiander M, Mayhew A, Weir MC, et al. Improving quality of care for persons with diabetes: an overview of systematic reviews - what does the evidence tell us? Syst Rev 2013 May 07;2:26 [FREE Full text] [doi: 10.1186/2046-4053-2-26] [Medline: 23647654]
13. Snoek FJ, Kersch NYA, Eldrup E, Harman-Boehm I, Hermanns N, Kokoszka A, et al. Monitoring of Individual Needs in Diabetes (MIND)-2: follow-up data from the cross-national Diabetes Attitudes, Wishes, and Needs (DAWN) MIND study. Diabetes Care 2012 Nov 26;35(11):2128-2132 [FREE Full text] [doi: 10.2337/dc11-1326] [Medline: 22837364]
14. Halliday JA, Hendrieckx C, Busija L, Browne JL, Nefs G, Pouwer F, et al. Validation of the WHO-5 as a first-step screening instrument for depression in adults with diabetes: results from Diabetes MILES - Australia. Diabetes Res Clin Pract 2017 Oct;132:27-35. [doi: 10.1016/j.diabres.2017.07.005] [Medline: 28783530]
15. Reddy J, Wilhelm K, Campbell L. Putting PAID to diabetes-related distress: the potential utility of the problem areas in diabetes (PAID) scale in patients with diabetes. Psychosomatics 2013 Jan;54(1):44-51. [doi: 10.1016/j.psym.2012.08.004] [Medline: 23295006]
16. Wieringa TH, de Wit M, Twisk JW, Snoek FJ. Improving interpretability of individual Diabetes Symptom Checklist-Revised (DSC-R) scores: the role of patient characteristics. BMJ Open Diabetes Res Care 2020 Apr 01;8(1):e001146 [FREE Full text] [doi: 10.1136/bmjdrc-2019-001146] [Medline: 32241781]
17. Lavallee DC, Chenok KE, Love RM, Petersen C, Holve E, Segal CD, et al. Incorporating patient-reported outcomes into health care to engage patients and enhance care. Health Aff (Millwood) 2016 Apr;35(4):575-582. [doi: 10.1377/hlthaff.2015.1362] [Medline: 27044954]
18. Wieringa TH, Rodriguez-Gutierrez R, Spencer-Bonilla G, de Wit M, Ponce OJ, Sanchez-Herrera MF, et al. Decision aids that facilitate elements of shared decision making in chronic illnesses: a systematic review. Syst Rev 2019 May 20;8(1):121 [FREE Full text] [doi: 10.1186/s13643-019-1034-4] [Medline: 31109357]
19. Rogers E, Yost K, Rosedahl J, Linzer M, Boehm D, Thakur A, et al. Validating the Patient Experience with Treatment and Self-Management (PETS), a patient-reported measure of treatment burden, in people with diabetes. Patient Relat Outcome Meas 2017 Nov;Volume 8:143-156. [doi: 10.2147/prom.s140851]
20. Nano J, Carinci F, Okunade O, Whittaker S, Walbaum M, Barnard-Kelly K, Diabetes Working Group of the International Consortium for Health Outcomes Measurement (ICHOM). A standard set of person-centred outcomes for diabetes mellitus: results of an international and unified approach. Diabet Med 2020 Dec 20;37(12):2009-2018. [doi: 10.1111/dme.14286] [Medline: 32124488]
21. Porter I, Gonçalves-Bradley D, Ricci-Cabello I, Gibbons C, Gangannagaripalli J, Fitzpatrick R, et al. Framework and guidance for implementing patient-reported outcomes in clinical practice: evidence, challenges and opportunities. J Comp Eff Res 2016 Aug;5(5):507-519. [doi: 10.2217/cer-2015-0014] [Medline: 27427277]
22. Greenhalgh J, Long AF, Flynn R. The use of patient reported outcome measures in routine clinical practice: lack of impact or lack of theory? Soc Sci Med 2005 Feb;60(4):833-843. [doi: 10.1016/j.socscimed.2004.06.022] [Medline: 15571900]
23. Scholle S, Morton S, Homco J, Rodriguez K, Anderson D, Hahn E, et al. Implementation of the PROMIS-29 in routine care for people with diabetes: challenges and opportunities. J Ambul Care Manage 2018;41(4):274-287. [doi: 10.1097/JAC.0000000000000248] [Medline: 29923844]
24. Nielsen AS, Kidholm K, Kayser L. Patients' reasons for non-use of digital patient-reported outcome concepts: a scoping review. Health Informatics J 2020 Dec 30;26(4):2811-2833 [FREE Full text] [doi: 10.1177/1460458220942649] [Medline: 32731773]
25. Engström M, Leksell J, Johansson U, Gudbjörnsdottir S. What is important for you? A qualitative interview study of living with diabetes and experiences of diabetes care to establish a basis for a tailored Patient-Reported Outcome Measure for the Swedish National Diabetes Register. BMJ Open 2016 Mar 24;6(3):e010249 [FREE Full text] [doi: 10.1136/bmjopen-2015-010249] [Medline: 27013595]
26. Deane K, Delbecque L, Gorbenko O, Hamoir AM, Hoos A, Nafria B, et al. Co-creation of patient engagement quality guidance for medicines development: an international multistakeholder initiative. BMJ Innov 2019 Jan 02;5(1):43-55 [FREE Full text] [doi: 10.1136/bmjinnov-2018-000317] [Medline: 31645992]
27. Santana M, Feeny D. Framework to assess the effects of using patient-reported outcome measures in chronic care management. Qual Life Res 2014 Jun 7;23(5):1505-1513. [doi: 10.1007/s11136-013-0596-1] [Medline: 24318085]
28. Greenhalgh J, Gooding K, Gibbons E, Dalkin S, Wright J, Valderas J, et al. How do patient reported outcome measures (PROMs) support clinician-patient communication and patient care? A realist synthesis. J Patient Rep Outcomes 2018 Dec;2:42 [FREE Full text] [doi: 10.1186/s41687-018-0061-6] [Medline: 30294712]
29. Skovlund SE, Troelsen LH, Nørgaard LM, Pietraszek A, Jakobsen PE, Ejskjaer N. Feasibility and Acceptability of a Digital Patient Reported Outcomes (PRO) Tool in Routine Outpatient Diabetes Care: A Mixed-Method Formative Pilot Study. JMIR Form Res (Forthcoming) . [doi: 10.2196/28329]

30. Baumeister H, Nowoczin L, Lin J, Seifferth H, Seufert J, Laubner K, et al. Impact of an acceptance facilitating intervention on diabetes patients' acceptance of internet-based interventions for depression: a randomized controlled trial. Diabetes Res Clin Pract 2014 Jul;105(1):30-39. [doi: 10.1016/j.diabres.2014.04.031] [Medline: 24862240]
31. Harris J, Haltbakk J, Dunning T, Austrheim G, Kirkevold M, Johnson M, et al. How patient and community involvement in diabetes research influences health outcomes: a realist review. Health Expect 2019 Oct;22(5):907-920 [FREE Full text] [doi: 10.1111/hex.12935] [Medline: 31286639]
32. Lloyd N, Kenny A, Hyett N. Evaluating health service outcomes of public involvement in health service design in high-income countries: a systematic review. BMC Health Serv Res 2021 Apr 20;21(1):364 [FREE Full text] [doi: 10.1186/s12913-021-06319-1] [Medline: 33879149]
33. Skovlund PC, Ravn S, Seibaek L, Thaysen HV, Lomborg K, Nielsen BK. The development of PROmunication: a training-tool for clinicians using patient-reported outcomes to promote patient-centred communication in clinical cancer settings. J Patient Rep Outcomes 2020 Feb 11;4(1):10 [FREE Full text] [doi: 10.1186/s41687-020-0174-6] [Medline: 32048085]
34. Mejdahl CT, Schougaard LM, Hjollund NH, Riiskjær E, Lomborg K. Patient-reported outcome measures in the interaction between patient and clinician - a multi-perspective qualitative study. J Patient Rep Outcomes 2020 Jan 09;4(1):3 [FREE Full text] [doi: 10.1186/s41687-019-0170-x] [Medline: 31919602]
35. Haugstvedt A, Hernar I, Graue M, Strandberg RB, Lie SS, Sigurdardottir AK, et al. Nurses' and physicians' experiences with diabetes consultations and the use of dialogue tools in the DiaPROM pilot trial: a qualitative study. Diabet Med 2021 Jun 20;38(6):e14419. [doi: 10.1111/dme.14419] [Medline: 33035378]
36. Valderas JM, Kotzeva A, Espallargues M, Guyatt G, Ferrans CE, Halyard MY, et al. The impact of measuring patient-reported outcomes in clinical practice: a systematic review of the literature. Qual Life Res 2008 Mar 4;17(2):179-193. [doi: 10.1007/s11136-007-9295-0] [Medline: 18175207]
37. Dickinson JK, Guzman SJ, Maryniuk MD, O'Brian CA, Kadohiro JK, Jackson RA, et al. The use of language in diabetes care and education. Diabetes Educ 2017 Dec;43(6):551-564. [doi: 10.1177/0145721717735535] [Medline: 29040034]
38. Speight J, Conn J, Dunning T, Skinner T, Diabetes Australia. Diabetes Australia position statement. A new language for diabetes: improving communications with and about people with diabetes. Diabetes Res Clin Pract 2012 Sep;97(3):425-431. [doi: 10.1016/j.diabres.2012.03.015] [Medline: 22513346]
39. Bootle S, Skovlund SE, editorial group of the 5th DAWN International Summit. Proceedings of the 5th International DAWN Summit 2014: Acting together to make person-centred diabetes care a reality. Diabetes Res Clin Pract 2015 Jul;109(1):6-18 [FREE Full text] [doi: 10.1016/j.diabres.2015.04.004] [Medline: 25979275]
40. Kwan BM, McGinnes HL, Ory MG, Estabrooks PA, Waxmonsky JA, Glasgow RE. RE-AIM in the real world: Use of the RE-AIM framework for program planning and evaluation in clinical and community settings. Front Public Health 2019 Nov 22;7:345 [FREE Full text] [doi: 10.3389/fpubh.2019.00345] [Medline: 31824911]
41. Kayser L, Karnoe A, Duminski E, Somekh D, Vera-Muñoz C. A new understanding of health related empowerment in the context of an active and healthy ageing. BMC Health Serv Res 2019 Apr 24;19(1):242 [FREE Full text] [doi: 10.1186/s12913-019-4082-5] [Medline: 31014350]
42. McGuire BE, Morrison TG, Hermanns N, Skovlund S, Eldrup E, Gagliardino J, et al. Short-form measures of diabetes-related emotional distress: the Problem Areas in Diabetes Scale (PAID)-5 and PAID-1. Diabetologia 2010 Jan 20;53(1):66-69. [doi: 10.1007/s00125-009-1559-5] [Medline: 19841892]
43. Young-Hyman D, de Groot M, Hill-Briggs F, Gonzalez JS, Hood K, Peyrot M. Psychosocial care for people with diabetes: a position statement of the American Diabetes Association. Diabetes Care 2016 Dec 22;39(12):2126-2140 [FREE Full text] [doi: 10.2337/dc16-2053] [Medline: 27879358]
44. Wozniak L, Rees S, Soprovich A, Al SF, Johnson ST, Majumdar SR, et al. Applying the RE-AIM framework to the Alberta's Caring for Diabetes Project: a protocol for a comprehensive evaluation of primary care quality improvement interventions. BMJ Open 2012;2(5):e002099 [FREE Full text] [doi: 10.1136/bmjopen-2012-002099] [Medline: 23103609]
45. Glasgow RE, Nelson CC, Strycker LA, King DK. Using RE-AIM metrics to evaluate diabetes self-management support interventions. Am J Prev Med 2006 Jan;30(1):67-73. [doi: 10.1016/j.amepre.2005.08.037] [Medline: 16414426]
46. Stetler CB, Legro MW, Wallace CM, Bowman C, Guihan M, Hagedorn H, et al. The role of formative evaluation in implementation research and the QUERI experience. J Gen Intern Med 2006 Feb;21(S2):1-8. [doi: 10.1111/j.1525-1497.2006.00355.x] [Medline: 16637954]
47. Brown CA, Lilford RJ. The stepped wedge trial design: a systematic review. BMC Med Res Methodol 2006 Nov 08;6(1):54 [FREE Full text] [doi: 10.1186/1471-2288-6-54] [Medline: 17092344]
48. Skovlund SE, Nørgaard LM, Stefansen S, De Lichtenberg TH, Troelsen L, Pietraszek A, et al. 839-P: Outcomes of systematic user involvement and user research in a national patient-reported outcomes diabetes initiative. Diabetes 2019 Jun 04;68(Supplement 1):839-P. [doi: 10.2337/db19-839-p]
49. Skovlund SE, Nørgaard L, Stefansen S, De Lichtenberg TH, Troelsen L, Pietraszek A, et al. 1267-P: Psychometric development of a multidimensional patient-reported outcomes questionnaire and clinical dialogue platform for routine diabetes care. Diabetes 2019 Jun 04;68(Supplement 1):1267-P. [doi: 10.2337/db19-1267-p]
50. Bandura A. Social cognitive theory: an agentic perspective. Annu Rev Psychol 2001 Feb;52:1-26. [doi: 10.1146/annurev.psych.52.1.1] [Medline: 11148297]

51. Williams GC, Freedman ZR, Deci EL. Perceived competence scales. Diabetes Care 1998;21(10):1644-1651 [FREE Full text]
52. Rossi MC, Lucisano G, Funnell M, Pintaudi B, Bulotta A, Gentile S, BENCH-D Study Group. Interplay among patient empowerment and clinical and person-centered outcomes in type 2 diabetes. The BENCH-D study. Patient Educ Couns 2015 Sep;98(9):1142-1149. [doi: 10.1016/j.pec.2015.05.012] [Medline: 26049679]
53. Stokols D. Translating social ecological theory into guidelines for community health promotion. Am J Health Promot 1996 Aug 26;10(4):282-298. [doi: 10.4278/0890-1171-10.4.282] [Medline: 10159709]
54. de Wit M, Winterdijk P, Aanstoot H, Anderson B, Danne T, Deeb L, DAWN Youth Advisory Board. Assessing diabetes-related quality of life of youth with type 1 diabetes in routine clinical care: the MIND Youth Questionnaire (MY-Q). Pediatr Diabetes 2012 Dec 22;13(8):638-646. [doi: 10.1111/j.1399-5448.2012.00872.x] [Medline: 23173877]
55. Varsi C, Nes LS, Kristjansdottir OB, Kelders SM, Stenberg U, Zangi HA, et al. Implementation strategies to enhance the implementation of ehealth programs for patients with chronic illnesses: realist systematic review. J Med Internet Res 2019 Sep 27;21(9):e14255 [FREE Full text] [doi: 10.2196/14255] [Medline: 31573934]
56. Proctor E, Silmere H, Raghavan R, Hovmand P, Aarons G, Bunger A, et al. Outcomes for implementation research: conceptual distinctions, measurement challenges, and research agenda. Adm Policy Ment Health 2011 Mar 19;38(2):65-76 [FREE Full text] [doi: 10.1007/s10488-010-0319-7] [Medline: 20957426]
57. Brownson CA, Miller D, Crespo R, Neuner S, Thompson J, Wall JC, et al. A quality improvement tool to assess self-management support in primary care. Jt Comm J Qual Patient Saf 2007 Jul;33(7):408-416. [doi: 10.1016/s1553-7250(07)33047-x]
58. King A, Hoppe RB. "Best practice" for patient-centered communication: a narrative review. J Grad Med Educ 2013 Sep;5(3):385-393 [FREE Full text] [doi: 10.4300/JGME-D-13-00072.1] [Medline: 24404300]
59. Nicolucci A, Burns KK, Holt RI, Lucisano G, Skovlund SE, Kokoszka A, et al. Correlates of psychological outcomes in people with diabetes: results from the second Diabetes Attitudes, Wishes and Needs (DAWN2(™) study. Diabet Med 2016 Sep 15;33(9):1194-1203. [doi: 10.1111/dme.13178] [Medline: 27353119]
60. Mokkink LB, Prinsen CA, Bouter LM, Vet HC, Terwee CB. The COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) and how to select an outcome measurement instrument. Braz J Phys Ther 2016 Jan 19;20(2):105-113 [FREE Full text] [doi: 10.1590/bjpt-rbf.2014.0143] [Medline: 26786084]
61. Terwee CB, Prinsen CA, Chiarotto A, Westerman MJ, Patrick DL, Alonso J, et al. COSMIN methodology for evaluating the content validity of patient-reported outcome measures: a Delphi study. Qual Life Res 2018 May 17;27(5):1159-1170 [FREE Full text] [doi: 10.1007/s11136-018-1829-0] [Medline: 29550964]
62. Castleberry A, Nolen A. Thematic analysis of qualitative research data: is it as easy as it sounds? Curr Pharm Teach Learn 2018 Jun;10(6):807-815. [doi: 10.1016/j.cptl.2018.03.019] [Medline: 30025784]
63. Stenberg U, Haaland-Øverby M, Fredriksen K, Westermann KF, Kvisvik T. A scoping review of the literature on benefits and challenges of participating in patient education programs aimed at promoting self-management for people living with chronic illness. Patient Educ Couns 2016 Nov;99(11):1759-1771. [doi: 10.1016/j.pec.2016.07.027] [Medline: 27461944]
64. Forman J, Heisler M, Damschroder LJ, Kaselitz E, Kerr EA. Development and application of the RE-AIM QuEST mixed methods framework for program evaluation. Prev Med Rep 2017 Jun;6:322-328 [FREE Full text] [doi: 10.1016/j.pmedr.2017.04.002] [Medline: 28451518]
65. de Visser RO, Graber R, Hart A, Abraham C, Scanlon T, Watten P, et al. Using qualitative methods within a mixed-methods approach to developing and evaluating interventions to address harmful alcohol use among young people. Health Psychol 2015 Apr;34(4):349-360. [doi: 10.1037/hea0000163] [Medline: 25822051]
66. Tariq S, Woodman J. Using mixed methods in health research. JRSM Short Rep 2013 Jun;4(6):2042533313479197 [FREE Full text] [doi: 10.1177/2042533313479197] [Medline: 23885291]
67. Stuckey HL, Mullan-Jensen CB, Reach G, Burns KK, Piana N, Vallis M, et al. Personal accounts of the negative and adaptive psychosocial experiences of people with diabetes in the second Diabetes Attitudes, Wishes and Needs (DAWN2) study. Diabetes Care 2014 Sep 27;37(9):2466-2474. [doi: 10.2337/dc13-2536] [Medline: 24973437]
68. Stuckey H, Peyrot M. Living with diabetes: literature review and secondary analysis of qualitative data. Diabet Med 2020 Mar 26;37(3):493-503. [doi: 10.1111/dme.14255] [Medline: 31984543]
69. ICMJE. Recommendations for the conduct, reporting, editing, and publication of scholarly work in medical journals. Chin Nurs Res 2015 Dec;2(4):I-XIII. [doi: 10.1016/j.cnre.2016.01.001]
70. Fenwick EK, Rees G, Holmes-Truscott E, Browne JL, Pouwer F, Speight J. What is the best measure for assessing diabetes distress? A comparison of the Problem Areas in Diabetes and Diabetes Distress Scale: results from Diabetes MILES-Australia. J Health Psychol 2018 Apr 22;23(5):667-680. [doi: 10.1177/1359105316642006] [Medline: 27106085]
71. Dennick K, Sturt J, Speight J. What is diabetes distress and how can we measure it? A narrative review and conceptual model. J Diabetes Complications 2017 May;31(5):898-911. [doi: 10.1016/j.jdiacomp.2016.12.018] [Medline: 28274681]
72. Palamenghi L, Carlucci MM, Graffigna G. Measuring the quality of life in diabetic patients: a scoping review. J Diabetes Res 2020 May 22;2020:5419298 [FREE Full text] [doi: 10.1155/2020/5419298] [Medline: 32566680]

Abbreviations

HCP: health care professional
M-PRODIA: multicenter patient-reported outcome diabetes study
PRO: patient-reported outcome
RE-AIM: Reach, Efficacy, Adoption, Implementation and Maintenance
VBHC-PRO-DIA: Value Based Health Care and PRO in Diabetes Project

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Protocol

Using Gaze Tracking as a Research Tool in the Deaf Health Literacy and Access to Health Information Project: Protocol for a Multisite Mixed Methods Study and Preliminary Results

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Abstract

Background: Previous studies have identified the internet as a major source of health information. Reliable and accessible sources of web-based health information are critical for cultivating patient-centered care. However, the accessibility and use of web-based health information remains largely unknown for deaf individuals. We used gaze-tracking technology to understand the navigation and use of web-based health information by deaf adults who communicate with sign language and by hearing adults.

Objective: This paper discusses our protocol for implementing gaze-tracking technology in a study that included both deaf and hearing participants. We report the preliminary results and lessons learned from the implementation of the protocol.

Methods: We conducted gaze-tracking sessions with 450 deaf signers and 450 hearing participants as a part of a larger, multisite mixed methods research study. Then, we conducted qualitative elicitation interviews with a subsample of 21 deaf and 13 hearing participants, who engaged in a search task and reviewed their gaze recordings. To our knowledge, no study has implemented a similar research protocol to better understand the experiences of deaf adults. As such, we also examined research staff notes and observations from team meetings regarding the conduct of gaze-tracking data to delineate lessons learned and best practices for research protocols in this area.

Results: Findings from the implementation of this study protocol highlight the use of gaze technology with deaf participants. We developed additional protocol steps to minimize gaze disruption from either lipreading or communicating in sign language. For example, research assistants were often unable to maintain eye contact with participants while signing because of the need to simultaneously point at the computer monitor to provide instructions related to gaze study components, such as the calibration process. In addition to developing ways to effectively provide instructions in American Sign Language, a practice exercise was included in the gaze tracker session to familiarize participants with the computer and technology. The use of the playback feature permitted a deeper dialogue between researchers and participants, which we found vital for understanding the experiences of deaf participants.

Conclusions: On the basis of our experience using the study protocol through a large research project, incorporating gaze-tracking technology offers beneficial avenues for better understanding how individuals interact with health information. Gaze tracking can determine the type and placement of visual content that attracts attention from the viewers of diverse backgrounds, including deaf individuals. The lessons learned through this study will help future researchers in determining ideal study designs, such as suitable protocols and participant characteristics (eg, deaf signers), while including gaze trackers in their projects. This approach

explored how different ways of presenting health information can affect or enable visual learners to engage and use health information effectively.

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KEYWORDS

gaze tracking; deaf; disabilities; accessibility; online health information; health information seeking; mobile phone

Introduction

Background

Between 40% and 60% of adults in the United States report regularly engaging in an internet search for information about a health topic [1,2]. Recent data from Google Health suggest that 7% of daily searches on the engine are for health topics [3]. The internet remains the most accessed source of health information, beyond health care professionals, traditional media, friends, and family [1]. This is to be expected, as changes within the health care system, including patient-centered care, require that individuals become more actively involved in their own health, including pursuing and managing information [4,5]. Adults are expected to take charge of their health decisions. Similarly, the development of health information technology (HIT), such as electronic health care records, patient portals, health apps for smartphones, and wearable technology, adds to the ways adults can directly monitor their health and participate as engaged communicators and consumers of health care.

Although these advancements can improve health outcomes for some, research suggests that they exacerbate health disparities for many, including those with disabilities [6-11]. The COVID-19 pandemic again exposed these inequities as it "ushered in a new era of telehealth" [11]. This has resulted in an increased need for medical visits provided through virtual options [11,12] and the dissemination of information through web-based sources [13]. During the rapidly evolving health crisis, those with disabilities were left behind, with critical health information often not made available in other languages or access options [14,15]. For example, the White House did not include American Sign Language (ASL) interpreters at their COVID-19 press briefings [14]. Telehealth options remained mostly inaccessible to those with disabilities or without reliable internet access [11]. Hence, a health *infodemic* was born, in which health information available on the internet often contained incorrect or outdated recommendations [13,16]. These injustices are likely to persist without more research and consideration of how web-based health information and HIT are developed [11].

Goldberg et al [17] argue, "missing from the national efforts toward pervasive ability for HIT for adults, families, doctors, and health care facilities is a programmatic and policy-based effort to ensure that people with disabilities (PWD) are able to participate equally in all the opportunities that new Health 2.0 networks and tools have to offer...". Indeed, health information websites have historically been found to be inconsistent in the extent to which accessibility requirements were met, which affects who can use this content and how they use it [18]. Unfortunately, this is a vicious cycle as a majority of the existing research on web-based health information seeking has been conducted with adults without disabilities, which severely limits the understanding of how people with disabilities access this content and opportunities for improvement. More work is needed to understand people with disabilities' access to and experience with web-based information.

Deaf Adults and Health Information on the Web

The national estimates suggest that nearly one million Americans are deaf signers [19]. The internet is a primary source of health information for this audience and played an important role for deaf adults during the pandemic [20]. Greater attention in improving the accessibility and user experience of health information on the internet is especially imperative for deaf adults, for whom there is relatively little available research [6,21]. Specific calls have been made to software developers and designers to improve the accessibility of web-based health information and technologies [11]. Deaf individuals encounter significant communication barriers, resulting in lower patient-provider satisfaction, adherence, inappropriate health care utilization, and decreased engagement in health-related decision-making [21,22]. As a result, deaf individuals are almost seven times more likely to have less than adequate health literacy. To help with the low availability of health knowledge (defined as limitation in one's factual knowledge base as compared with the general population) due to inaccessible information and loss of incidental learning opportunities [23], deaf adults must then turn to community peer exchanges, print media, family and friends, and the internet to obtain health information [24].

One study demonstrated that 79% of deaf individuals use the internet daily and are almost three times more likely to search the internet for health information than their hearing peers [25]. However, deaf adults may find navigating the internet to be a challenging task [26]. Some deaf individuals display competency in navigating visual targets but struggle with categorical decision-making (often based on semantics rather than visual cues) to make a more refined search, such as navigating through a series of pages to reach information that exists deep within a website [27]. Most web-based health information requires more categorical decision-making because of the level of semantics and textual-based graphics.

Although it is known that deaf adults access the internet at higher rates to retrieve health information and guidance [25], the navigation, barriers, and specifics of these searches are underresearched. Exploring these actions can shed light on the objective ways this community engages in web-based health information seeking. Karras and Rintamaki [6] describe the

potential for the internet to serve as a "double-edged sword in that it provides boons and challenges for deaf people." It is important to devote greater research attention on how deaf adults access and use health information on the internet [6], including the steps taken, assessments of content credibility, and accessibility of this information for various audiences. Specific consideration should be devoted to deaf adults so that health disparities among these populations can be reduced.

Objectives

The purpose of this paper is to introduce a research methodology, the use of gaze tracking and visualization, to gain new insights into this specific population. Gaze-tracking technology affords numerous research opportunities and can be implemented with participants of all ages and many different backgrounds but has not been widely implemented in people with different types of disabilities. For health communication researchers, gaze-tracking data can contribute to naturalistic, objective findings about information seeking and engagement that cannot be assessed in other ways. Although there are numerous benefits to this useful tool, there are a number of best practices and recommendations that researchers should consider before choosing to embark on this endeavor. We outline the preliminary results observed while implementing this protocol in the context of a larger study.

Researchers interested in the extent and ways in which deaf adults engage with health information can benefit from studying these adults' eye behaviors. A great deal of health information is visual in nature. This includes pamphlets, web-based content, videos, infographics, recommendations and guidelines, health procedure prep instructions, handwritten notes, drawings, graphs, and countless other forms. The exploration of how deaf adults direct their visual attention is essential for the work of health communication scholars, as it can help us understand what draws adults to specific information and thus guide best practices for designing health content that is engaging and accessible for adults of different backgrounds. In addition, design quality and visual design assessments have been shown to affect the perceived credibility of health content as well as influence attitudes and comprehension [28,29].

In the remainder of this paper, we provide an overview of gaze-tracking technology and how we implemented this protocol in a large-scale, multisite mixed methods research study involving both deaf and hearing participants. The goal of the gaze-tracking component was to better understand deaf participants' search and information scanning behaviors in response to examples of internet health information websites. Finally, recommendations for using this methodology are outlined, based on the preliminary results.

Methods

Overview of Gaze Tracking

Humans are not physically equipped to attend to all possible visual stimuli; thus, we engage in selective attention to conserve cognitive resources. When adults perform searches, scan, read, or extract details about health topics, they are engaged in selective visual attention—deciding where to spend time looking and processing information. Studying eye movements and visual attention sheds light on the "what" and "where" conditions under which stimuli gain attention [30]. Humans move objects of interest into a visible field so that they may examine them further. This results in a gaze path that reflects different points of visual attention exhibited by a viewer [30].

A gaze-tracking system is a type of technology that measures a participant's eye movements in response to a visual stimulus. As a methodology, gaze tracking offers quantitative data regarding how long a participant spends looking at a given stimulus as well as the specific aspects that gain the most attention. Previous reports suggest that pairing patient-reported survey data with gaze tracking and qualitative responses, or "methodological triangulation," can offer deeper interpretations of this behavior [31].

Gaze tracking is one of only a limited set of objective assessments that capture attention in a naturalistic setting and is perhaps the leader in affordability, practicality of use, and the ease of data interpretation [31,32]. Visual attention can also be captured using brain imaging techniques such as functional magnetic resonance imaging [33,34], but this methodology warrants steeper learning curves and higher costs for the user.

Gaze tracking is a true-to-life research methodology that can capture the eye movements and patterns in everyday life with minimal intrusion. Understanding real-time, naturalistic searching and reading is essential for building content for adults—this starts with understanding what they are already doing, rather than guessing and building ineffective interventions.

Study Design and Participants

A large, multisite, explanatory sequential mixed methods study was conducted with deaf and hearing participants at three locations [26]. The participants self-identified their hearing status and the languages they use. All study materials were provided to deaf participants in ASL. As such, we recruited only deaf signers.

The overall study aimed to address the factors influencing health literacy in each of these two groups. The goal of the gaze-tracking component of the study was to assess and understand participants' search and information scanning behaviors in response to examples of health information websites. Given the limited research in this area, we aimed to outline these factors using quantitative gaze tracking and survey assessments in the first phase of the study and then explore them in greater depth using qualitative methods in the second phase of the study. Thus, the mixed methods design allowed us to examine not just *what* participants looked at on the internet and the factors that influenced this search (phase 1) but also *how* they found this information and *why* they pursued specific content (phase 2). This was designed based on previous work by a mixed methodologist on the team [35-38] and was an appropriate fit for the goals of the project. Through this National Institutes of Health–funded grant, we were able to explore the capabilities and limitations of gaze-tracking research in the context of how deaf and hearing adults find, use, and understand health information on the internet.

In the first phase of the study, a series of quantitative cross-sectional survey items and tasks were implemented among 450 deaf and 450 hearing participants to identify the predictors and moderators of health literacy between these groups. We integrated a gaze-tracking component into this phase of a larger study. In this experimental aspect of the study, participants viewed the US Centers for Disease Control and Prevention (CDC) webpages of four health conditions and answered questions about the page. The development of these stimuli and procedures are described in greater detail in the *Developing Study Stimuli* section. Participants viewed the CDC webpages on a laptop to simulate what they might do if they were looking for health information on the internet in their everyday lives.

Through this first phase of the study, we assessed the predictors for adequate health literacy and the ability to use web-based health information and found several key variables, such as age, race and ethnicity, language fluency, and reading literacy. A diverse set of participants with these backgrounds stratified by health literacy adequacy were invited back for the second phase, which incorporated a task performance and an elicitation interview.

In the second phase, this sample of participants, selected using the quantitative data obtained in the first phase, was asked to perform a search task and review their gaze-tracking results through the technology's playback feature and engage in elicitation interviews in response to these results. This qualitative component was guided by previous research and study design that implemented video elicitation interviews [36,37]. This second phase provided greater clarity on how and why deaf individuals access and understand web-based health information, as it explored both the "complex cognitive or decision-making processes and participants' reactions to or assessments of their own actions" while accessing web-based health information [36].

Equipment Used

We implemented the Tobii Pro X3 system for this project. This gaze-tracking system is easy to use and highly mobile given its small size (approximately 7 inches in length). The multisite nature of this project enabled the research team to store, pack, and move the system with ease. To set up the system for data collection, the bar-shaped tracker was clipped to a computer monitor using a strong magnet. As such, the tracker could be easily reattached to other screens and computers with the addition of a magnet to each new screen. The X3 is designed to capture gaze data on laptop and computer monitor screens [39]. We selected the 120 Hz version as we were interested in examining participants' scanning of several visual areas of interest (AOIs) and the nuanced attention on specific words on the screen. This model has since been discontinued by Tobii, but a similar model, the Tobii Pro Fusion, is comparable.

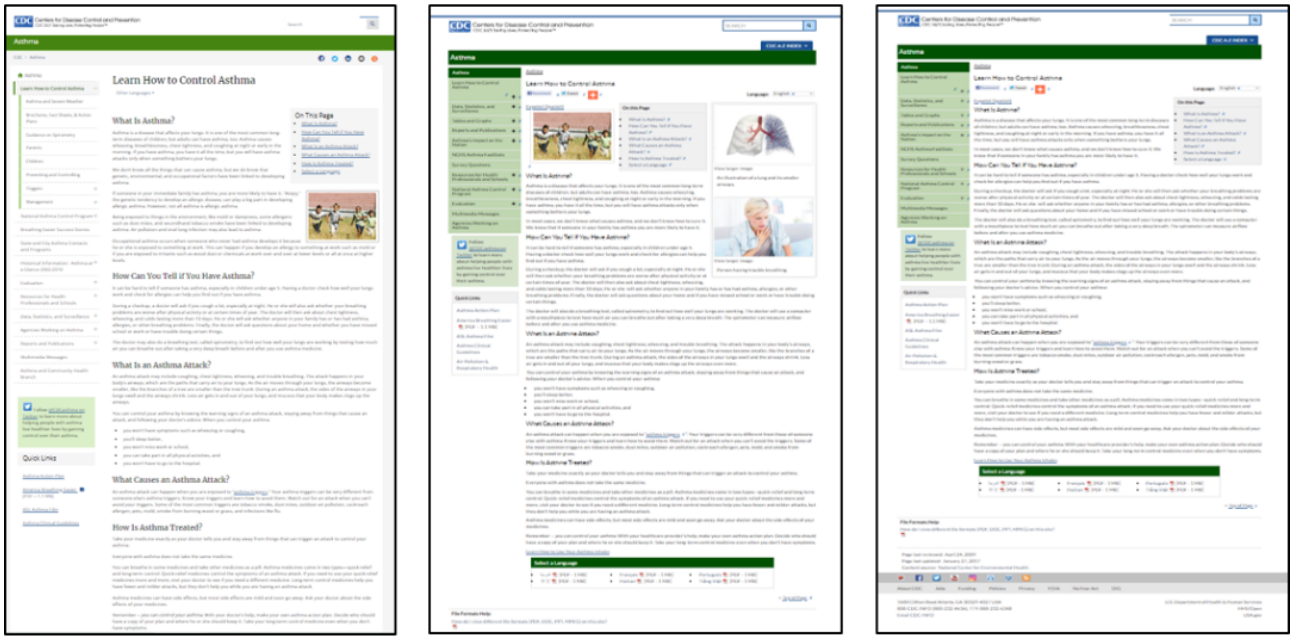
Developing Study Stimuli

The Tobii X3 system can accommodate many forms of media, including real-time website browsing, static images (such as nutrition or medicine labels, consent forms, decision aids, and messages), videos, surveys, and other components. We implemented a *web element* and *questionnaire* elements for this study. Furthermore, we created multiple sessions or *conditions* through which participants viewed content for comparison.

One aim of the study was to explore the types of content on a health website that would gain attention from deaf and hearing participants from varied personal backgrounds. We found that using a *live* webpage (directly linked to a CDC webpage) would not suffice, as content could be changed or updated by the page owner on the site at any time. If the page owners changed the content during the span of data collection, this would introduce unwanted variability in our visual stimuli. Furthermore, using *live* content on the internet would lend authenticity and generalizability to the study; however, it would not allow us to manipulate the conditions. We included four health conditions, selected through pilot testing. Two were commonly known topics (asthma and sinusitis) and two were lesser known (Sjogren syndrome and staphylococcal food poisoning). We were also interested in how deaf and hearing adults would peruse and evaluate visual content. Each health condition also featured a version of the page with and without pictures (Figure 1).

We created static website images or *screenshots* for use within the study. We created PDF pages that mimicked the real content seen on the CDC website but were still able to manipulate the content as needed. Following this, we created links to each page on our lab server. Creating these links, and having the images available on the internet, allowed the use of the web element within the Tobii Studio software, which recorded the participant's gaze pattern as they scrolled down a page, just as they would with a live website. Participants viewed the page content and answered questions based on what they read.

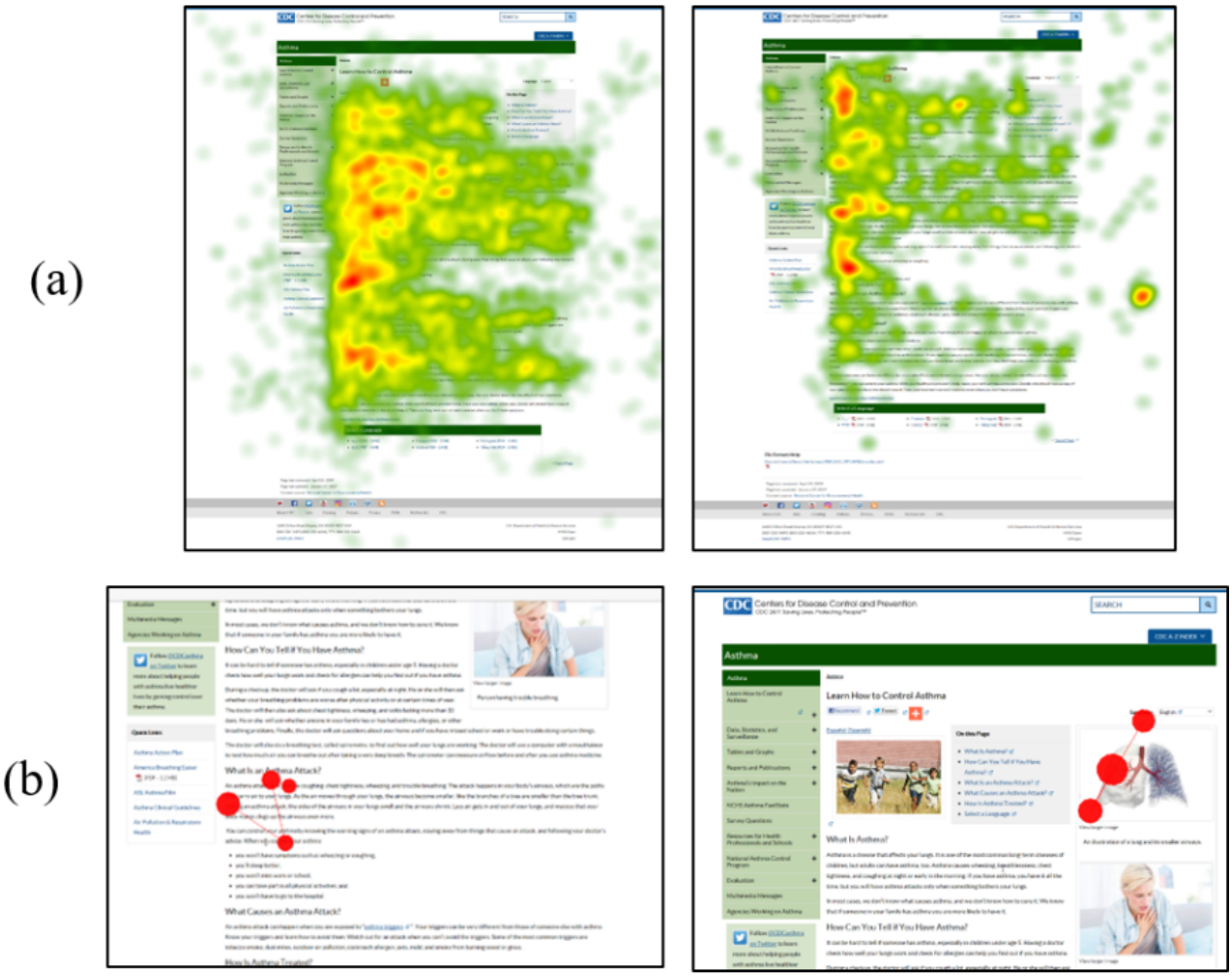
Figure 1. Sample stimuli from left to right: (1) actual Centers for Disease Control and Prevention webpage, (2) experimental study stimuli with pictures, (3) experimental study stimuli without pictures.



Measures

To capture attention, gaze trackers record a participant's eye movements using built-in sensors and cameras. In many models, near-infrared light is projected from the gaze tracker onto a participant's pupils [40]. The length of time a participant spends on a given stimulus (a variable referred to as *fixation duration*, reflected in seconds), the number of times a participant returns to the stimulus (*fixation count*, reflected in counts or hits), and the gaze path a participant performs while scanning the visual information are calculated in response to the ways in which the near-infrared light reflects off the pupil. These three variables (fixation duration, fixation count, and eye gaze paths) are common measures exported from a gaze-tracking system and were used in this study to reflect attention given to the various areas of the webpage. The first two variables capture the quantitative assessments of visual attention, whereas the gaze paths are presented in high-quality visualization images, such as heat maps and gaze diagrams (Figure 2), which allow for other forms of data analysis.

Figure 2. Examples of heat maps and gaze diagrams collected in this study: (a) Example heat map: group of low health literacy hearing participants (left), group of low health literacy deaf participants (right)—the gradient of colors (green to red) indicate the density of visual attention (low to high, respectively); (b) Example gaze plot of asthma survey component.

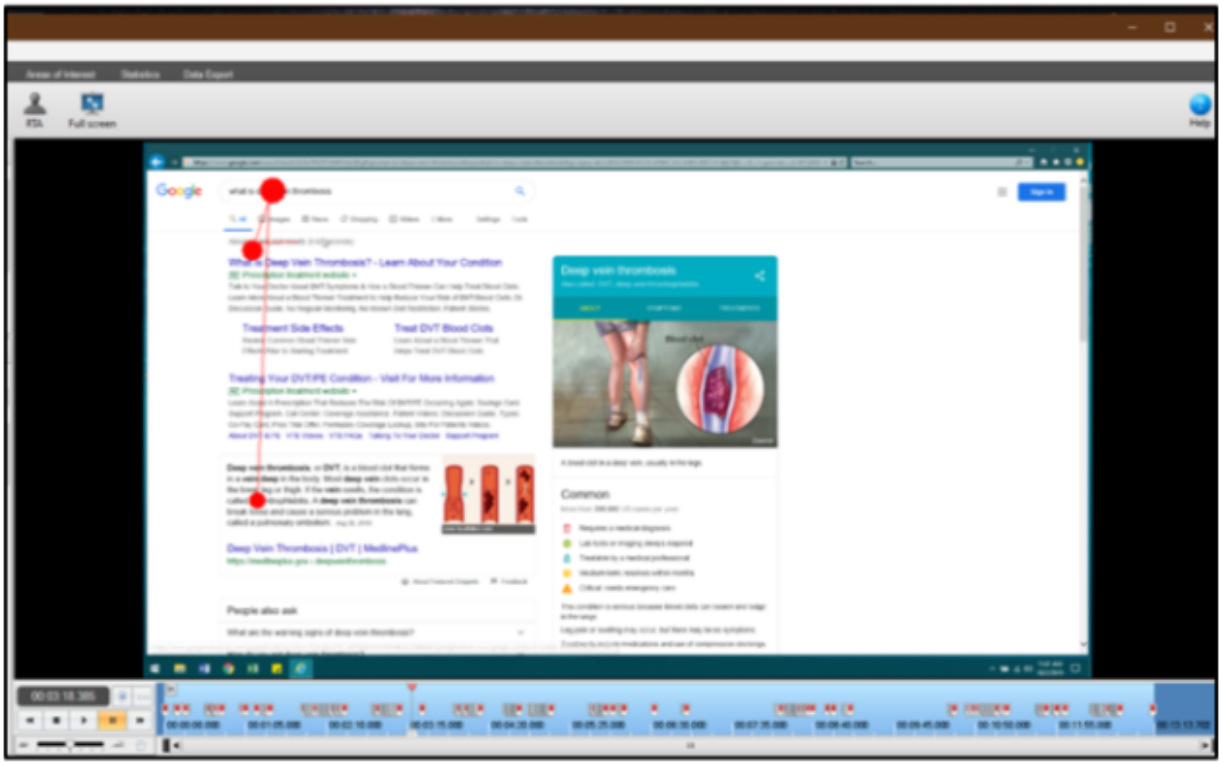


Moreover, we used the Tobii AOI tool to create visual *areas* by drawing boxes or shapes around specific visual content of focus (Figure 3). In our study, we were interested in how much visual attention was garnered by pictures included on a given website page. Using the AOI tool, we drew a box around the picture to create a visual area. The Tobii Studio software provides the aforementioned information (eg, fixation duration) for the AOI, in this case, a picture. AOIs can be created for any visual element on a page, such as headlines, click buttons, captions, and infographics.

Figure 3. Example Area of Interest tool.

For the qualitative elicitation interviews in phase 2 of the study, we implemented the playback video tool to review and discuss gaze-tracking recordings with the participant (Figure 4). After a gaze-tracking session, Tobii provides an opportunity to immediately view a recording of the participants' gaze as they scan various stimuli. After completing the first phase of the study, we invited several participants back to peruse additional health information in a separate free search task (in which the participant was provided with a vignette and asked to find information on their own about the health topic, using any web-based searching methods and terms) and discuss how they made decisions to search and look at specific information.

Figure 4. Example video replay. The participant searches for information about deep vein thrombosis.



Recruitment and Screening

The recruitment and screening guidelines were essential components of this study. Importantly, we asked participants about their vision. During recruitment, we asked if participants had any visual impairments. If so, they were then asked whether they were able to see a computer screen easily. Participants indicated whether they wore eyeglasses, contacts, no glasses, had vision limitations, or were color blind. To avoid data collection or scheduling issues when participants forgot to bring their glasses, our research team was also equipped with a tray providing multiple reading glasses ranging from a +1.25 to +2.0 power in +0.25 power increments. Tobii [41] advises that glasses-wearing participants clean their eyewear before the study. As a result, glass cleaners and cloths were offered during the study session.

Session Setup

Overview

In phase 1, the gaze-tracking component of this project was included in a battery of other tests included in the larger study. When it was their turn to complete the gaze-tracking task, the participant was asked to sit down in front of the laptop. Specifically, we selected a chair for participants that does not swivel and was both easy and comfortable to sit in, as participants may fidget or move in the chair, which can disrupt the collection of gaze data. The research assistant then performed the following phases.

Calibration

First, a research assistant performed a brief calibration process using the gaze-tracking software. Achieving an accurate calibration is important for data analysis, as this process will connect a participant's gaze path with the corresponding content appearing on the screen. The calibration process involved watching a dot scan across the screen to different corners of the computer screen. Following this, the participant observed the visual stimuli on the screen as they would normally. As many of the participants had not participated in a gaze-tracking study before, it was essential that detailed explanations and instructions were given before beginning a session.

Research assistants provided instructions and explanations for what to expect regarding the calibration process. Researchers explained the importance of sitting in one spot for the study and remaining on the angle of the monitor (to the best of their ability) due to the tracking devices needed to retrieve the data. In addition, assistants discussed resisting the urge to break visual connections with the computer monitor, as this could lose the gaze data.

Acquainting Participants With Gaze Tracking

During our pilot phase, we found that the calibration and initial steps in the gaze-tracking session were cumbersome for deaf participants because they had to look back and forth between the monitor and the research assistant to receive instructions in ASL. We were concerned that participants would still be getting a feel for the study and its procedures well into the first health topic test session. As such, we added a practice health topic that mirrored the format of the other topics, but it was not used for data collection purposes. In this case, we used a screenshot of the CDC's website about influenza (flu). In this practice session, participants read questions, viewed the page, and answered questions. This practice session helped put participants' minds at ease as they got a feel of the study procedures. Participants could ask questions if anything was unclear. The intention of this test was to get participants who liked to make eye contact or lacked computer skills to become well oriented with the gaze-tracking session. We also explained how gaze trackers work and asked them to focus on the computer screen until their task was completed. This helped in reducing the proportion of gaze tracker failures due to breaks in gazes.

Once participants completed the practice session and felt comfortable with the gaze tracker, we asked them to proceed with the four CDC health condition webpages. Participants were randomized to view these four conditions with or without relevant pictures or graphics included alongside the text. Each participant saw one of four versions of the study, each of which presented the health topics in a different order. Participants were asked questions about each of the illnesses, then viewed a website screenshot of the corresponding CDC page, and subsequently asked to again answer the questions they saw before viewing the web content.

Qualitative Elicitation Interviews

To gain a more in-depth understanding of the typical search and navigational abilities of our participants, a subsample of deaf and hearing participants with different levels of health literacy and other quantitative variables observed in phase 1 were invited back to participate in a second gaze-tracking session. Four brief clinical vignettes (ie, pneumonia, deep vein thrombosis, migraines, and appendicitis) with multiple-choice answers were provided to all participants as a way to prompt web-based searches. These vignette topics were selected through pilot testing and were chosen to avoid recall bias. The recording of the participants' web-based activities was then reviewed together with the research assistant and used as a part of an elicitation interview to elucidate how and why deaf and hearing individuals access and understand different types of health information. The captured data from the gaze tracker allowed the interviewer to ask more detailed questions on how and why such an action was chosen and the participant's thought process related to the web-based information. Similar to what was done in phase one, an influenza topic was used as a practice exercise to help participants become familiarized with the gaze tracker.

Results

Overview

Gaze-tracking technology provides an objective assessment of the visual content that draws attention from viewers of diverse backgrounds. We found that this type of data collection is especially useful while determining the barriers and challenges deaf adults have with health information on the internet and how it is presented. The gaze tracker recordings and their ability to play back or tag certain time points are useful for conducting elicitation or cognitive interviews or usability testing. It is important to note that we observed a learning curve while using this technology with deaf participants, namely, the importance

of explaining to participants what they could expect during the session and what they were being asked to do. We also learned about the limitations gaze-tracking systems and projects have with large numbers of participants, including large file sizes. We will now describe preliminary findings related to our research protocol.

Recruitment and Screening

Overall, we had high rates of participants who wore glasses. Having this information before the start of the study—and reminding participants that they will be reading information on a computer screen—is an important point for those who may use reading glasses. This will also help researchers understand what to expect before the participant arrives for the session. The Tobii gaze-tracking system has a "unique tolerance for eyewear" as compared with other systems and thus may be more conducive for use among participants with vision-related disabilities. Tobii [41] advises that glasses-wearing participants clean their eyewear before the study. Despite this, our research teams had difficulty in attaining successful calibration and gaze-tracking sessions with some glasses-wearing participants, particularly those who wore bifocals or progressives. For those with difficult calibration sessions due to their bifocal or progressive glasses, we encouraged participants to choose from our reading glasses of varying strengths to minimize this issue.

On the basis of our experience with this project, we would also include additional screening questions in future gaze-tracking projects, such as whether the participant can use a mouse with the computer and conduct a visual acuity and field screen to measure their visual abilities.

Session Setup

Calibration

This was difficult for deaf participants who were simultaneously watching the research assistant explain the process using ASL. The research assistant would, at times, need to break eye contact with the participant. This was difficult to manage, as the research assistants would ideally be able to maintain eye contact with participants to facilitate the provision of instruction. While working with deaf participants, the researchers would point at the calibration dot and provide time for the participant to see where they were pointing and then pause for them to look at the signer. Through our experience with calibration, it would also be helpful to change the calibration dot to another color (eg, blue or purple), which is typically red by default and not easily detected, especially by those who have red-green colorblindness. This is a possibility in the Tobii Studio software program by navigating to *Calibration* tab under *Global Settings*. Finally, through our experience, it can be difficult to obtain gaze data with participants who do not read content straight on but prefer to read at an angle.

It is also important to note that the research team experienced some challenges regarding the distance from the participants' eyes to the gaze tracker. There were instances in which researchers struggled with the seating angle of the participant to ensure that the visual distance was appropriate before testing. This was especially common among participants who were exceptionally short or tall. It can be helpful to have a practice text document open on the desktop of the computer to give participants an example of the text size included in the study materials. The participant may want to wear reading glasses or adjust how close they are to the screen. These adjustments should be made before starting the study session.

Session Duration and Complexity

Our project asked participants to complete a heavy amount of reading if they chose to read the entirety of the articles presented, which could be tiring for participants. For example, the page on asthma contained 725 words. In the case of our study, we wanted the gaze-tracking content to mimic a true, live webpage and thus chose to mirror our content, including its length, to that provided by the CDC. Likewise, the time of day can potentially play a role in the willingness or capability of a participant to engage with more content. Controlling for the time of day in which study sessions are scheduled (or counterbalancing through random assignment) can contribute to more accurate reflections of attention devoted to the study content.

During the qualitative elicitation interviews, upon completion of the clinical vignettes, participants were encouraged to take a short break of approximately 15 minutes. This break period allowed the research assistant to review the Tobii recording of the activity and video tag key times to use as prompts for the elicitation interviews. This step complemented the assistant's field observation notes in preparation for the 1:1 elicitation interview with the participant. When the participant returned from the short break, the assistant and participant reviewed their Tobii recording together. The recording would then be used to learn about the participant's thought processes during search queries, viewing patterns, and selection of websites.

However, because of participants' need for periodic breaks in gaze connections to read the clinical vignette-based questions, several options were explored to minimize this. Once the Tobii project is started, it does not allow for switching back and forth to different media displays (eg, Internet Explorer to Word document listing the questions). This forced us to print out the questions. Clipping them up next to the computer versus laying in front of the computer did not appear to make much difference in terms of visual breaks and loss of gaze tracking. Our piloting phase revealed that short intermittent visual breaks are permissible with Tobii gaze trackers as long as the breaks are not lengthy. However, actual testing, especially among those with lower literacy levels, required longer visual breaks than expected. These visual breaks would accumulate over a period of 10-15 minutes and often would eventually result in a loss of gaze-tracking abilities for the remainder of the test. For those with a loss of gaze tracking, other elements were captured. The data included the video footage of the subject (including eye movements and facial expression), websites visited, duration of page visited, number of clicks, and cursor activity. The use of clinical vignettes to encourage typical web-based searches resulted in rich data points that included participants' query formulations, navigation patterns, cursor activity, total search times, and number and nature of websites accessed, which can help explain the different abilities of deaf and hearing participants.

Data Storage

Another unique aspect of this study was the use of multiple data collection sites, which has not been well described in previous research. We learned many lessons about using gaze-tracking systems across multiple data collection sites. Using multiple systems on the same project can offer tremendous benefits in terms of generalizability, but this practice also comes with considerable challenges. While creating a project, the data and sessions will be stored and can be analyzed locally, only on the laptop or computer using the Tobii Studio software. Although a session can be created on this machine and transferred to another one, it is not possible to merge these files unless one large project is created at the outset (rather than two identical but unlinked projects on separate machines). This created limitations for our study. We advise researchers working in this area to create one large project on a *master* computer and then share with computers at other data collection sites, rather than creating a *new* project on each of the individual computers. This will streamline the ability to compile data from each site.

Although an inherent benefit of gaze-tracking investigations is the real-time, second-by-second data collection, this makes for sizable individual data files. Specifically, the gaze-tracking files attained in this study ranged from 14.9 MB to 68.6 MB, with an average file size of 40.0 MB. For the elicitation interviews that allowed participants to perform real-life web-based searches, the files were as large as 17 GB. We were specifically challenged by the data storage and sharing capacities for our large-scale study. Limited storage space on a computer can cause the Tobii system to crash while data collection is in progress. This is problematic as restarting a data collection session disrupts and compromises the benefits of naturalistic observations offered through this research methodology.

Training to use the machine is another consideration for researchers. However, the software was not intuitive. Some of our researchers had an assistant familiar with the software to help with software navigation. Having an additional person in the room may compromise the naturalistic process for participants while they navigate health information on the internet.

Discussion

Principal Findings

The purpose of this study was to highlight the benefits and complexities of using a gaze tracker system to assess how deaf adults access health information and provide preliminary results in response to the implementation of this protocol. We learned that deaf signers may find aspects of the gaze-tracking session, such as calibration, challenging; however, these can be addressed in future studies through the use of this protocol paper. Gaze tracking is an affordable and effective way to understand how adults search and spend time processing patient-facing health information, such as that available on the internet. Previous research has articulated the ways in which gaze tracking can be successfully implemented in a research setting. These capacities were also observed in this study. However, our research team also experienced clear limitations with the system, notably with large sample sizes and data collection across research sites. Lessons learned also included considerations for extensive training for research assistants, as the software and procedures are not self-explanatory.

Conclusions

The experiences learned through this study will help future researchers determine ideal study designs, such as suitable protocols and participant characteristics (eg, deaf signers), when including gaze trackers in their projects. The procedures we found most effective in working with these populations were discussed, and suggestions for future research were proposed.

Conflicts of Interest

None declared.

References

1. Jacobs W, Amuta AO, Jeon KC. Health information seeking in the digital age: an analysis of health information seeking behavior among US adults. Cogent Soc Sci 2017 Mar 13;3(1):1-11. [doi: 10.1080/23311886.2017.1302785]
2. Fox S, Duggan M. Health online 2013. Pew Research Center. 2013. URL: http://www.pewinternet.org/2013/01/15/health-online-2013/ [accessed 2021-07-15]
3. Murphy M. Dr Google will see you now: search giant wants to cash in on your medical queries. The Telegraph. 2019. URL: https://www.telegraph.co.uk/technology/2019/03/10/google-sifting-one-billion-health-questions-day/ [accessed 2021-07-15]
4. Barry MJ, Edgman-Levitan S. Shared decision making — the pinnacle of patient-centered care. N Engl J Med 2012 Mar;366(9):780-781. [doi: 10.1056/nejmp1109283]
5. Karnam S, Raghavendra P. Hybrid Doctors: The need risen from informed patients. J Clin Diagn Res 2017;11(2):ZI01-ZI04. [doi: 10.7860/jcdr/2017/23163.9200]
6. Karras E, Rintamaki LS. An examination of online health information seeking by deaf people. Health Commun 2012 Aug 19;27(2):194-204. [doi: 10.1080/10410236.2011.575539] [Medline: 21854224]
7. Mackert M, Mabry-Flynn A, Champlin S, Donovan EE, Pounders K. Health literacy and health information technology adoption: the potential for a new digital divide. J Med Internet Res 2016 Oct 04;18(10):e264 [FREE Full text] [doi: 10.2196/jmir.6349] [Medline: 27702738]
8. Mitsutake S, Shibata A, Ishii K, Oka K. Associations of eHealth literacy with health behavior among adult internet users. J Med Internet Res 2016 Jul 18;18(7):e192 [FREE Full text] [doi: 10.2196/jmir.5413] [Medline: 27432783]

9. Panzer K, Park J, Pertz L, McKee M. Teaming together to care for our deaf patients: insights from the deaf health clinic. J Am Deaf Rehab Asso 2020;53(2):60-77 [FREE Full text]
10. Suggs LS. A 10-year retrospective of research in new technologies for health communication. J Health Commun 2006 Jan;11(1):61-74. [doi: 10.1080/10810730500461083] [Medline: 16546919]
11. Valdez R, Rogers C, Claypool H, Trieshmann L, Frye O, Wellbeloved-Stone C, et al. Ensuring full participation of people with disabilities in an era of telehealth. J Am Med Inform Assoc 2021 Feb 15;28(2):389-392 [FREE Full text] [doi: 10.1093/jamia/ocaa297] [Medline: 33325524]
12. Koonin LM, Hoots B, Tsang CA, Leroy Z, Farris K, Jolly B, et al. Trends in the use of telehealth during the emergence of the COVID-19 pandemic - United States, January-March 2020. MMWR Morb Mortal Wkly Rep 2020 Oct 30;69(43):1595-1599 [FREE Full text] [doi: 10.15585/mmwr.mm6943a3] [Medline: 33119561]
13. Cuan-Baltazar J, Muñoz-Perez M, Robledo-Vega C, Pérez-Zepeda M, Soto-Vega E. Misinformation of COVID-19 on the internet: infodemiology study. JMIR Public Health Surveill 2020 Apr 09;6(2):e18444 [FREE Full text] [doi: 10.2196/18444] [Medline: 32250960]
14. Murray JJ. Improving signed language and communication accessibility during COVID-19 pandemic. Hearing J. 2020. URL: https://journals.lww.com/thehearingjournal/blog/onlinefirst/pages/post.aspx?PostID=66 [accessed 2021-07-16]
15. Paludneviciene R, Knight T, Firl G, Luttrell K, Takayama K, Kushalnagar P. Perception of COVID-19 physical distancing effectiveness and contagiousness of asymptomatic individuals: cross-sectional survey of deaf and hard of hearing adults in the United States. J Med Internet Res 2021 Feb 25;23(2):e21103 [FREE Full text] [doi: 10.2196/21103] [Medline: 33560996]
16. Limaye RJ, Sauer M, Ali J, Bernstein J, Wahl B, Barnhill A, et al. Building trust while influencing online COVID-19 content in the social media world. Lancet Dig Health 2020 Jun;2(6):277-278. [doi: 10.1016/s2589-7500(20)30084-4]
17. Goldberg L, Lide B, Lowry S, Massett H, O'Connell T, Preece J, et al. Usability and accessibility in consumer health informatics current trends and future challenges. Am J Prev Med 2011 May;40(5 Suppl 2):187-197. [doi: 10.1016/j.amepre.2011.01.009] [Medline: 21521594]
18. Zeng X, Parmanto B. Web content accessibility of consumer health information web sites for people with disabilities: a cross sectional evaluation. J Med Internet Res 2004 Jun 21;6(2):e19 [FREE Full text] [doi: 10.2196/jmir.6.2.e19] [Medline: 15249268]
19. Mitchell RE. How many deaf people are there in the United States? Estimates from the Survey of Income and Program Participation. J Deaf Stud Deaf Educ 2006 Oct 12;11(1):112-119. [doi: 10.1093/deafed/enj004] [Medline: 16177267]
20. Moreland CJ, Paludneviciene R, Park JH, McKee M, Kushalnagar P. Deaf adults at higher risk for severe illness: COVID-19 information preference and perceived health consequences. Patient Educ Couns 2021 Mar 17:A (forthcoming). [doi: 10.1016/j.pec.2021.03.020] [Medline: 33824053]
21. Barnett S, McKee M, Smith SR, Pearson TA. Deaf sign language users, health inequities, and public health: opportunity for social justice. Prev Chronic Dis 2011 Mar;8(2):A45 [FREE Full text] [Medline: 21324259]
22. Kushalnagar P, Hill C, Carrizales S, Sadler GR. Prostate-Specimen Antigen (PSA) screening and shared decision making among deaf and hearing male patients. J Cancer Educ 2020 Feb 23;35(1):28-35 [FREE Full text] [doi: 10.1007/s13187-018-1436-3] [Medline: 30353474]
23. Pollard RQ, Barnett S. Health-related vocabulary knowledge among deaf adults. Rehabil Psychol 2009 May;54(2):182-185. [doi: 10.1037/a0015771] [Medline: 19469608]
24. McKee MM, Paasche-Orlow MK, Winters PC, Fiscella K, Zazove P, Sen A, et al. Assessing health literacy in deaf American sign language users. J Health Commun 2015 Oct 29;20 Suppl 2(sup2):92-100 [FREE Full text] [doi: 10.1080/10810730.2015.1066468] [Medline: 26513036]
25. Valentine G, Skelton T. 'An Umbilical Cord to the World' : The role of the internet in D/deaf people's information and communication practices. Inf Commun Soc 2009 Feb;12(1):44-65. [doi: 10.1080/13691180802158573]
26. McKee MM, Hauser PC, Champlin S, Paasche-Orlow M, Wyse K, Cuculick J, et al. Deaf adults' health literacy and access to health information: protocol for a multicenter mixed methods study. JMIR Res Protoc 2019 Oct 09;8(10):e14889 [FREE Full text] [doi: 10.2196/14889] [Medline: 31599730]
27. Fajardo I, Abascal J, Canas J. The role of working memory and long term memory in Deaf users' hypertext navigation: review of guidelines for web accessibility. In: Stary C, Stephanidis C, editors. User-Centered Interaction Paradigms for Universal Access in the Information Society. Berlin: Springer; 2004:320-325.
28. Champlin S, Lazard A, Mackert M, Pasch KE. Perceptions of design quality: an eye tracking study of attention and appeal in health advertisements. J Comm Healthcare 2014 Dec 04;7(4):285-294. [doi: 10.1179/1753807614y.0000000065]
29. Robins D, Holmes J, Stansbury M. Consumer health information on the web: the relationship of visual design and perceptions of credibility. J Am Soc Inf Sci 2009 Oct 02;61(1):13-29. [doi: 10.1002/asi.21224]
30. Duchowski A. Eye Tracking Methodology: Theory and Practice. Switzerland: Springer; 2017:1-251.
31. Kok EM, Jarodzka H. Before your very eyes: the value and limitations of eye tracking in medical education. Med Educ 2017 Jan 01;51(1):114-122. [doi: 10.1111/medu.13066] [Medline: 27580633]
32. Falck-Ytter T, Bölte S, Gredebäck G. Eye tracking in early autism research. J Neurodev Disord 2013 Sep 26;5(1):28 [FREE Full text] [doi: 10.1186/1866-1955-5-28] [Medline: 24069955]

33. Tang I, Tsai Y, Lin Y, Chen J, Hsieh C, Hung S, et al. Using functional Magnetic Resonance Imaging (fMRI) to analyze brain region activity when viewing landscapes. Landsc Urban Plan 2017 Jun;162:137-144. [doi: 10.1016/j.landurbplan.2017.02.007]
34. Whelan ME, Morgan PS, Sherar LB, Orme MW, Esliger DW. Can functional magnetic resonance imaging studies help with the optimization of health messaging for lifestyle behavior change? A systematic review. Prev Med 2017 Jun;99:185-196. [doi: 10.1016/j.ypmed.2017.02.004] [Medline: 28214544]
35. Fetters M. The Mixed Methods Research Workbook: Activities for Designing, Implementing, and Publishing Projects. Thousand Oaks, California, United States: Sage Publications Inc; 2019:1-312.
36. Henry SG, Fetters MD. Video elicitation interviews: a qualitative research method for investigating physician-patient interactions. Ann Fam Med 2012 Mar 12;10(2):118-125 [FREE Full text] [doi: 10.1370/afm.1339] [Medline: 22412003]
37. Henry S, Forman J, Fetters M. 'How do you know what Aunt Martha looks like?' A video elicitation study exploring tacit clues in doctor-patient interactions. J Eval Clin Pract 2011 Oct;17(5):933-939. [doi: 10.1111/j.1365-2753.2010.01628.x] [Medline: 21210905]
38. Creswell J, Clark V. Designing and Conducting Mixed Methods Research. Thousand Oaks, California, United States: Sage Publications Inc; 2007:1-488.
39. Tobii Pro X3-120 - discontinued. Tobii Pro. URL: https://www.tobiipro.com/product-listing/tobii-pro-x3-120/ [accessed 2021-07-16]
40. What is eye tracking? Tobii Tech. URL: https://www.tobii.com/tech/technology/what-is-eye-tracking/ [accessed 2021-07-16]
41. Glasses, lenses, and eye surgery. Tobii Support. 2017. URL: https://help.tobii.com/hc/en-us/articles/210249865-Glasses-lenses-and-eye-surgery [accessed 2021-07-16]

Abbreviations

AOI: area of interest
ASL: American Sign Language
CDC: US Centers for Disease Control and Prevention
HIT: health information technology

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Protocol

Combined Use of Web-Based and In-Person Education on Ill Health Self-management Skills in Adults With Bipolar Disorder: Protocol for a Mixed Methods Study

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Abstract

Background: Addressing the enhancement of ill health self-management skills in adults diagnosed with bipolar disorder may be considered an important intervention for health care systems worldwide.

Objective: This protocol describes the study "Management of my Bipolarity" (MoB), which aims to develop an educational intervention for adults with bipolar disorder and assess its effectiveness. The objectives include (a) a literature review on bipolar disorder educational interventions; (b) a qualitative exploration of the educational needs of people with bipolar disorder; (c) development of an educational intervention based on objectives (a) and (b) (ie, the MoB educational intervention); and (d) exploration of the effectiveness of the intervention regarding participants' knowledge of their mental health condition and enhancement of their ill health self-management skills. The MoB educational intervention will consist of an in-person and a web-based intervention in the form of a digital platform.

Methods: The proposed interventional study is a combination of a qualitative and a quantitative design (mixed methods study). A focus group and content analysis will be implemented for the qualitative assessment of the educational needs of adults with bipolar disorder. The intervention will be developed based on the qualitative data of the study and relevant literature. The effectiveness of the acquired knowledge and self-management skills will be assessed according to (a) substance use behavior, (b) health locus of control, (c) impulse control, (d) adherence to pharmacotherapy, (e) relapse prevention, (f) improvement of quality of life, and (g) bipolar disorder knowledge level via structured instruments in the quantitative part of the study using descriptive and inferential statistics (SPSS version 24.0).

Results: A total of 13 patients with bipolar disorder have been interviewed (8 women, 5 men) to identify educational needs to be covered through the intervention. Moreover, a literature review on bipolar disorder educational interventions has been completed. These data have been incorporated in the design of the MoB in-person intervention and the digital platform. The digital platform is live, and the development of the MoB in-person intervention was completed at the end of 2020. The recruitment of the participants for the intervention (40 patients) and the control group (40 patients) began during the first semester of 2021. Moreover, by tracking the platform for 1.5 years, we have recorded that 2180 users have visited the platform with an average session duration of almost 2 minutes. Mobile and tablet devices are being used by 70% of the visitors.

Conclusions: Since new parameters regarding educational interventions will be explored, these findings are expected to provide evidence that participation in structured educational interventions offers patients the opportunity to improve adherence to pharmacotherapy and increase their quality of life.

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KEYWORDS

education; empowerment; bipolar disorders; self-management; bipolar; mental health

Introduction

Bipolar disorder (BD) is one of the main causes of disability, affecting approximately 45 million people globally [1,2]. The percentage of people with mood disorders, including BD, in Cyprus is approximately 13.8%, and the incidence per year of people with BD is approximately 0.6% [3]. The most prominent manifestations of BD (ie, cognitive, mood, and interpersonal deficiencies) are all linked with decreased quality of life [4,5]. Therefore, BD has a significant effect on the personal, social, and professional lives of both patients and their families/significant others [6,7]. Most importantly, BD is linked to high mortality rates due to suicide, as well as comorbidities with other types of illness (eg, cardiovascular disease) [8-10]. All of the above highlight the need for support and empowerment of people with BD as one of the key objectives of health care systems worldwide [11].

Empowerment in the context of health care emerges out of the promotion of independence of service users and the restriction of disability and incapacitation, at both personal and social levels [12]. One of the main methods of empowering people with chronic illness is through reinforcement of their capacity to manage the illness themselves (ie, self-management capacity) [12], while reducing health care professionals' involvement to the minimum possible [13]. Enhancement of ill health self-management capacity is achieved through educational and training interventions [14]. Educational interventions, as therapeutic approaches, include information intake and training in skills regarding the ability to effectively deal with ill health issues such as self-monitoring of symptoms, medication adherence, or fulfillment of daily needs [14,15]. A plethora of positive effects have been associated with enhancement of ill health self-management skills through educational interventions, such as decreased frequency and duration of relapse episodes and hospitalization, and improvement of quality of life [14]. Educational interventions for self-management of disease symptoms have been described for chronic mental diseases, including psychosis and BD [16,17]. Computer software applications have also been incorporated in educational interventions aiming to increase knowledge and health literacy [18,19]. Specifically, web-based interventions present certain advantages such as more opportunities for participation, as they are available throughout the day and provide accessibility to a larger network of people, establishing this method of training as one with a significant financial advantage [20,21]. Moreover, participation in web-based educational interventions may be more favorable for people encountering the social stigma of mental illness, on national and international levels [22,23].

Although previous data support the effectiveness of structured educational interventions for people with BD, the data remain insufficient regarding relevant interventions in northern European countries, including Cyprus, as well as in relation to combined in-person and web-based interventions [14]. Specifically, there are no relevant structured interventions available in the Greek language. In addition, to the best of our knowledge, only one study reported to date used a combination of in-person training alongside a respective web-based intervention [24]. Although numerous digital educational interventions and relevant platforms for BD exist, the degree to which they have been developed according to any theoretical background or empirical data on the needs of patients is not clear. Notably, no digital platforms aiming to increase the knowledge and educate people in BD or enhance relevant ill health self-management skills have been found in the Greek language, and the implementation of such interventions appears to be almost absent in the health care systems of Greece and Cyprus.

Previous data support difficulty in impulse control [25], and high rates of substance use [26] and nonadherence to pharmacotherapy [27] in people diagnosed with BD, which are all linked to increased relapse rates and decreased quality of life [4,5]. Thus, interventions, mainly psychotherapeutic, toward addressing these issues need to be further explored [28]; the combination of in-person and web-based interventions is highly recommended for effective management of symptoms [29]. Other studies support that performance of ill health self-management skills is associated with one's self-perception about the health-related locus of control and related health literacy level [30,31]. Overall, educational interventions targeted to people with chronic disorders, including BD, should constitute a basic service offered by health care systems and mental health service structures at the international level [11].

The proposed protocol focuses on a study aiming to develop an educational intervention for patients with BD, and explores the null hypothesis that patients who solely receive pharmacotherapy will show the same improvement in important aspects of their lives, such as relapse rate and quality of life, compared to those who receive pharmacotherapy and structured educational interventions. The effectiveness of the proposed intervention will be tested in relation to improvement with respect to (a) impulse control, (b) substance use attitudes, (c) adherence to pharmacotherapy, (d) relapse prevention, (e) BD knowledge

level, and (f) self-perceived quality of life and locus of health-related control. Thus, the findings of the proposed study are expected to provide data on the effectiveness of a structured educational intervention, which combines in-person and digital interventions, regarding enhancement of ill health self-management skills.

Methods

Aim

The aim of the study entitled "Management of my Bipolarity," hereafter referred to as MoB, is to develop and test an educational intervention for patients with BD. The stages of the study include: (1) a literature review on BD educational interventions; (2) exploration of the educational needs of adults with BD; (3) development of the MoB educational intervention, encompassing in-person sessions and a digital platform; and (4) exploration of the effectiveness of the MoB intervention in adults diagnosed with BD regarding (i) their knowledge about this disorder, and (ii) the empowerment of ill health self-management skills in relation to the improvement of impulse control, adherence to pharmacotherapy, relapse frequency, quality of life, and substance use attitudes.

Design

This study is based on a mixed method design and consists of four stages.

Stage 1 includes a qualitative exploration of the educational needs of patients, aiming to develop an experimental educational intervention according to these needs. Moreover, a literature review on BD educational interventions was performed in this stage to support this objective according to the steps described by Tawfik et al [32] for systematic reviews. Stage 1 has been completed.

Stage 2 includes the design of the MoB intervention both in person and with the digital platform. The design of the in-person intervention relies on the Colom and Vieta [33] model, in which cognitive behavioral techniques are incorporated according to existing literature [34] and the results of Stage 1 (all relevant findings of the literature review and data acquired in the qualitative research of educational needs). The structure of the MoB digital platform has been designed by the researchers of this study and a web developer, partially based on the preferences and needs of the participants (as determined in Stage 1). Stage 2 has also been completed. The digital platform will be further enriched based on the qualitative and quantitative findings from platform evaluation techniques and interactive educational features in Stage 4.

Stage 3 includes implementation of the MoB in-person educational intervention and the quantitative evaluation of its effectiveness regarding the acquired knowledge and self-management skills of the participants at four time points (ongoing).

Stage 4 includes the qualitative and quantitative assessment of the applicability of the digital platform (ongoing).

Settings and Sampling

The target population is adults diagnosed with BD who are under treatment. The recruitment will be implemented in collaboration with the mental health services used by the participants. Specifically, both private and public mental health services in Cyprus have been informed about the objectives and procedures of the study through a specific communication process. Through this process, several patients have already been referred to the research team by their psychiatrists/therapeutic team coordinator to participate in Stage 1. As a result, convenience sampling will be combined with snowball sampling, according to study inclusion criteria set in every stage. The study is also posted on social media and groups related to BD (health care service users, health care professionals).

To promote participant retention, an action plan has been developed. Specifically, the principal investigator (AH) will arrange one or two social meetings with the participants of Stage 1 and Stage 3 to achieve some degree of intimacy, emphasize confidentiality, and ensure engagement with the study. The cost of these social meetings is covered by the Nursing Department of Cyprus University of Technology. Regarding the control group of Stage 3, the principal investigator (AH) will also make a phone call once or twice per month to reassure their participation in the study, as follows: "Hello, I am Anna from the MoB project. I'm calling to see how you are, and if you are still interested in participating in the project. The next appointment will be on date X. Is this okay with you, or do you have any other arrangements for the day?"

Stage 1

Objectives

The objective of Stage 1 is to perform a literature review on BP educational interventions and define the educational needs of adults with BD via empirical exploration of their living experience, aiming to integrate data in the MoB intervention. This stage has been completed. Specifically, the objectives of the systematic review included exploration of the educational methods applied to individuals with BD and their effectiveness regarding enhancement of ill-health self-management skills in relation to (i) relapse prevention, (ii) adherence to pharmacotherapy, and (iii) enhanced quality of life. This stage also evaluated the BD literacy needs in people with BD. An additional objective of the review was to inform the design of Stage 3 regarding eligible outcome measures for assessment of the effectiveness of the proposed intervention.

An advanced search in the CINAHL Medline, Scopus, Psych INFO, and Cochrane Library databases was performed between December 2018 and June 2020 by two researchers (MK and AH). The following key words were used singly and in combination: "bipolar disorder," "manic-depress*," "mania," "depress*," "education*," "self-management," "intervention," "program*," "empowerment," "psycho-education," "e-health," and "literacy." The following inclusion criteria were set: (a) an empirical, quantitative study; and (b) published in the English language in a peer-reviewed journal between 2007 and 2020. The methodological accuracy of the included studies was

assessed with the Health Evidence Quality Assessment Tool [35].

Inclusion Criteria and Sampling for Qualitative Exploration of Patients' Educational Needs

The inclusion criteria were set as follows: (a) sufficient experience (more than 6 months) as a patient under BD treatment; (b) willingness to communicate the living experience of BD; and (c) ability to reflect on the living experience of BD, as it will be drawn from the narrative content [36]. The final sample size was based on theoretical and data saturation of emergent themes [37-39].

Data Collection and Analysis

The form of the data collection interview, focus group or personal interview, was designed to be assigned according to the participant's convenience. Since Cyprus is a small island with approximately 1 million citizens, some of the participants were reluctant to participate in focus group discussions due to the social stigma of mental illness [40]. Participation in personal interviews was expected to preserve their anonymity.

A semistructured guide with open-ended questions, set up by the research team according to relevant literature, was used for data collection in this stage. The interview guide included the following questions:

1. Please tell us what you know about your mental health condition/BD.
2. Please describe what you would like to know about bipolar disorders.
3. Please describe in what way and on what topics you would like to be educated and increase your knowledge on bipolar disorders?
4. Please describe your expectations from an educational intervention regarding its impact on your everyday living.
5. Would you like this intervention to be implemented one-on-one or in a group?
6. How long would you like the intervention to last?
7. What is your level of engagement with the internet?
8. Are you familiar with computer use?

The original intention was to have two focus groups (6-10 people per group); however, in the process of the research, only one focus group was ultimately deemed to be necessary. The focus group participants met two to three times. In the second meeting, the themes revealed in the first meeting were verified and enriched where possible. During the third meeting, the researchers interpreted the data, followed by a discussion with the participants. This method was also applied to personal interviews (2-3 meetings with each participant). Data analysis was based on the conventional mode of content analysis [41].

Stage 2

The purpose of the development of the MoB in-person intervention is to create an applicable, feasible, and effective intervention to enhance BD knowledge and ill-health self-management skills in people diagnosed with BD. Specifically, a textbook has been devised explaining in detail the step-by-step process and the techniques of the experimental educational method of the MoB in-person intervention.

The goal of the development of the MoB digital platform is to create an ecosystem where people with BD will be educated and empowered to make use of the platform via a computer, tablet, or mobile phone. The owner of the platform is the Nursing Department of Cyprus University of Technology and the administrator is the principal investigator (AH). The participants of the proposed study will have the opportunity to access the platform during and after completion of the study.

Stage 3

Inclusion and Exclusion Criteria

The following inclusion criteria have been set for participation in the MoB intervention: (1) clinical diagnosis based on the Diagnostic and Statistical Manual of Mental Disorders-5 for BD; (2) aged between 18 and 65 years; (3) signed the informed consent form; (4) stable mood status at the beginning of the MoB in-person intervention based on clinical assessment, conducted by the principal investigator (AH); (5) experience of the illness for at least 1 year based on the medical record; (6) adequate awareness of the illness, based on the following guide: (a) are you aware of the reason(s) you are using mental health services/under medication? and (b) are you aware of the aim of the educational intervention in which you may participate?; and (7) familiarity with computer use.

The exclusion criteria are: (1) intellectual disability (IQ<70), based on the Wechsler Adult Intelligence Scale [42]; (2) brain damage (eg, following a stroke) based on diagnostic tests; (3) acute phase of the illness, based on clinical assessment and use of the Young Mania Rating Scale (YMRS; total score <12) [43] and/or Beck Depression Inventory (total score <17) [44]; and (4) substance use problems at the beginning of this stage according to the Alcohol Use Disorders Identification Test (AUDIT; total score <9) [45] and Drug Use Disorders Identification Test (DUDIT; total score <2 for women or <6 for men) [46].

All eligible participants will be randomly assigned (in terms of gender, age, duration of illness) into the intervention group and the control (waiting) group. With the aim of obtaining a moderate correlation effect, with 80% statistical power and .05 level of statistical significance, 40 participants are needed in the intervention group and 40 participants are needed in the control (waiting) group.

The criteria for discontinuing participation in the intervention group are disorder relapse and nonadherence to pharmacotherapy (discontinuation of medication).

Intervention Procedure

The form of this intervention will be in groups or in person according to the participant's choice (similar to the data collection process as detailed above). Additionally, all participants of this group will have access to the MoB digital platform and will be assessed via a checklist on the frequency and extent to which they use the digital platform in each in-person session.

The implementation methodology of the MoB in-person intervention will include videos and PowerPoint presentations,

as well as interactive learning methods such as role playing, empowerment exercises, and live discussions.

The MoB in-person intervention will comprise a total of 12 educational sessions. Each session will have a duration of 1.5 hours and the maximum number of participants in the groups will be 12 patients. At the beginning of each session, the participants will be given the opportunity to record their feedback for the previous session and the impact of the training intervention so far for themselves and for their families/significant others. The intervention will be performed at Cyprus University of Technology and will be implemented by the principal investigator (AH). Participation in the educational intervention is free of charge. Moreover, there is no financial benefit for those participating in the study (participants, researchers) in terms of reimbursement or any other material benefit.

Those who wish to withdraw participation prior to completion of the intervention will be able to continue to receive information/knowledge about their illness through the digital platform.

The control (waiting) group will only have access to the MoB digital platform. Yet, it should be noted that the control (waiting) group will also receive the MoB in-person intervention if its effectiveness is shown at the end of the study. In this way, all participants will be given the chance to receive the MoB intervention.

Effectiveness Evaluation

Evaluation of the effectiveness of the MoB in-person intervention will be based on the degree of improvement in the following outcome variables defined according to the findings of the literature review completed in Stage 1: (1) self-perceived quality of life level, as measured by the World Health Organization Quality of Life Assessment (WHOQOL) tool [47]; (2) self-perceived health-related locus of control, as measured by the Multidimensional Health Locus of Control (MHLC) scale [48]; (3) ability to control impulses, as reflected in one's sexual and aggressive behavior, measured by the items "aggressive behavior" and "sexual interest" of the YMRS [43]; (4) substance use problems, measured by the AUDIT (alcohol use) [45] and DUDIT (drug use) [46] tools; (5) adherence to pharmacotherapy, measured by the Drug Attitude Inventory (DAI-30) tool [49]; (6) frequency of relapses assessed by the reduction of the number and duration of hospitalizations for the 2 years following the end of the educational intervention; and (7) BD knowledge level assessed by the Bipolar Disorder Knowledge Scale (BDKS) [50].

The degree of self-perceived quality of life will be measured by the total score in the WHOQOL scale assessment. This is a 1-5 Likert-type scale including 26 items. The minimum score in the scale is 26 and the maximum is 130; higher scores indicate a better outcome. The BD level of knowledge will be measured by the total score in the BDKS. This is a 25-item, true-false scale. The items address diagnosis, etiology, disease course, symptoms, treatment, and life impact BD-related knowledge. The ratio of "true" to "false" responses is assessed; a higher percentage of correct values indicates a better outcome. The degree of ability to control impulses will be measured by the total score in the YMRS. This is a 0-4 Likert scale, including 11 items. The total score of the scale ranges from 0 to 44; a lower total score indicates a better outcome. The degree of adherence to pharmacotherapy will be measured by the total score in the DAI-30. This is a 30-item true-false scale. The ratio of "true" to "false" responses is assessed; a higher percentage of correct values indicates a better outcome. Drug use will be measured by the total score in the DUDIT scale. This is a 1-5 Likert, 11-item scale (total score range: 1-55); a lower total score indicates a better outcome. Alcohol use will be measured by the total score in the AUDIT. This is a 0-4 Likert, 10-item scale (total score range: 0-40); lower scores indicate a better outcome. The degree of self-perceived health-related locus of control will be assessed by the MHLC tool, which is a 6-point Likert (scored from 1 to 6), 18-item scale (Form A). These items are grouped in three subscales corresponding to three different loci of control (ie, internal, others, and fate/luck); higher sum scores in each of the 3 subscales indicate a stronger locus of control. The frequency of relapses will be measured by the number of hospitalizations after completion of the in-person intervention. The number of hospitalizations will be measured as the sum of individual hospitalizations in a high-security psychiatric hospital/setting; the lower the number of hospitalizations, the better the outcome. The duration of relapses will be assessed by the duration of inpatient hospitalizations in days after completion of the in-person intervention. The duration of inpatient hospitalizations will be measured as the sum of the days of hospitalization in a high-security psychiatric hospital/setting; the lower the duration in days of hospitalization, the better the outcome.

There will be four evaluation time points. The first evaluation time point will be prior to implementation of the MoB in-person intervention, the second will take place immediately after completion of the MoB in-person intervention, and the third and fourth evaluations will be applied at 6 and 12 months, respectively, after completion of the MoB in-person intervention. These time points have been determined according to the systematic review completed in Stage 1 [14].

The control group will be assessed via the same evaluation tools as the intervention group, and at the same time periods. This will test the null hypothesis that patients who solely receive pharmacotherapy demonstrate the same improvement as the intervention group.

The educational meetings will be held at Cyprus University of Technology in a room specially designed for this purpose that is soundproof, without windows, and chairs placed in a circular arrangement to allow for eye contact, along with small tables on either side to keep notes.

Data Analysis

The means (SD) will be calculated for the scale numeric (sum) scores (YMRS, WHOQOL, MHLC, BDKS, DUDIT, DAI-30, AUDIT, relapse frequency/duration) and frequencies will be calculated for categorical variables (gender, age groups, sex, years in illness groups). Parametric tests (analysis of variance, *t* test) will be applied for comparisons between groups. For all statistical tests, *P* values of .05 or lower will be considered

statistically significant. Data will be analyzed through the Statistical Package for Social Sciences (SPSS Inc, version 25.00). To test the relationship between two or more variables, logistic and linear regression analyses will be used. The multiple imputation method will be applied to handle missing data.

Stage 4

Assessment of the applicability of the MoB digital platform will be based on qualitative (users' feedback) and quantitative (data analysis) testing. The qualitative assessment will be based on the experience of the users with the platform and on the degree to which they were positively affected by its use. Specifically, the focus of the interviews will be on the impact of the platform on their everyday life, as well as on enhancement of ill health self-management skills according to the participants' responses to the following open-ended questions: (a) "How would you describe your experience with the use of the MoB digital platform?" (b) "What was the impact of use of the MoB digital platform on your life?" and (c) "What was the impact of the MoB digital platform on your ill health self-management skills?" This process will take place via focus groups discussions. Specifically, two focus groups with 8-12 participants each will be recruited including participants who (a) attended the MoB in-person intervention and had used the platform and (b) solely used the MoB digital platform.

The quantitative testing involves anonymous questionnaires provided to users of the MoB digital platform, who will have to answer predefined questions regarding satisfaction parameters relevant to the platform. The first outcome assessed will be the level of users' satisfaction with the MoB digital platform, measured by the score on a 3-item Likert scale (low, moderate/accepted, high) self-questionnaire exploring users' perceptions of overall experience; utility, according to their present medical condition and clinical state; practicality on daily usage; improvement of self-management skills; and technical difficulties experienced [51]. The second outcome is the degree of improvement in users' knowledge as measured by the score on the BDKS [50].

Patient and Public Involvement

Although patients with BD have not been included as members of the present research team, their input in the development of this study will be constant and accounted for during various stages of this project. Patient/participant involvement is registered as follows. Once enrolled in the study, participants' feedback and reactions will be collected by the research team and used for improvement of the implementation of the study protocol. Respect for the rights, experiences, and personalities of the patients involved is one of the key priorities and motivations of the research team. During stage 1, the qualitative (empirical) exploration of the educational needs of patients with BD will be assessed. During the development of the MoB in-person intervention, the features, methods, and stages described by the participants (data from Stage 1) will be taken into account. Participant perspectives will also be addressed during preparation of the research questions on the effectiveness of the MoB in-person intervention. These questions are expected to be finalized according to the preliminary input resulting from the participants' narratives on the clinical areas that need to be addressed by the MoB in-person intervention and the expected impact of the intervention on their lives (data from Stage 1). The issue of the participants' burden of the MoB in-person intervention is included in the interview guide. Relevant data were used to define the duration of the MoB in-person intervention and the assessment periods of the intervention (data from Stage 1). The participants are expected to introduce the proposed study to their peers, since a snowball sampling technique will be applied in Stage 3 aiming to recruit the participants of the intervention and control group. Finally, the participants who will be involved in Stage 4 will assess the applicability of the MoB digital platform via qualitative and quantitative data.

Due to the limited population of the Republic of Cyprus, attracting an adequate number of participants for the study is one of the challenges faced. However, the research team will disseminate the call to patients and providers' associations as well as through other available means to ensure patient participation.

Members of the public, or the significant others/family members of the participants, will not be involved in the study. However, should the intervention be considered successful, significant effort and work will be exerted to alleviate the effects of the stigma of BD in society, both in Cyprus and internationally. A collaborative effort will be undertaken by the researchers to engage with members of the public to highlight the experience of BD, and the significance and effectiveness of the MoB intervention.

Registration and Ethics

This protocol was approved by the Cyprus National Committee of Bioethics (ΕΕΒΚ/ΕΠ/2018/27) on September 30, 2018, and was registered at the Research Committee Review board of the Ministry of Health of the Republic of Cyprus ($5.34.01.7.6^{E}$/0490/2018) on February 18, 2019. Moreover, the research protocol has been registered in ClinicalTrials.gov (ID: NCT04643210). All participants have/will sign the consent form for participation in the study, which includes the parameter of data publication. The questionnaires included in this study protocol have been previously published elsewhere and all relevant references to the questionnaires are cited in the manuscript.

Results

Stage 1

Literature Review

The literature review has been completed, and these data have been published [14]. Specifically, 15 studies were included in the review, showing that effective management of BD was mainly based on the combination of pharmacotherapy and structured educational interventions. Participation in structured educational interventions was associated with improvement in global functionality, adherence to pharmacotherapy, and early detection of relapse symptoms, all resulting in reduced frequency of hospitalization and experiences of mental illness social stigma. However, none of the reviewed studies assessed

important areas of functioning (ie, cognition, delinquency, and impulse control). In relation to the mode of the educational intervention, both digital and in-person interventions were identified. Regarding the structure of the reviewed educational interventions, the majority were developed according to modified versions of the Colom and Vieta model [33], and their duration ranged with 7-8 in-person sessions and 6-21 group sessions. Moreover, personal interventions were linked to an increased frequency of drop-off and decreased duration of positive effects compared with those of group-based interventions. However, additional research on the effectiveness of in-person interventions compared to group-based interventions was suggested. Although this review described evidence on the effectiveness of web-based educational interventions, relevant data were not sufficient or of adequate quality to further support their usefulness. Nevertheless, it was revealed that web-based interventions were associated with advantages such as availability throughout the day and subsequently more opportunities for participation, accessibility to a larger network of people, and cost-effectiveness. Moreover, web-based interventions were more attractive to those encountering social stigma and younger participants. Additionally, the vast majority of the studies reported on the increased patient satisfaction from participation in educational interventions, and the most frequent reasons for quitting these interventions were increased job demands, relapse, and lack of time. Moreover, those with a duration of illness of more than 15 years did not benefit significantly from educational interventions. In conclusion, this review suggests the need for further intervention studies in educating BD clinical groups, combining in-person and web-based interventions, and further assessment of their effectiveness in areas such as substance use, delinquency, and impulse control.

Empirical Qualitative Exploration of Educational Needs

Regarding the qualitative exploration of the educational needs of ill-health self-management skills in people diagnosed with BD, a total of 13 participants were interviewed (8 women, 5 men). Specifically, since participation in interviews was designed to include both personal and focus group modes, we completed one focus group with 6 participants and 7 personal interviews (May to September 2020). The simultaneous data collection and analysis of emerged themes allowed us to determine thematic saturation up to this sample size. Thus, we did not proceed to an additional focus group as intended. Moreover, the fact that the participants came from different educational, social, and professional backgrounds supported the criterion of data saturation. By April 2021, all three meetings had been completed with all 13 participants. Relevant data defined the design of the MoB intervention and are expected to be published by the end of 2021.

Specifically, the participants only partially described the main symptomatology and the risks stemming for inadequate management of BD, and subsequently the impact of BD on their lives; notably, none of the participants reported any type of participation in a structured educational intervention on BD. Furthermore, the internet was identified as the primary source of education about their illness, with health care professionals (ie, psychiatrists and mental health nurses) listed as the second, yet ineffective, source of knowledge. Regarding BD-related educational needs, the participants mainly focused on the necessity to become familiar with the pathophysiology and symptomatology of BD, but most importantly the etiology behind the onset of this disorder and the factors that might have triggered BD. Moreover, they clearly described their need to enhance their knowledge about pharmacotherapy, side effects, and the rationale behind particular types of psychotropic agents, as well as effective management of the adverse effects of pharmacotherapy. Substance use was also included in the agenda of the participants regarding their educational needs. Additionally, the participants reported their need to be educated on how to manage human/patient rights violations against them, mainly in relation to consent to treatment, participation in clinical decision-making, and capacity to make legal decisions. The participants also described their need to enhance knowledge about the therapeutic procedures applied in other countries, as well as in relation to complementary therapeutic options. Female participants expressed their need to learn more about the link between BD and reproductive and sex-life health issues, with focus on fertility and the link between pharmacotherapy side effects and menstrual disturbances, childbirth, and hormones regulation. Employment-related issues were also raised, especially with respect to lack of knowledge regarding sick-leave issues and disclosure issues about their health status to their employers and coworkers. The participants also provided input regarding the frequency, duration, and mode of educational sessions. Most importantly, the participants underlined their need to be practically educated on how to implement all of the provided information into their daily lives, and mainly on how to identify and self-manage (if possible) early symptoms to prevent relapse.

Regarding the above topics, those referring to (a) sexual and reproductive health, (b) patient/human rights, (c) employment issues, and (d) alternative and complementary therapeutic options were incorporated into the MoB intervention, since these topics were not included or adequately covered in the Colom and Vieta [33] module. Moreover, the participants' suggestions about the frequency (once a week), duration (90 minutes per session/12 sessions), and mode (both personal and group-oriented options to participate in the MoB intervention, combination of in-person and online modules via a digital platform) were also taken into consideration during development of the MoB intervention.

Beyond educational needs, the participants spontaneously provided descriptions about social needs, and specifically expressed their need to belong to a certain group or society, as well as their willingness to support others in need. Based on this input, a session on social skills training and information about how to engage in volunteering was incorporated in the design of the MoB intervention.

Stage 2

MoB In-Person Intervention

A textbook explaining the detailed, step-by-step process and the techniques of the experimental educational method of the MoB in-person education has been devised. According to the data acquired in Stage 1, the MoB in-person intervention

comprises a total of 12 in-person educational sessions, with one session per week. Each session has a duration of 1.5 hours and the maximum number of participants in the groups is 12 patients.

MoB Digital Platform

The interactive part of the platform is under development, while the informative part is live [52] and accessible to the participants in the current study, as well as to any interested person (eg, family members of people with BP) or caregivers providing updated information related to BD (platform users). The platform is in the form of a dynamic website with user-generated content as well as static information, following a responsive design (ie, accessible with all types of devices). The informative part, so far, includes the following functionalities: self-management action plan, homework exercises, self-assessment tools, and scientific articles relevant to BD. Entry into the platform functionalities (scientific articles excluded) is password-protected.

Users can register in the platform by filling in their personal profile and can log out/log in and revisit at their convenience. Regarding self-management functionalities, the platform will contain subject units where personal relapse symptoms may be registered, a life events table, personal risk factors for relapse, and a weekly program of activities. Input of relevant information will be provided through open-ended questions and checklists. Participants of the MoB in-person intervention who visit the platform will find that these subject units (chapters) are topics on which they will be educated on. Additional features will be incorporated according to development of Stage 1 (eg, new training needs as described by participants in the focus groups).

Another subject unit will be the personal therapy file, where users will have the chance to keep tabulated notes related to their therapy, including information about the dose and type of medication treatment, as well as pending medical tests (eg, blood tests) and other relevant information. The therapeutic team of the user will have the ability to access the information by registering in the platform under approval of the user with the aim to support continuity and share information.

Stage 3

The recruitment of the participants of the intervention group (40 patients) and the control group (40 patients) began during the first semester of 2021.

Stage 4

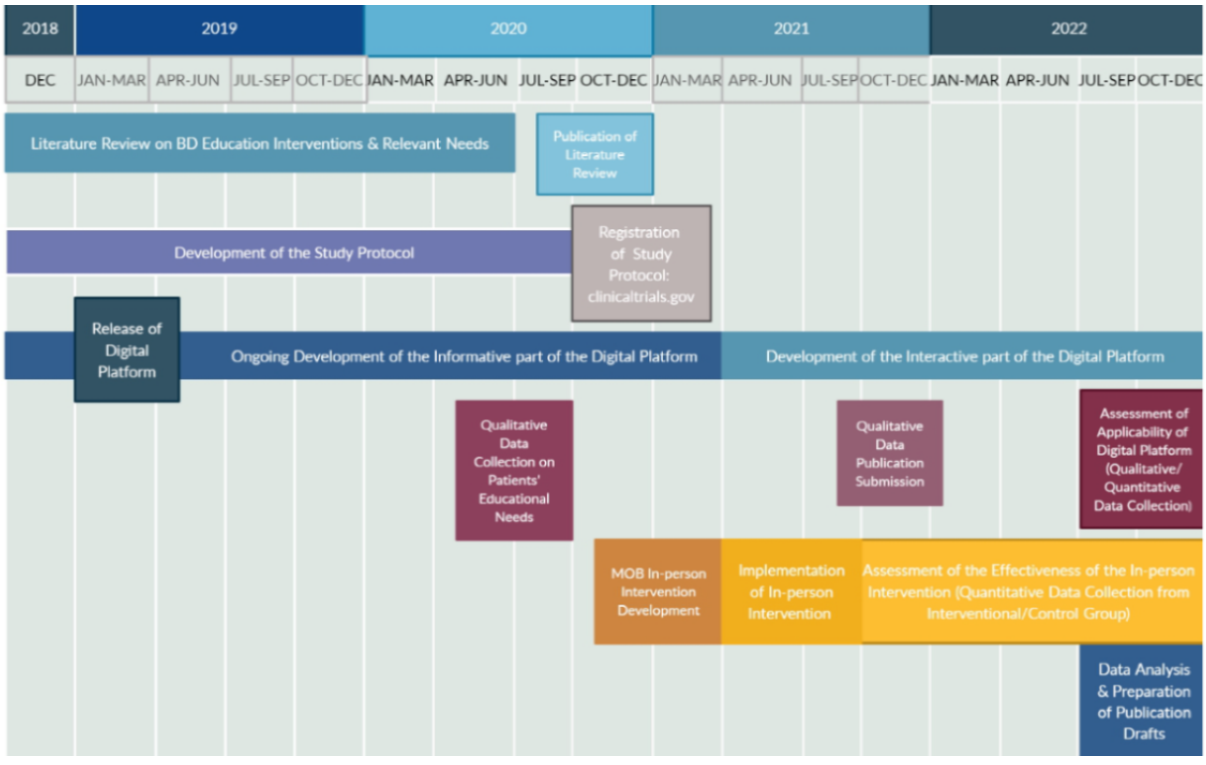
User behavior data have been analyzed through Google Analytics by tracking the platform for approximately 1.5 years (January 2019 to October 2020). Specifically, we have recorded that 2180 users have visited the platform with an average session duration of almost 2 minutes. The bounce rate of these visits is 68%, which calls for improvement. The returning visitor rate is approximately 10%, and 70% of the visitors are accessing the platform via mobile and tablet devices.

The website has a total of 7100 page views. Each user has an average of 2.6 pages per visit. In terms of search appearance, it seems that 72% of the traffic is derived from organic searches, which means that search engine optimization fundamentals have been applied to the highest level. Usability testing is being performed to ensure that the website is improving the lives of the users.

The full development and release of the interactive part of the digital platform is expected to be finalized by the second semester of 2022, at which time the assessment of the applicability of the platform will take place.

The timeline of the proposed study is presented in Figure 1.

Figure 1. Timeline of the Management of my Bipolarity (MoB) study. BD: bipolar disorder.



Confidentiality and Dissemination

Ethics and Data Management

Participation in all stages of the study will follow the provision of informed consent. The participants will be informed both orally and in written form about the purpose and process of the study, as well as about confidentiality issues regarding the revealed experiences and the safe storage of the collected data. The principal investigator (AH) will answer all questions. The consent form will include a telephone number and email address for expressing complaints relating to the procedures of the study. Participants will be able to withdraw at any point as they wish, with no repercussions in the therapeutic procedure they already follow.

Each interview will be recorded with the participant's permission. Moreover, the participants will be reassured that no data that could reveal their real identity would be presented or reported at any point of the study. Pseudonyms will be used for participation in the study. Although there is no identified psychosocial or other type of danger or harm related to participation in this study, the research team will provide psychosocial supportive services to those in need during the study and for up to 1 year after its completion.

Dissemination Policy

Dissemination of the results will take place through publications in international and national scientific journals. There will also be presentations of the data in nursing and medical conferences at national and international levels. All publications and presentations that will be held will include the names of all the collaborators who contributed to the implementation of this study. The aim of the dissemination is to inform health professionals and researchers interested in the follow-up of similar methodological planning for intervention studies.

Data Management

The data collected from each participant will be encoded as a letter according to the group to which they will be assigned (ie, "I" for the intervention group or "C" for the control group) and the sequence number of entering this group (eg, I1 or C1). This algorithm is expected to produce a unique code for each participant. All data will be safely stored in a locked cabinet in the office of the main supervisor, MK. Access is granted only to MK and AH. The data will also be stored on the computer of the main supervisor. When the data are stored on the computer, AH and MK will perform a double check to assure that the questionnaires have been completed accurately. The data will be published immediately in scientific publications for their verification. Mechanisms to protect data, based on the General Data Protection Regulation, have been taken into account to ensure the security of sensitive information provided on the digital platform by its users. In relation to security of data linked to any kind of communication within the environment of the platform, the HTTPS encryption system will be applied. Moreover, in relation to privacy issues, a cookies system will be applied. Access to personal files will be password-protected and all relevant information will be encrypted. Identification issues will also be taken into consideration. Overall, further investigation on security, privacy, and identification issues will be ongoing.

Discussion

Projected Findings and Significance

The findings of the proposed protocol will shed some light on the characteristics of structured educational interventions applied to people with BD and the educational needs of this clinical population. Most importantly, the proposed study is expected to provide data on the effectiveness of a structured educational intervention regarding enhancement of ill health self-management skills in this clinical population. The development of a relevant digital platform is also expected to contribute to this goal. Structured educational interventions include knowledge provision and experiential exercises to adapt effective attitudes regarding the self-management of BD [20,53-66], while the degree of self-management of chronic mental disorders is further linked with improved patient quality of life [67,68].

The review performed in Stage 1 of this protocol revealed that control of the symptoms of BD is a complex process, which appears to be based on the combination of pharmacotherapy, psychotherapy, and structured education [20,53-66]. Moreover, this review confirmed that participation of people with BD in structured educational interventions gives them the opportunity to improve important life parameters such as functionality in terms of fulfillment of everyday life activities and work engagement [16], adherence to pharmacotherapy, early detection of relapse symptoms, reduction in the frequency and length of hospitalization [69], and limitation of social stigma [65]. Additionally, it became clear that individuals with BD who participate in training interventions have fewer symptoms of intensity, resulting in a decrease in the amount of medication received [70]. Moreover, based on this review, it was shown that the duration of relevant educational interventions varies according to the form of the training intervention (individual- or group-oriented). Specifically, 6 to 21 training sessions seem to be necessary for group interventions and 7-8 sessions are needed for individual interventions [16,54,60]. Another factor found to be related to the effectiveness of education was the chronicity of the disorder. Those who described a chronic state of the disorder with a duration of more than 15 years did not benefit significantly from educational interventions [47]. Subsequently, priority should be given to educational interventions in the early stages of diagnosis of the disorder to achieve the highest possible efficacy. On this basis, since both the intervention and control groups in the proposed study will include individuals with a variety of illness durations, caution will be taken during data analysis to control this confounder.

Integration of the qualitative data of Stage 1 into the development of the MoB intervention was achieved in relation to both the curriculum of the intervention and the delivery mode. Most importantly, since the participants confirmed a lack of structured, culturally adapted educational interventions in the Greek language, we may assume the necessity of applying the proposed educational intervention to people diagnosed with BD and their families in an accessible and friendly mode; thus,

implementation of advanced, web-based educational interventions accessible to both clinical and nonclinical populations may be supported. Nevertheless, the internet was identified as the primary source of education for the participants, which was also described as a useful source of knowledge. Consequently, the development of a culturally sensitive platform providing reliable and updated information and knowledge to the public may be deemed necessary. Overall, based on the above, the research team confirmed the need to combine in-person sessions with a digital platform in the form of a dynamic website with user-generated content as well as static information, while these data have been integrated into the design and assessment of the applicability of the MoB digital platform.

Regarding the context of the MoB educational sessions, several new topics were introduced: (a) sexual and reproductive health, beyond lithium-related topics and sexual impulse control in mania/hypomania, which are already included in the Colum and Vieta [33] model; (b) patient/human rights; (c) employment issues; and (d) alternative and complementary therapeutic options, beyond the stress-control techniques already included in the Colum and Vieta [33] model. Additionally, aiming to support the participants' social needs, a session on social skills training and information on how to engage in volunteering was incorporated into the MoB intervention.

Based on the preliminary metrics related to the digital platform, despite low rates of engagement, bearing in mind the rate of visitations, we may conclude that there is an interest in the digital platform. The numbers of visitations may further suggest that we have developed a user-friendly platform following the latest technological trends. Nevertheless, it would be useful to know how many visitors typically visit other similar websites regarding patient education, and to further compare the rate of visitations of the digital platform with the typical rates for such resources. Currently, due to a lack of websites in the Greek language on psychiatric patient education, a relevant comparison was not possible. Overall, further improvements will be made based on ongoing data retrieval and testing, with special focus on ways to increase the duration of engagement in the platform. The qualitative and quantitative assessment of the platform is still ongoing, which is expected to be finalized at the end of 2021.

Approximately 5.7 million adults in the United States are diagnosed with BD annually, a percentage corresponding to 2.6% of the total adult population [70,71], while BD is the second most prevalent neurobiological (mental) disorder in the Republic of Cyprus, following psychotic thought disorder [71]. The median age of onset for BD is 25 years, although the illness can start in early childhood or late adulthood, having a long-term impact on one's life [72]. An equal number of men and women develop BD, and this condition is found in all ethnic groups and social classes [72]. Most importantly, BD results in a 9.2-year reduction in expected lifespan, and as many as 1 in 5 individuals with BD attempts suicide [72]. Additionally, a prolonged lack of diagnosis or false diagnosis at some point of the illness trajectory is a common phenomenon among people with BD [73]. As a result of delayed effective treatment, the symptoms of the disorder become more severe, along with an increased frequency of relapse [74,75]. All of the above constitute the application of innovative, multidimensional, and effective therapeutic approaches aiming to increase the quality of life of this clinical group and adequately empower patients as an imperative goal. Empowerment in the context of health care refers to the status in which service users may function under the highest degree of autonomy, achieve their personal life goals, and gain the optimum level of quality of life [76,77]. Studies on the effectiveness of therapeutic methods aiming to empower ill health self-management skills in people with chronic illness, including BD, have been reported to be necessary [78,79].

Several changes have been made to mental health services in Cyprus; today, the majority of services are provided in community rather than institutional settings. According to the goals of the Ministry of Health of the Republic of Cyprus, advanced, evidence-based mental health clinical practices are considered an integral part of the therapeutic interprofessional approach toward clinical populations [71]. However, to our knowledge, there is no evidence of the extent to which empowering-oriented approaches toward individuals diagnosed with BD have been incorporated to the recent modification of mental health services. Implementation of the proposed intervention is expected to contribute to this goal in Cyprus.

Limitations

Regarding the limitations of the proposed study, only adults will be involved (18-65 years), which will limit the ability to obtain a comprehensive depiction of the effectiveness of the MoB intervention in populations of different ages (eg, adolescents, the elderly). Additionally, the interventions will be developed only in the Greek language, excluding non-Greek–speaking participants, leading to limited generalizability of the findings.

Conclusion

This is the first study, to the best of our knowledge, on structured education of adults with BD that combines in-person and web-based interventions. The outcome of robust evidence on the effectiveness of the MoB educational intervention is expected to contribute to the development of knowledge and documentation on the subject, locally in the Greek-Cypriot area, but internationally as well. New parameters regarding educational interventions will be explored, while data from the proposed study are expected to support the incorporation of the MoB educational intervention into mental health care services, thereby enhancing mental health nursing practice, both in Cyprus and globally.

Authors' Contributions

AH, as the principal investigator of the study, has designed and written the study protocol, designed the MoB digital platform, will collect quality data, and will provide the educational intervention. MK is the lead supervisor of the study and has equally

contributed with AH to the design and writing of the study protocol, and is responsible for the overall scientific supervision of the study. AH and MK are responsible for data management. EP and AC are members of the research team of AH, and have provided critical review to the development of the study protocol. VSK has contributed to the editing and critical review of the protocol. All authors have read and approved the manuscript and ensure that this is the case.

Conflicts of Interest

None declared.

References

1. American Psychiatric Association. The Diagnostic and Statistical Manual of Mental Disorders. 5th edition. Washington, DC: American Psychiatric Association; 2013:65-92.
2. GBD 2017 DiseaseInjury IncidencePrevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2018 Nov 10;392(10159):1789-1858 [FREE Full text] [doi: 10.1016/S0140-6736(18)32279-7] [Medline: 30496104]
3. Population and social conditions (2018). Cyprus Statistical Office. URL: https://www.mof.gov.cy/mof/cystat/statistics.nsf/populationcondition_23main_gr/populationcondition_23main_gr?OpenForm&sub=3&sel=4 [accessed 2020-11-21]
4. Bonnín CDM, Reinares M, Martínez-Arán A, Jiménez E, Sánchez-Moreno J, Solé B, et al. Improving functioning, quality of life, and well-being in patients with bipolar disorder. Int J Neuropsychopharmacol 2019 Aug 01;22(8):467-477 [FREE Full text] [doi: 10.1093/ijnp/pyz018] [Medline: 31093646]
5. Marwaha S, Durrani A, Singh S. Employment outcomes in people with bipolar disorder: a systematic review. Acta Psychiatr Scand 2013 Sep;128(3):179-193. [doi: 10.1111/acps.12087] [Medline: 23379960]
6. Sylvia LG, Montana RE, Deckersbach T, Thase ME, Tohen M, Reilly-Harrington N, et al. Poor quality of life and functioning in bipolar disorder. Int J Bipolar Disord 2017 Dec;5(1):10 [FREE Full text] [doi: 10.1186/s40345-017-0078-4] [Medline: 28188565]
7. Sharif F, Mahmoudi A, Shooshtari AA, Vossoughi M. The effect of family-centered psycho-education on mental health and quality of life of families of adolescents with bipolar mood disorder: a randomized controlled clinical trial. Int J Community Based Nurs Midwifery 2016 Jul;4(3):229-238 [FREE Full text] [Medline: 27382589]
8. Johnson SL, Cuellar AK, Gershon A. The influence of trauma, life events, and social relationships on bipolar depression. Psychiatr Clin North Am 2016 Mar;39(1):87-94 [FREE Full text] [doi: 10.1016/j.psc.2015.09.003] [Medline: 26876320]
9. Crump C, Sundquist K, Winkleby MA, Sundquist J. Comorbidities and mortality in bipolar disorder: a Swedish national cohort study. JAMA Psychiatry 2013 Sep;70(9):931-939. [doi: 10.1001/jamapsychiatry.2013.1394] [Medline: 23863861]
10. Hayes JF, Miles J, Walters K, King M, Osborn DPJ. A systematic review and meta-analysis of premature mortality in bipolar affective disorder. Acta Psychiatr Scand 2015 Jun;131(6):417-425 [FREE Full text] [doi: 10.1111/acps.12408] [Medline: 25735195]
11. Shields GE, Buck D, Elvidge J, Hayhurst KP, Davies LM. Cost-effectiveness evaluations of psychological therapies for schizophrenia and bipolar disorder: a systematic review. Int J Technol Assess Health Care 2019;35(4):317-326 [FREE Full text] [doi: 10.1017/S0266462319000448] [Medline: 31328702]
12. Collins C, Rochfort A. Promoting self-management and patient empowerment in primary care. In: Capelli O, editor. Primary care in practice - integration is needed. England: InTechOpen; 2018:150-170.
13. Baiardini I, Heffler E. The Patient-Centered Decision System as per the 4Ps of Precision Medicine. In: Agache I, Hellings P, editors. Implementing Precision Medicine in Best Practices of Chronic Airway Diseases. Cambridge, MA: Academic Press; 2019:147-151.
14. Hatzioannou A, Papastavrou E, Chatzittofis A, Karanikola M. Exploration of the effectiveness of structured education in empowering people with a Bipolar Disorder. Nurs Care Res 2020;55:246-274.
15. Rahmani F, Ebrahimi H, Ranjbar F, Razavi SS, Asghari E. The effect of group psychoeducation program on medication adherence in patients with bipolar mood disorders: a randomized controlled trial. J Caring Sci 2016 Dec;5(4):287-297 [FREE Full text] [doi: 10.15171/jcs.2016.030] [Medline: 28032073]
16. Li H, Shapiro D, Seidman L. Handbook of attenuated psychosis syndrome across cultures. Switzerland: Springer; 2019.
17. Chen R, Zhu X, Capitão LP, Zhang H, Luo J, Wang X, et al. Psychoeducation for psychiatric inpatients following remission of a manic episode in bipolar I disorder: A randomized controlled trial. Bipolar Disord 2019 Feb;21(1):76-85. [doi: 10.1111/bdi.12642] [Medline: 29578271]
18. Lauder S, Cosgrove VE, Gliddon E, Grimm D, Dodd S, Berk L, et al. Progressing MoodSwings. The upgrade and evaluation of MoodSwings 2.0: An online intervention for bipolar disorder. Contemp Clin Trials 2017 May;56:18-24 [FREE Full text] [doi: 10.1016/j.cct.2017.02.008] [Medline: 28257919]
19. Gliddon E, Barnes SJ, Murray G, Michalak EE. Online and mobile technologies for self-management in bipolar disorder: A systematic review. Psychiatr Rehabil J 2017 Sep;40(3):309-319. [doi: 10.1037/prj0000270] [Medline: 28594196]

20. Barnes CW, Hadzi-Pavlovic D, Wilhelm K, Mitchell PB. A web-based preventive intervention program for bipolar disorder: outcome of a 12-months randomized controlled trial. J Affect Disord 2015 Mar 15;174:485-492. [doi: 10.1016/j.jad.2014.11.038] [Medline: 25554993]
21. Joas E, Bäckman K, Karanti A, Sparding T, Colom F, Pålsson E, et al. Psychoeducation for bipolar disorder and risk of recurrence and hospitalization - a within-individual analysis using registry data. Psychol Med 2020 Apr;50(6):1043-1049 [FREE Full text] [doi: 10.1017/S0033291719001053] [Medline: 31057138]
22. Brijnath B, Protheroe J, Mahtani KR, Antoniades J. Do web-based mental health literacy interventions improve the mental health literacy of adult consumers? Results from a systematic review. J Med Internet Res 2016 Jun 20;18(6):e165 [FREE Full text] [doi: 10.2196/jmir.5463] [Medline: 27323907]
23. Lam NHT, Tsiang JT, Woo BKP. Exploring the role of YouTube in disseminating psychoeducation. Acad Psychiatry 2017 Dec;41(6):819-822. [doi: 10.1007/s40596-017-0835-9] [Medline: 29022242]
24. Depp CA, Ceglowski J, Wang VC, Yaghouti F, Mausbach BT, Thompson WK, et al. Augmenting psychoeducation with a mobile intervention for bipolar disorder: a randomized controlled trial. J Affect Disord 2015 Mar 15;174:23-30 [FREE Full text] [doi: 10.1016/j.jad.2014.10.053] [Medline: 25479050]
25. Rai S, Mishra BR, Sarkar S, Praharaj SK, Das S, Maiti R, et al. Higher impulsivity and HIV-risk taking behaviour in males with alcohol dependence compared to bipolar mania: a pilot study. Community Ment Health J 2018 Feb;54(2):218-223. [doi: 10.1007/s10597-017-0139-2] [Medline: 28456858]
26. Grunze H, Schaefer M, Scherk H, Born C, Preuss UW. Comorbid bipolar and alcohol use disorder-a therapeutic challenge. Front Psychiatry 2021;12:660432 [FREE Full text] [doi: 10.3389/fpsyt.2021.660432] [Medline: 33833701]
27. Bauer M, Glenn T, Alda M, Bauer R, Grof P, Marsh W, et al. Trajectories of adherence to mood stabilizers in patients with bipolar disorder. Int J Bipolar Disord 2019 Sep 04;7(1):19 [FREE Full text] [doi: 10.1186/s40345-019-0154-z] [Medline: 31482209]
28. Crowe M, Eggleston K, Douglas K, Porter RJ. Effects of psychotherapy on comorbid bipolar disorder and substance use disorder: A systematic review. Bipolar Disord 2021 Mar;23(2):141-151. [doi: 10.1111/bdi.12971] [Medline: 32615028]
29. Konstantinou P, Kassianos AP, Georgiou G, Panayides A, Papageorgiou A, Almas I, et al. Barriers, facilitators, and interventions for medication adherence across chronic conditions with the highest non-adherence rates: a scoping review with recommendations for intervention development. Transl Behav Med 2020 Dec 31;10(6):1390-1398. [doi: 10.1093/tbm/ibaa118] [Medline: 33231691]
30. Mirzania M, Khajavi A, Kharazmi A, Moshki M. Health literacy and quality of life among Iranian pregnant women: The mediating role of health locus of control. Med J Islam Repub Iran 2020;34:161 [FREE Full text] [doi: 10.47176/mjiri.34.161] [Medline: 33816360]
31. Kassianos AP, Raats MM, Gage H. Post-diagnostic dietary changes in prostate cancer: associations with patients' wellbeing and the perceptions of GPs. Eur J Cancer Care (Engl) 2017 Jul;26(4):e12599. [doi: 10.1111/ecc.12599] [Medline: 27774678]
32. Tawfik GM, Dila KAS, Mohamed MYF, Tam DNH, Kien ND, Ahmed AM, et al. A step by step guide for conducting a systematic review and meta-analysis with simulation data. Trop Med Health 2019;47:46 [FREE Full text] [doi: 10.1186/s41182-019-0165-6] [Medline: 31388330]
33. Colom F, Vieta E. Psychoeducation manual for bipolar disorder. New York: Cambridge University Press; 2006.
34. Ramirez Basco M, Ruch AJ. Cognitive-behavioral therapy for bipolar disorder. Second edition. New York: The Guilford Press; 2007.
35. Quality Assessment Tool - Review Articles. Health Evidence. URL: https://www.healthevidence.org/documents/our-appraisal-tools/quality-assessment-tool-dictionary-en.pdf [accessed 2021-08-16]
36. Holloway I, Wheeler S. Qualitative research in nursing Immy Holloway Qualitative research in nursing and Stephanie Wheeler Blackwell 304 £18.99 0632052848 0632052848 [Formula: see text]. Nurse Res 2003 Oct 01;11(1):87. [doi: 10.7748/nr.11.1.87.s16] [Medline: 27702197]
37. Saunders B, Sim J, Kingstone T, Baker S, Waterfield J, Bartlam B, et al. Saturation in qualitative research: exploring its conceptualization and operationalization. Qual Quant 2018;52(4):1893-1907 [FREE Full text] [doi: 10.1007/s11135-017-0574-8] [Medline: 29937585]
38. Munhall P. Nursing research: A qualitative perspective. Sudbury, Ontario: Jones & Bartlett Learning; 2012.
39. Morse JM. "Data were saturated . . . ". Qual Health Res 2015 May;25(5):587-588. [doi: 10.1177/1049732315576699] [Medline: 25829508]
40. Kaite CP, Karanikola MN, Vouzavali FJD, Koutroubas A, Merkouris A, Papathanassoglou EDE. The experience of Greek-Cypriot individuals living with mental illness: preliminary results of a phenomenological study. BMC Psychiatry 2016 Oct 06;16(1):343 [FREE Full text] [doi: 10.1186/s12888-016-1051-y] [Medline: 27716117]
41. Karanikola MN. Content analysis in critical and emergency care: a discussion paper. World Crit Care Nurs 2019 Aug 29;13(1):8-23. [doi: 10.1891/1748-6254.13.1.8]
42. Kaufman AS. Test Review: Wechsler, D. Manual for the Wechsler Adult Intelligence Scale, Revised. New York: Psychological Corporation, 1981. J Psychoeduc Assess 1983;1(3):309-313. [doi: 10.1177/073428298300100310]
43. Young RC, Biggs JT, Ziegler VE, Meyer DA. A rating scale for mania: reliability, validity and sensitivity. Br J Psychiatry 1978 Nov;133:429-435. [doi: 10.1192/bjp.133.5.429] [Medline: 728692]

44. Beck Depression Inventory-II manual. Brown School of Public Health. 1996. URL: https://www.brown.edu/academics/public-health/research/mens-health-initiative/bdiii [accessed 2020-03-06]
45. Babor TF, Higgins-Biddle JC, Saunders JB, Monteiro MG. AUDIT: the Alcohol Use Disorders Identification Test (AUTIT): Guidelines for use in primary health care. World Health Organization. 2001. URL: https://apps.who.int/iris/handle/10665/67205 [accessed 2020-11-10]
46. Berman A, Bergman H, Palmstierna T, Schlyter F. Drug Use Disorders Identification Test (DUDIT). European Monitoring Centre for Drugs and Drug Addiction. 2005. URL: https://www.emcdda.europa.eu/drugs-library/drug-use-disorders-identification-test-dudit_en [accessed 2020-11-10]
47. World Health Organization. World Health Organization Quality of Life Instruments (WHOQOL-BREF) Introduction, administration, scoring and generic version of the assessment. URL: https://www.who.int/mental_health/media/en/76.pdf [accessed 2020-11-10]
48. Wallston KA. The validity of the multidimensional health locus of control scales. J Health Psychol 2005 Sep;10(5):623-631. [doi: 10.1177/1359105305055304] [Medline: 16033784]
49. Hogan TP, Awad AG, Eastwood R. A self-report scale predictive of drug compliance in schizophrenics: reliability and discriminative validity. Psychol Med 1983 Feb;13(1):177-183. [doi: 10.1017/s0033291700050182] [Medline: 6133297]
50. Stump TA, Eng ML. The development and psychometric properties of the bipolar disorders knowledge scale. J Affect Disord 2018 Oct 01;238:645-650. [doi: 10.1016/j.jad.2018.05.043] [Medline: 29957482]
51. Hidalgo-Mazzei D, Mateu A, Reinares M, Murru A, Del Mar Bonnín C, Varo C, et al. Psychoeducation in bipolar disorder with a SIMPLe smartphone application: Feasibility, acceptability and satisfaction. J Affect Disord 2016 Aug;200:58-66. [doi: 10.1016/j.jad.2016.04.042] [Medline: 27128358]
52. MOB (Management of my Bipolarity) platform. URL: https://mob.com.cy/ [accessed 2021-08-07]
53. Even C, Thuile J, Kalck-Stern M, Criquillion-Doublet S, Gorwood P, Rouillon F. Psychoeducation for patients with bipolar disorder receiving lithium: short and long term impact on locus of control and knowledge about lithium. J Affect Disord 2010 Jun;123(1-3):299-302. [doi: 10.1016/j.jad.2009.09.008] [Medline: 19815295]
54. Eker F, Harkın S. Effectiveness of six-week psychoeducation program on adherence of patients with bipolar affective disorder. J Affect Disord 2012 May;138(3):409-416. [doi: 10.1016/j.jad.2012.01.004] [Medline: 22316565]
55. Faria AD, de Mattos Souza LD, de Azevedo Cardoso T, Pinheiro KAT, Pinheiro RT, da Silva RA, et al. The influence of psychoeducation on regulating biological rhythm in a sample of patients with bipolar II disorder: a randomized clinical trial. Psychol Res Behav Manag 2014;7:167-174. [doi: 10.2147/PRBM.S52352] [Medline: 25061340]
56. Proudfoot J, Parker G, Manicavasagar V, Hadzi-Pavlovic D, Whitton A, Nicholas J, et al. Effects of adjunctive peer support on perceptions of illness control and understanding in an online psychoeducation program for bipolar disorder: a randomised controlled trial. J Affect Disord 2012 Dec 15;142(1-3):98-105. [doi: 10.1016/j.jad.2012.04.007] [Medline: 22858215]
57. Kurdal E, Tanriverdi D, Savas HA. The effect of psychoeducation on the functioning level of patients with bipolar disorder. West J Nurs Res 2014 Mar;36(3):312-328. [doi: 10.1177/0193945913504038] [Medline: 24025221]
58. Candini V, Buizza C, Ferrari C, Caldera MT, Ermentini R, Ghilardi A, et al. Is structured group psychoeducation for bipolar patients effective in ordinary mental health services? A controlled trial in Italy. J Affect Disord 2013 Oct;151(1):149-155. [doi: 10.1016/j.jad.2013.05.069] [Medline: 23816448]
59. Van Dijk S, Jeffrey J, Katz MR. A randomized, controlled, pilot study of dialectical behavior therapy skills in a psychoeducational group for individuals with bipolar disorder. J Affect Disord 2013 Mar 05;145(3):386-393. [doi: 10.1016/j.jad.2012.05.054] [Medline: 22858264]
60. Javadpour A, Hedayati A, Dehbozorgi G, Azizi A. The impact of a simple individual psycho-education program on quality of life, rate of relapse and medication adherence in bipolar disorder patients. Asian J Psychiatr 2013 Jun;6(3):208-213. [doi: 10.1016/j.ajp.2012.12.005] [Medline: 23642977]
61. de Barros Pellegrinelli K, de O Costa LF, Silval KID, Dias VV, Roso MC, Bandeira M, et al. Efficacy of psychoeducation on symptomatic and functional recovery in bipolar disorder. Acta Psychiatr Scand 2013 Feb;127(2):153-158. [doi: 10.1111/acps.12007] [Medline: 22943487]
62. Todd NJ, Jones SH, Hart A, Lobban FA. A web-based self-management intervention for Bipolar Disorder 'living with bipolar': a feasibility randomised controlled trial. J Affect Disord 2014 Dec;169:21-29. [doi: 10.1016/j.jad.2014.07.027] [Medline: 25129531]
63. Çuhadar D, Çam MO. Effectiveness of psychoeducation in reducing internalized stigmatization in patients with bipolar disorder. Arch Psychiatr Nurs 2014 Feb;28(1):62-66. [doi: 10.1016/j.apnu.2013.10.008] [Medline: 24506989]
64. Rahmani F, Ranjbar F, Ebrahimi H, Hosseinzadeh M. The effects of group psychoeducational programme on attitude toward mental illness in families of patients with schizophrenia, 2014. J Caring Sci 2015;4(3):243-251 [FREE Full text] [doi: 10.15171/jcs.2015.025] [Medline: 26464841]
65. Gumus F, Buzlu S, Cakir S. Effectiveness of individual psychoeducation on recurrence in bipolar disorder; a controlled study. Arch Psychiatr Nurs 2015 Jun;29(3):174-179. [doi: 10.1016/j.apnu.2015.01.005] [Medline: 26001717]
66. Chen C, Lo F, Chen B, Lu M, Hsin Y, Wang R. Pathways of emotional autonomy, self-care behaviors, and depressive symptoms on health adaptation in adolescents with type 1 diabetes. Nurs Outlook 2017;65(1):68-76. [doi: 10.1016/j.outlook.2016.07.015] [Medline: 27640101]

67. Bipolar Disorder: the assessment and management of bipolar disorder in adults, children and young people in primary and secondary care. National Institute for Health and Care Excellence (NICE). 2014. URL: https://www.nice.org.uk/guidance/cg185 [accessed 2020-12-13]
68. Goodwin GM, Haddad PM, Ferrier IN, Aronson JK, Barnes T, Cipriani A, et al. Evidence-based guidelines for treating bipolar disorder: Revised third edition recommendations from the British Association for Psychopharmacology. J Psychopharmacol 2016 Jun;30(6):495-553 [FREE Full text] [doi: 10.1177/0269881116636545] [Medline: 26979387]
69. Bond K, Anderson IM. Psychoeducation for relapse prevention in bipolar disorder: a systematic review of efficacy in randomized controlled trials. Bipolar Disord 2015 Jun;17(4):349-362. [doi: 10.1111/bdi.12287] [Medline: 25594775]
70. Bipolar disorder. National Institute of Mental Health. URL: https://www.nimh.nih.gov/health/statistics/bipolar-disorder [accessed 2021-08-16]
71. Health hospital statistics. Cyprus Statistical Office. URL: https://www.mof.gov.cy/mof/cystat/statistics.nsf/All/F9690C2D35652CB5C2257726003DDA8F/$file/HEALTH_HOSPITAL_STATS-2018-EL-130520.pdf [accessed 2020-09-21]
72. Marwaha S, Sal N, Bebbington P. Bipolar disorder. Adult Psychiatric Morbidity Survey. 2014. URL: http://wrap.warwick.ac.uk/83135/1/WRAP_apms-2014-bipolar%20(1).pdf [accessed 2020-12-13]
73. Fountoulakis KN, Kasper S, Andreassen O, Blier P, Okasha A, Severus E, et al. Efficacy of pharmacotherapy in bipolar disorder: a report by the WPA section on pharmacopsychiatry. Eur Arch Psychiatry Clin Neurosci 2012 Jun;262(Suppl 1):1-48. [doi: 10.1007/s00406-012-0323-x] [Medline: 22622948]
74. Joyce K, Thompson A, Marwaha S. Is treatment for bipolar disorder more effective earlier in illness course? A comprehensive literature review. Int J Bipolar Disord 2016 Dec;4(1):19 [FREE Full text] [doi: 10.1186/s40345-016-0060-6] [Medline: 27613276]
75. Lublóy Á, Keresztúri JL, Németh A, Mihalicza P. Exploring factors of diagnostic delay for patients with bipolar disorder: a population-based cohort study. BMC Psychiatry 2020 Feb 19;20(1):75 [FREE Full text] [doi: 10.1186/s12888-020-2483-y] [Medline: 32075625]
76. Chiapperino L, Tengland P. Empowerment in healthcare policy making: three domains of substantive controversy. Health Promot J Austr 2015 Dec;26(3):210-215. [doi: 10.1071/HE15035] [Medline: 26650538]
77. Kayser L, Karnoe A, Duminski E, Somekh D, Vera-Muñoz C. A new understanding of health related empowerment in the context of an active and healthy ageing. BMC Health Serv Res 2019 Apr 24;19(1):242 [FREE Full text] [doi: 10.1186/s12913-019-4082-5] [Medline: 31014350]
78. Yang L, Wu Q, Hao Y, Cui Y, Liang L, Gao L, et al. Self-management behavior among patients with diabetic retinopathy in the community: a structural equation model. Qual Life Res 2017 Feb;26(2):359-366. [doi: 10.1007/s11136-016-1396-1] [Medline: 27592109]
79. Lloyd C, Campion DP. Occupational stress and the importance of self-care and resilience: focus on veterinary nursing. Ir Vet J 2017;70:30 [FREE Full text] [doi: 10.1186/s13620-017-0108-7] [Medline: 29021894]

Abbreviations

AUDIT: Alcohol Use Disorders Identification Test
BD: bipolar disorder
BDKS: Bipolar Disorder Knowledge Scale
DAI-30: Drug Attitude Inventory
DUDIT: Drug Use Disorders Identification Test
MHLC: Multidimensional Health Locus of Control
MoB: Management of my Bipolarity
WHOQOL: World Health Organization Quality of Life Assessment B
YMRS: Young Mania Rating Scale

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Protocol

Health Behavior Survey Among People Who Use Opioids: Protocol for Implementing Technology-Based Rapid Response Surveillance in Community Settings

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Abstract

Background: In 2018, 2 million Americans met the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition diagnostic criteria for an opioid use disorder, and 9.9 million Americans had misused prescription pain relievers the previous year. Despite a rapid increase in opioid misuse, opioid use disorders, and overdoses, data are limited on the behavioral and contextual risks as well as the protective factors fueling the opioid epidemic in some hard hit US cities—Atlanta, Los Angeles, and Las Vegas. Opioid use also contributes to the risk of other health problems such as HIV and hepatitis C virus infections or mental health disorders and is linked to behavioral and environmental risks (eg, homelessness, experiences of violence, involvement in the justice system). Knowledge of the relationships between these linked vulnerabilities and how they influence service utilization is critical to effective policy and interventions.

Objective: This survey explores the relationships between demographic and economic characteristics, behavioral and environmental risk factors, and service utilization of people who use opioids to inform public health practice, policy, and future efforts to mitigate the risks faced by this population experiencing multiple health, social, and economic vulnerabilities. The results of this survey will be used to identify needs and intervention points for people who use drugs currently served by public health organizations.

Methods: We implemented a community-engaged strategy that involved development and execution of a two-stage purposive sampling plan involving selection of partner organizations (syringe exchange programs in urban settings) and recruitment and enrollment of participants aged 18-69 years served by these organizations in Atlanta, Los Angeles, and Las Vegas from 2019 to 2020. The recruited participants completed a survey, including a variety of measures to assess health (physical and mental) and health behaviors such as sexual behavior, vaccine receipt, and HIV/ hepatitis C virus infection testing. Additional items assessed drug use and misuse, syringe exchange and health service utilization, sex exchange, histories of interpersonal violence, and vaccine confidence.

Results: This protocol was successfully implemented despite challenges such as real-time technology issues and rapidly finding and surveying a difficult-to-reach population. We sampled 1127 unique participants (248 in Atlanta, 465 in Los Angeles, and 414 in Las Vegas).

Conclusions: The establishment and utilization of strong community partnerships enabled the rapid collection of data from a typically difficult-to-reach population. Local efforts such as these are needed to develop policies and practices that promote harm reduction among people who use opioids.

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KEYWORDS

substance use; opioid; opioid crisis; social determinants; hidden populations; health equity

Introduction

Modifications in use and prescription practices of opioids in the late 1990s caused a major shift in the mindset toward opioids among the general public as well as among health care professionals [1]. Aggressive marketing campaigns from pharmaceutical companies created an increase in the number of prescriptions written to combat noncancer pain in patients. As an October 2020 settlement with the United States Department of Justice stipulates, the industry adopted practices that led to a rapid proliferation of abuse of both prescription and nonprescription opioids.

According to the National Survey on Drug Use and Health, over 10 million people in the United States aged 12 years or older (roughly 4% of the total population) misused opioids in 2018 [2]. Nearly 10 million of these individuals reported prescription pain reliever misuse, and 808,000 reported using heroin [2]. That same year, an estimated 2 million people aged 12 years or older had an opioid use disorder (less than 1% of the population) [2]. However, among those who met the criteria for an opioid use disorder, only about 400,000 (19.7%) received drug use treatment at a specialty facility in the past year (eg, inpatient hospital, inpatient or outpatient drug or alcohol rehabilitation facility, inpatient or outpatient mental health center) [2].

Synthetic opioids have become a major contributor to the significant increase in opioid-related overdose deaths in the United States [3]. The United States Centers for Disease Control and Prevention reported that more than 31,000 fentanyl-related fatalities occurred in the United States in 2018, accounting for the most deaths among any type of opioids [4]. More specifically, death rates associated with synthetic opioids increased by 10% from 2017 to 2018 [4]. Other data suggest that many people who inject drugs were unaware or suspect that their drugs contain fentanyl more often than not [5,6], thereby exponentially increasing their risk of opioid-related overdose and death. Furthermore, data from 2018 estimated that, on a daily basis, 128 Americans die as a result of opioid-related overdoses, which reiterates a serious national and public health concern [7].

The impact of the opioid epidemic in the United States on public health extends beyond opioid-related fatalities. Additional public health consequences related to opioid misuse and opioid use disorders include an increase in HIV/hepatitis C virus infections and other infections among persons who inject drugs [8-10]. The United States Centers for Disease Control and Prevention reported that, in 2018, 1 in 15 new HIV diagnoses in the United States occurred among persons who inject drugs [11]. Additional concerns included increased risk of neonatal abstinence syndrome and other fetal and birth complications [12], health and safety of children whose parents are active users [13], impact on mental health [14], impact on first responders and other health care professionals [15], and economic costs [16].

More recently, opioid drug overdoses have increased as a result of the COVID-19 pandemic [17]. More than 40 states have reported not only increases in opioid-related mortalities but also concerns for those experiencing mental illness or substance use disorders [17]. According to the Overdose Detection Mapping Application Program, the proportion of suspected overdoses in the United States has jumped from 18% in March 2020 to 42% in May 2020 [18]. Some attribute this rise in overdoses to the directives for social distancing resulting in isolation, while others have noted considerable increases in alcohol and other substance use since the COVID-19 pandemic began [19]. It has also been suggested that impacts to the drug supply have resulted in users turning to new substances or dealers [19].

Given these findings regarding the public health consequences associated with opioid use, it is vital to gain additional information relative to the behavioral and contextual risk and protective factors fueling the current epidemic. Prior studies have identified correlations between opioid abuse and behavioral and environmental risks, including high-risk sexual behavior [20,21], homelessness [22,23], experiences of violence [24], and involvement in the justice system [25]. Further, previous studies have indicated that people who use opioids also display higher rates of serious mental illness [26], which can compound other issues of substance abuse [27]. However, many of these domains are sparse, and studies are often restricted to emergency room patients or are limited in scope and geographic coverage. Additionally, to our knowledge, no prior research has estimated vaccination coverage or confidence among people who use opioids. Strategies focused on harm reduction will not only inform public health practice and policy but also mitigate the risks faced by vulnerable populations. Our project has been developed to expand our knowledge of these behavioral and contextual risks and to address our limited knowledge of these barriers and intervention points.

Through the development and maintenance of strong partnerships with community organizations serving people who use opioids, we were able to work with client populations that are normally difficult to engage in data collection efforts related to their health behaviors and drug use. To characterize the health status and behaviors of people who use opioids and utilize services at community organizations, we partnered with community organizations providing syringe exchange services in 3 US cities to recruit people who use opioids to participate in a comprehensive health and behavior questionnaire, which was designed to capture the following project goals:

1. Assess the behavioral (drug use patterns, vaccination status, pre-exposure prophylaxis use, sexual behavior, etc) and environmental (homelessness, experiences with violence, etc) health risks faced by people who use opioids who are clients of community health organizations.
2. Examine barriers and facilitators of access to health and life services, such as financial support, insurance, access to transportation, and social support networks.

3. Determine utilization of health and life services from the partner community health organizations and from other sources to identify service gaps that could be targeted by interventions and community organizations.

The results of these analyses will be used to identify needs and intervention points for people who use opioids who use services at community health organizations and to help inform service provision and policy.

Methods

Site and Partnering Organization Selection

The sampling strategy included a recruitment plan of up to 1200 individuals who identified as clients of partnering organizations. Data collection sites were chosen based on characteristics of the population of people using opioids, particularly those who may be vulnerable to HIV, viral hepatitis, vaccine-preventable diseases, and opioid use. The selected cities were Atlanta, Georgia; Los Angeles, California; and Las Vegas, Nevada. We engaged partners with whom the project leadership team has spent several years cultivating collaborative relationships. These partnerships have emerged from the project faculty reaching out to organizations to gauge interest in partnering on various field-based efforts related to service provision, health outcomes, and public policies that impact their client populations. The partners engaged in our efforts had well-established syringe services and a demonstrated track record of success serving diverse clients in a variety of settings. Atlanta's primary partner organization provides syringe services through a mobile program, with established locations in the community where individuals can come on set days/times, as well as community outreach at homeless encampments and other known drug use locations. Our primary Los Angeles partner is a community-based health care and social services organization working to identify and address emerging health issues faced by the Latino and lesbian, gay, bisexual, transgender, and queer (LGBTQ+) communities. They provide syringe services at one of their brick-and-mortar sites as well as through a mobile program. The Las Vegas partner provides services at a brick-and-mortar site and through a mobile program, as well as through local vending machines and delivering materials to their clients' homes via FedEx. The organization aims to reduce the risk of negative behavioral consequences while eliminating the stigma associated with drug use. These community partners were selected in part for variation in operations, as this would provide for a better assessment of the differences in their operations and their ability to provide services. As needed, we supplemented our sample with participants recruited from similar entities servicing these communities; in Atlanta, we supplemented with another organization, and in Los Angeles, we supplemented with 2 additional agencies.

Participant Inclusion and Exclusion Criteria

Eligible participants included those who had accessed the designated partner's services. Potential participants reported using opioids at least once in the previous 6 months, being 18-69 years of age, having English or Spanish language comprehension (reading or speaking), and were able to voluntarily consent to participation. Exclusion criteria were inability to provide voluntary consent (for any reason) and failure to meet other inclusion criteria. Pregnant women were not a target population for this survey project; yet, they were not explicitly excluded if they met all the inclusion criteria.

Sampling Plan and Sample Size

We used a two-stage purposive sampling plan: (1) selection of the partner organizations and (2) recruitment and enrollment of clients utilizing services from these entities. Sites were selected based on being operational for at least two years and having a variety of service delivery modes (eg, entirely mobile, combination brick and mortar/mobile services). Recruitment and enrollment of participating individuals were based on the eligibility criteria and sampling frame. Purposive sampling is based on having strong theoretical reasons for inclusion of cases in the sample. In contrast to probabilistic methods, purposive sampling draws on theory and empirical data to select the most information-rich cases to inform the project aims in question while having sufficient variation to allow for analytic comparisons [17]. Variations for this project included selected partner sites, each of which operates under different state-based regulations and differs in service provision. We also sought to have varied distribution by race, ethnicity, and gender identity across the 3 sites. The planned variation by these characteristics was based on anecdotal data about the differences in this population's lived experiences and perceived needs, barriers, and facilitators to accessing services. We were also mindful of capturing a spectrum of ages across the eligible 18-69 years of age range. A sampling target of 400 per city (total of 1200) was chosen to fit within funding restraints while providing an adequate sample size for city-specific and comparative analyses. This sampling target also ensured adequate samples of subpopulations such as LGBTQ+ gender identity.

Staff Training

Project staff were recruited to the team by the University of Nevada, Las Vegas and the University of California, Los Angeles project leaders, including community members, students, and young professionals who expressed interest in the topic area and had demonstrated exemplary skills, subject matter knowledge, and experience in similar roles with the populations of interest. At the outset of the training process, all field staff were required to complete Collaborative Institutional Training Initiative trainings related to ethics and procedures. Survey-specific training included a full-day review of best practices in survey methods as well as methods for interacting with at-risk socially and economically disadvantaged populations. The staff discussed appropriate methods for selecting participants in field settings and team-based assessment procedures to ensure that potential participants were not currently under the influence of impairing drugs or alcohol prior to consent. The training detailed the manner in which partner staff were provided an opportunity to identify potential participants, given their experience and knowledge of clients in the local population. During the training events in each selected city, the team also took time to navigate the survey on the tablet to become comfortable with the format and to identify strategies to address potential issues that participants might experience. As diverse staff were hired to conduct the survey,

including those bilingual in English and Spanish, project leaders spent considerable time during training to ensure that survey procedures, instructions, and domain items were clear to all team members by using both languages prior to field initiation. This process also allowed the team to check survey skip and display logic to ensure proper survey flow and item interpretation. Quality assurance procedures were also identified and discussed in the one-day trainings, including details on potential mitigation strategies. All project staff conducting surveys, as well as its team leaders in each city, participated in face-to-face and follow-up trainings on the instruments and procedures, including a review of acceptable strategies to approach potential participants for data collection.

Field Recruitment Process

The partner organizations assisted in identifying the best approaches for recruitment of their clients, scheduling data collection periods, and performing data collection in diverse field settings (eg, during mobile outreach services). Participating partners designated point-of-contact community-based organization (CBO) staff who could answer questions about the project and redirect those interested in speaking to designated project recruiters as needed. Potentially eligible participants were screened in-person at specific locations during data collection events. All recruiters assessed eligibility via the established electronic tablet-based screener. The screening tool allowed the team to collect data confidentially as no identifying information was needed from participants and provided us the opportunity to collect consent electronically without collecting the name or signature on consent documents. In addition to determining eligibility, the screening process also included basic demographic questions (eg, age, race/ethnicity). Screening took no more than 3 minutes to complete.

Informed Consent

Survey procedures involved a two-stage consent process. Initial consent, conducted at the beginning of the screening process, took place before any questions were asked. This initial abridged consent described the project aims, including the length of time required for participation, the participants' rights not to answer any question(s) they did not wish to answer, the right to leave at any time, and notice that the information they provided would be destroyed if they chose not to participate, and concluded by asking for their consent to proceed. The initial consent was used because the screeners included eligibility as well as demographic questions. These data were linked via a unique identification number to the survey; thus, we sought to ensure that participants understood and accepted this process prior to answering any questions. At the end of the screening process, the survey automatically directed eligible participants to our web-based informed consent form where participants provided consent and were able to continue to the rest of the survey questions. The web-based consent process reiterated the information previously shared during the initial consent. During both consent processes, participants were given an opportunity to ask questions and receive additional information before providing consent. The reading level for the electronic consent was no higher than an eighth-grade level on the Flesch-Kincaid reading scale. Participants were recruited and surveyed at sites where they already received services of value to their health. At each location, participants were able to take a nominal well-being item typically available at the sites for clients (eg, hand sanitizer, hygiene kit, sunscreen).

Data Collection Instruments

In addition to the informed consent form and screener, data were collected using a Qualtrics-based questionnaire on a Wi-Fi–enabled iPad. A high-quality data collection instrument was developed to address the constructs of interest, maximize participant engagement, minimize missing data, and minimize participant burden. These goals guided the development of the screener and the survey. Program staff from participating organizations and other subject matter experts provided feedback on the survey which the team used to refine survey questions. The survey took approximately 20-30 minutes to complete (median 23 minutes, IQR 17-31 minutes). Our survey instruments in English and Spanish asked about participant sociodemographic data, health behaviors (including sexual behavior, vaccination, HIV and hepatitis C virus testing), health literacy, co-occurring psychiatric symptoms, legal issues (including knowledge of Good Samaritan laws and incarceration history), history of traumatic experiences, social networks, drug and alcohol usage, media use, intervention access, and CBO service utilization. A description of the content domains and example items are available in Multimedia Appendix 1 (Table S1). Psychometric instruments were drawn from valid and reliable measures: vaccine confidence was assessed using a version of the Emory Vaccine Confidence Index modified for adult vaccination [28], mental distress was measured using the K6 scale [29], health literacy assessment used the 3-item scale of Chew et al [30], and the DUDIT-E instrument was used to measure the motivation to change substance abuse behavior [31]. Other items were drawn from prior surveys when available and from subject area expertise.

Technology Adoption and Data Collection Procedures

Participants were identified by an identification number only. We obtained demographic information during the screener and survey, which was collected on a Health Insurance Portability and Accountability Act (HIPAA)–compliant survey administration platform, that is, Qualtrics (Provo, UT). HITECH (Health Information Technology for Economic and Clinical Health Act) updated HIPAA rules to ensure that data were properly protected and the best security practices followed. Qualtrics safeguards all data and uses secure data centers to ensure the highest protection per HITECH requirements.

Data Analysis

The protocol data analysis plans include univariate and multivariate statistical techniques to understand factors related to opioid use as well as perceived needs related to HIV/hepatitis C virus infections and other partner agency services among people who use opioids in and across the 3 cities. Planned analyses include assessments of the following:

1. Vaccination coverage and vaccine confidence.
2. Acceptability of injectable pre-exposure prophylaxis among people who inject drugs.

3. Prevalence of mental distress and its association with violence and victimization.
4. Knowledge of and attitudes toward Good Samaritan laws.
5. Current CBO service and other health services utilization, desired services, and potential barriers to service utilization.
6. Patterns of substance use, including alcohol and tobacco, and attitudes toward substance abuse.

These assessments will also include comprehensive analyses of the associated risk and protective factors. Estimates of bivariate associations will be used to describe population-level trends, while appropriate multivariable models will allow adjustment for relationships between independent factors. Data analyses associated with specific survey construct domains are described in Table S1 of Multimedia Appendix 1.

Institutional Review Board Approval

Project protocols were reviewed and given an exempt determination by the University of Nevada, Las Vegas Institutional Review Board, followed by independent institutional review board reviews with Emory University, University of California, Los Angeles, and College of Mount Saint Vincent for secondary analyses determination.

Results

Through data collection, 1368 individual surveys were started across the 3 sites from May 2019 through February 2020. The majority (1127/1368, 82.4%) of the participants who started the survey completed it and met our eligibility criteria. In total, 1127 participants met the eligibility criteria and completed the survey (Atlanta, n=248; Los Angeles, n=465; Las Vegas, n=414).

Discussion

Procedural Advantages of Technology Adoption

Our use of tablets allowed us to strengthen our recruitment efforts for opioid users who may have variable transience among the population and be harder to reach. Utilizing the tablets allowed our team members to conduct recruitment while in brick-and-mortar partner agency locations and participate in mobile outreach, which occurred in all 3 of our sites. Our use of technology also allowed our recruiters to troubleshoot issues in survey completion while participants self-administered the survey. For example, some participants had issues with visual impairment, making use of the electronic tablets difficult to complete the survey in a timely manner; however, we were able to adjust the font size to be easier to read for our participants. Lastly, embracing the web-based Qualtrics platform for survey completion across our 3 sites facilitated immediate review and assessment of collected data and planning for additional data collection needs. Project staff were able to immediately examine patterns in data collection across the 3 sites to identify effective recruitment strategies and modalities in each site (eg, brick-and-mortar compared to mobile outreach). We were also able to identify any potentially problematic questions within the survey and to assess response patterns across the 3 sites to identify participants simply skipping through the survey. Tracking of our participants through web-based channels and close communication with CBO staff members also ensured that no individual participant completed the survey more than once.

Limitations

This effort focused on people who use opioids and reside in 3 cities highly impacted by the US opioid crisis and who receive services through the partnering organizations. We excluded other groups who were known to underutilize HIV, hepatitis C virus, and other prevention and treatment services, such as individuals of 13-17 years of age and people who do not use opioids. Despite efforts to develop an instrument with health literacy in mind (eg, Flesch-Kincaid lower than the eighth-grade reading level), we experienced some item response gaps as some participants were unable to respond to some questions without excessive clarification or direction from staff and were therefore unable to provide complete survey responses. We also encountered a handful of participants who were too inexperienced with technology and could not successfully complete the survey. Finally, across sites, there were other competing ongoing research efforts among the target population, often with higher or more desirable incentives for participation.

Conclusion

We successfully implemented our web-based, tablet-based survey of opioid users across 3 urban sites by enrolling over 1300 unique client participants. Based on our eligibility framework, over 1100 quality answers remained for use during data analysis. Our project was able to successfully navigate collaboration with local agencies to facilitate participant recruitment. Forging relationships with each of the collaborating entities ensured our successful implementation of the survey across our 3 sites while navigating the needs for recruitment in diverse settings (eg, brick-and-mortar facilities, mobile outreach). We avoided any data duplication from participants completing the survey more than once. Our project demonstrated that recruitment of opioid users in these 3 cities is possible by using appropriate methodology by reaching out to this population in environments where they are comfortable, instead of clinical settings. We believe investigators need to understand the participant population and meet them where they are—not only the physical location but also the provision of a survey that is accessible to the various needs of this population. Lessons learned for future in-person data collection with opioid-using populations in these cities include considering staff-facilitated administration of surveys to ensure comprehension of the survey questions, thereby reducing the time needed for survey completion. Additional technological advances could aid in the implementation of the survey. Specifically, because some participants identified low experience with technology (iPad) and limited literacy level or visual impairments, the capability of the survey to automatically be read to the participant, if they choose, could have been immensely useful among this population. Considering these adaptations when developing and designing future research projects focused on this population would facilitate efficient data collection and capture of quality data.

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Authors' Contributions

The details of the HBOU study team are as follows. The subject matter experts were Max Gahk, JD, MPH; Sarah Hunt, PhD; Brian Labus, MPH, PhD; Ayako Miyashita, JD; and Matthew Archibald, PhD. The study staff/data collectors were Mehret Girmay, John Olawepo, Sfurti Maheshwari, Katy Berteau, Elizabeth Wu, Evan Kreuger, Ashleigh Herrera, Tasha Perdue, Mohammed Ahmed, Alberto Gonzales, Do Kin Luong, Cassandra DeWitt, Alicia Morales Perez, Francisco Rodriguez, Jade Dalton, Arthur Sun, Sarah Fiskin, Antonio Shallowhorn, Bernice Lopez, Alexandra (Alex) Michel, Katherine Maxwell, Stephanie Richardson, Allen Welty-Green, Priscilla Smith, and Tracy Thompson. The community partners were Chelsi Cheatom, Robert Contreras, Joanna Barreras, Hugo Aguilar, Esmeralda Limeta, Terri Reynolds, Mojgan Zare, Mona Bennett, and Tracy Thompson.

Conflicts of Interest

ACS's research is in part funded by Gilead. She also serves as a consultant and is on the advisory board for Gilead. ACS receives non-research support from Gilead, Abbvie, Merck, bioLytical Sciences, and Guardian.

Multimedia Appendix 1
Content domains and example items and data analyses associated with specific survey construct domains.
[DOC File , 60 KB - resprot_v10i9e25575_app1.doc]

References

1. Dayer LE, Painter JT, McCain K, King J, Cullen J, Foster HR. A recent history of opioid use in the US: Three decades of change. Subst Use Misuse 2019;54(2):331-339. [doi: 10.1080/10826084.2018.1517175] [Medline: 30572776]
2. Key substance use and mental health indicators in the United States: Results from the 2018 national survey on drug use and health. Substance Abuse and Mental Health Services Administration. URL: https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/NSDUHNationalFindingsReport2018/NSDUHNationalFindingsReport2018.pdf [accessed 2021-06-19]
3. Han Y, Yan W, Zheng Y, Khan MZ, Yuan K, Lu L. The rising crisis of illicit fentanyl use, overdose, and potential therapeutic strategies. Transl Psychiatry 2019 Nov 11;9(1):282 [FREE Full text] [doi: 10.1038/s41398-019-0625-0] [Medline: 31712552]
4. Wilson N, Kariisa M, Seth P, Smith H, Davis NL. Drug and Opioid-Involved Overdose Deaths - United States, 2017-2018. MMWR Morb Mortal Wkly Rep 2020 Mar 20;69(11):290-297 [FREE Full text] [doi: 10.15585/mmwr.mm6911a4] [Medline: 32191688]
5. Park JN, Weir BW, Allen ST, Chaulk P, Sherman SG. Fentanyl-contaminated drugs and non-fatal overdose among people who inject drugs in Baltimore, MD. Harm Reduct J 2018 Jul 05;15(1):34 [FREE Full text] [doi: 10.1186/s12954-018-0240-z] [Medline: 29976195]
6. Amlani A, McKee G, Khamis N, Raghukumar G, Tsang E, Buxton JA. Why the FUSS (Fentanyl Urine Screen Study)? A cross-sectional survey to characterize an emerging threat to people who use drugs in British Columbia, Canada. Harm Reduct J 2015 Nov 14;12:54 [FREE Full text] [doi: 10.1186/s12954-015-0088-4] [Medline: 26577516]
7. Overdose death rates involving opioids, by type, United States 2000-2017. Centers for Disease Control and Prevention. 2020. URL: https://www.cdc.gov/drugoverdose/images/data/OpioidDeathsByTypeUS.PNG [accessed 2021-06-21]
8. Gostin LO, Hodge JG, Noe SA. Reframing the Opioid Epidemic as a National Emergency. JAMA 2017 Oct 24;318(16):1539-1540. [doi: 10.1001/jama.2017.13358] [Medline: 28832871]
9. Powell D, Alpert A, Pacula RL. A Transitioning Epidemic: How The Opioid Crisis Is Driving The Rise In Hepatitis C. Health Aff (Millwood) 2019 Feb;38(2):287-294. [doi: 10.1377/hlthaff.2018.05232] [Medline: 30715966]
10. Anderson ES, Russell C, Basham K, Montgomery M, Lozier H, Crocker A, et al. High prevalence of injection drug use and blood-borne viral infections among patients in an urban emergency department. PLoS One 2020;15(6):e0233927 [FREE Full text] [doi: 10.1371/journal.pone.0233927] [Medline: 32497108]
11. Hess K, Johnson S, Hu X. Diagnoses of HIV infection in the United States and dependent areas, 2017. Centers for Disease Control and Prevention. 2018. URL: https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-2017-vol-29.pdf [accessed 2021-06-19]

12. Jilani SM, Frey MT, Pepin D, Jewell T, Jordan M, Miller AM, et al. Evaluation of State-Mandated Reporting of Neonatal Abstinence Syndrome - Six States, 2013-2017. MMWR Morb Mortal Wkly Rep 2019 Jan 11;68(1):6-10 [FREE Full text] [doi: 10.15585/mmwr.mm6801a2] [Medline: 30629576]
13. Feder KA, Letourneau EJ, Brook J. Children in the Opioid Epidemic: Addressing the Next Generation's Public Health Crisis. Pediatrics 2019 Jan;143(1):e20181656 [FREE Full text] [doi: 10.1542/peds.2018-1656] [Medline: 30514782]
14. Khoury L, Tang YL, Bradley B, Cubells JF, Ressler KJ. Substance use, childhood traumatic experience, and Posttraumatic Stress Disorder in an urban civilian population. Depress Anxiety 2010 Dec;27(12):1077-1086 [FREE Full text] [doi: 10.1002/da.20751] [Medline: 21049532]
15. International Association of Fire Fighters (IAFF). EMS response to opioid overdose and fire fighter health center for excellence. 2018 Presented at: 2018 National Rx Drug Abuse and Heroin Summit; April 2-5; Atlanta, GA URL: https://vendome.swoogo.com/2018-rx-summit/session/59223/ems-response-to-opioid-overdose-and-fire-fighter-behavioral-health-center-of-excellence-hosted-by-international-association-of-fire-fighters-iaff
16. Florence C, Zhou C, Luo F, Xu L. The Economic Burden of Prescription Opioid Overdose, Abuse, and Dependence in the United States, 2013. Med Care 2016 Oct;54(10):901-906 [FREE Full text] [doi: 10.1097/MLR.0000000000000625] [Medline: 27623005]
17. Issue brief: Nation's drug-related overdose and death epidemic continues to worsen. American Medical Association. 2020. URL: https://www.ama-assn.org/system/files/2020-12/issue-brief-increases-in-opioid-related-overdose.pdf [accessed 2021-06-19]
18. Wan W, Long H. 'Cries for help': Drug overdoses are soaring during the coronavirus pandemic. The Washington Post. 2020. URL: https://www.washingtonpost.com/health/2020/07/01/coronavirus-drug-overdose/ [accessed 2021-06-19]
19. Weiner S. COVID-19 and the opioid crisis: When a pandemic and an epidemic collide. Association of American Medical Colleges. 2020. URL: https://www.aamc.org/news-insights/covid-19-and-opioid-crisis-when-pandemic-and-epidemic-collide [accessed 2021-06-19]
20. Meade CS, Bevilacqua LA, Moore ED, Griffin ML, Gardin JG, Potter JS, et al. Concurrent substance abuse is associated with sexual risk behavior among adults seeking treatment for prescription opioid dependence. Am J Addict 2014;23(1):27-33 [FREE Full text] [doi: 10.1111/j.1521-0391.2013.12057.x] [Medline: 24313238]
21. Friedman SR, Mateu-Gelabert P, Ruggles KV, Goodbody E, Syckes C, Jessell L, et al. Sexual Risk and Transmission Behaviors, Partnerships and Settings Among Young Adult Nonmedical Opioid Users in New York City. AIDS Behav 2017 Apr;21(4):994-1003 [FREE Full text] [doi: 10.1007/s10461-016-1672-7] [Medline: 28058567]
22. Doran KM, Rahai N, McCormack RP, Milian J, Shelley D, Rotrosen J, et al. Substance use and homelessness among emergency department patients. Drug Alcohol Depend 2018 Jul 01;188:328-333 [FREE Full text] [doi: 10.1016/j.drugalcdep.2018.04.021] [Medline: 29852450]
23. Yamamoto A, Needleman J, Gelberg L, Kominski G, Shoptaw S, Tsugawa Y. Association between homelessness and opioid overdose and opioid-related hospital admissions/emergency department visits. Soc Sci Med 2019 Dec;242:112585 [FREE Full text] [doi: 10.1016/j.socscimed.2019.112585] [Medline: 31634808]
24. Stone R, Rothman EF. Opioid Use and Intimate Partner Violence: a Systematic Review. Curr Epidemiol Rep 2019 May 1;6(2):215-230. [doi: 10.1007/s40471-019-00197-2]
25. Winkelman TN, Chang VW, Binswanger IA. Health, Polysubstance Use, and Criminal Justice Involvement Among Adults With Varying Levels of Opioid Use. JAMA Netw Open 2018 Jul 06;1(3):e180558 [FREE Full text] [doi: 10.1001/jamanetworkopen.2018.0558] [Medline: 30646016]
26. Jones CM, McCance-Katz EF. Co-occurring substance use and mental disorders among adults with opioid use disorder. Drug Alcohol Depend 2019 Apr 01;197:78-82. [doi: 10.1016/j.drugalcdep.2018.12.030] [Medline: 30784952]
27. Lewer D, Freer J, King E, Larney S, Degenhardt L, Tweed EJ, et al. Frequency of health-care utilization by adults who use illicit drugs: a systematic review and meta-analysis. Addiction 2020 Jun;115(6):1011-1023 [FREE Full text] [doi: 10.1111/add.14892] [Medline: 31705770]
28. Frew PM, Murden R, Mehta CC, Chamberlain AT, Hinman AR, Nowak G, et al. Development of a US trust measure to assess and monitor parental confidence in the vaccine system. Vaccine 2019 Jan 07;37(2):325-332 [FREE Full text] [doi: 10.1016/j.vaccine.2018.09.043] [Medline: 30503657]
29. Furukawa TA, Kessler RC, Slade T, Andrews G. The performance of the K6 and K10 screening scales for psychological distress in the Australian National Survey of Mental Health and Well-Being. Psychol Med 2003 Feb;33(2):357-362. [doi: 10.1017/s0033291702006700] [Medline: 12622315]
30. Chew LD, Bradley KA, Boyko EJ. Brief questions to identify patients with inadequate health literacy. Fam Med 2004 Sep;36(8):588-594 [FREE Full text] [Medline: 15343421]
31. Berman AH, Palmstierna T, Källmén H, Bergman H. The self-report Drug Use Disorders Identification Test: Extended (DUDIT-E): reliability, validity, and motivational index. J Subst Abuse Treat 2007 Jun;32(4):357-369. [doi: 10.1016/j.jsat.2006.10.001] [Medline: 17481459]

Abbreviations

CBO: community-based organization
HIPAA: Health Insurance Portability and Accountability Act
HITECH: Health Information Technology for Economic and Clinical Health Act
LGBTQ: lesbian, gay, bisexual, transgender, and queer

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Protocol

Virtual Clinical and Precision Medicine Tumor Boards—Cloud-Based Platform–Mediated Implementation of Multidisciplinary Reviews Among Oncology Centers in the COVID-19 Era: Protocol for an Observational Study

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Abstract

Background: Multidisciplinary tumor boards play a pivotal role in the patient-centered clinical management and in the decision-making process to provide best evidence-based, diagnostic, and therapeutic care to patients with cancer. Among the barriers to achieve an efficient multidisciplinary tumor board, lack of time and geographical distance play a major role. Therefore, the elaboration of an efficient virtual multidisciplinary tumor board (VMTB) is a key point to successfully obtain an oncology team and implement a network among health professionals and institutions. This need is stronger than ever during the COVID-19 pandemic.

Objective: This paper presents a research protocol for an observational study focused on exploring the structuring process and the implementation of a multi-institutional VMTB in Sicily, Italy. Other endpoints include analysis of cooperation between participants, adherence to guidelines, patients' outcomes, and patient satisfaction.

Methods: This protocol encompasses a pragmatic, observational, multicenter, noninterventional, prospective trial. The study's programmed duration is 5 years, with a half-yearly analysis of the primary and secondary objectives' measurements. Oncology care health professionals from various oncology subspecialties at oncology departments in multiple hospitals (academic and general hospitals as well as tertiary centers and community hospitals) are involved in a nonhierarchic manner. VMTB employs an innovative, virtual, cloud-based platform to share anonymized medical data that are discussed via a videoconferencing system both satisfying security criteria and compliance with the Health Insurance Portability and Accountability Act.

Results: The protocol is part of a larger research project on communication and multidisciplinary collaboration in oncology units and departments spread in the Sicily region. The results of this study will particularly focus on the organization of VMTBs, involving oncology units present in different hospitals spread in the area, and creating a network to allow best patient care pathways and a hub-and-spoke relationship. The present results will also include data concerning organization skills and pitfalls, barriers, efficiency, number, and types with respect to clinical cases and customer satisfaction.

Conclusions: VMTB represents a unique opportunity to optimize patient management through a patient-centered approach. An efficient virtualization and data-banking system is potentially time-saving, a source for outcome data, and a detector of possible holes in the hull of clinical pathways. The observations and results from this VMTB study may hopefully be useful to design nonclinical and organizational interventions that enhance multidisciplinary decision-making in oncology.

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KEYWORDS

virtual tumor board; multidisciplinary collaboration; oncology; multidisciplinary communication; health services; multidisciplinary oncology consultations; virtual health; digital health; precision medicine; tumor; cancer; cloud-based; platform; implementation; oncology; COVID-19

Introduction

Background

Cancer treatment represents a complex pathway that requires the collaboration of various health professionals with complementary skills who work together to share the latest evidence, pool their skills, and exchange information through a regular communication flow [1,2]. Advances in technology and the ability to customize patient treatment plans (target, molecular medical therapy, and radiotherapy) have further increased the need for regular interactions among health care professionals from different areas of expertise [3]. Consequently, in recent decades, scientific evidence has shown that cancer care has increasingly been delivered through multidisciplinary interventions by dedicated teams, the so-called multidisciplinary tumor board (MTB) [4-6].

An MTB is a team of health professionals from different clinical specialties who work together to decide the recommended best clinical pathway for an individual patient [7]. MTB members come together to discuss a series of patients to obtain a definitive staging and formulate a shared treatment plan, considering the best evidence available for personalized treatment options and appropriate follow-up [8,9]. In most cases, the multidisciplinary approach represents a useful platform for coordinating cancer care, as well as a tool for optimizing decision-making and communication processes [10,11]. As a result, MTBs improve health care delivery and the expertise for participating health professionals. Additionally, MTB participants share treatment decisions and clinical responsibility [9,12].

Despite medical literature reporting that the concept of a multidisciplinary approach to cancer treatment since 1975, MTBs in real clinical practice started in the late 1990s. From that point on, the multidisciplinary approach has continually increased, becoming a milestone in many cancer centers and a key moment in treatment plans and guidelines [13]. Over time, MTBs have evolved into a more collaborative structure with teams that pay attention to all aspects of cancer care, including rehabilitation, nutrition, psychosocial needs, and long-term care [12-16]. A few years ago, only a relatively small percentage of patients with cancer benefited from MTB-based care. Such teams currently exist for some cancers in some hospitals, but this is not the rule. Moreover, the increasing complexity of clinical pathways require a stronger interaction between high-volume centers and low-volume and community centers [13]. Before the creation of MTBs, patient evaluations were often carried out, and the oncological treatments often provided, by specialists without all the necessary knowledge and skills related to a specific tumor in terms of continuous training and adherence to local, national, and international guidelines [8,17]. The medical staff often worked in isolation owing to brief and infrequent opportunities for discussion among doctors, surgeons, radiologists, pathologists, and oncologists on the clinical, radiological, and pathological characteristics of individual cases [3,9]. Consequently, some factors relevant to decision-making were overlooked and, in some cases, patients were not considered for other treatments when these might have been useful [18].

More recently, technological advances have made collaboration between MTB members easier by introducing the possibility of “virtual” meetings when team members are not available in person [19,20]. Even if in recent years, the medical/scientific community has rightly focused on the realization of MTB, with the widespread perception that teamwork has brought benefits to patients and improved decision-making, it is necessary to focus on how MTBs function and how they will have to evolve in light of the epochal changes that SARS-CoV-2 induces in the short, medium, and long terms. Awareness of the actual provision of oncological services can help guarantee the quality of services in the face of growing demand and tight budgets through planning of actions that improve the effectiveness or efficacy of health care provision [21]. Thus, there is a need to explore new systems that allow health services professionals to access a multidisciplinary cancer treatment board regardless of their geographic location [7]. Health information technology (HIT) systems and solutions could easily solve many of the problems related to access, collection, organization, and presentation of information for MTBs, thus reducing the need for digitization of workflows [18,22].

The recent COVID-19 pandemic has augmented the necessity of reorganizing MTBs using virtual, commercially available, web-based conversation platforms [23]. Therefore, implementation of virtual multidisciplinary tumor boards (VMTBs) is a research priority which requires, regardless of technical aspects, a cultural, behavioral, and organizational change [5].

Objectives

The aim of the project is to implement a regional wide clinical and precision medicine network and to scale the available platform to optimize its use in most common malignancies such as urogynecologic, gastrointestinal, and thoracic cancers, including breast neoplasms. Implementation of a cloud-based platform may be thwarted by physician-related barriers such as lack of time. The VMTB would support clinical decision-making, reduce unwarranted practice variation across a cancer care system, give comprehensive information about the distance between patients and a potential treatment center, and may avoid costs at hospitals lacking molecular diagnostic

facilities. The VMTB would also facilitate the reporting of key statistics about each case, which will allow administrators to monitor key metrics such as improvements in time from diagnosis to treatment and the impact on patient outcomes.

Methods

Study Design

The study is a pragmatic, observational, multicenter, prospective trial. The study's programmed duration is 5 years, with a half-yearly analysis of the achievement of primary and secondary objectives.

Study Objectives

The aim of this study is to design and implement a VMTB based on the concept of precision and molecular medicine, in the form of a retrospective and prospective observational study within the existing regional oncological care pathways. The study is aimed at allowing: (1) participation of the health professionals involved in oncology management regardless of their location, device used, and timing, so that they can provide information on cases at the best time for them; (2) participation in real-time videoconferencing from anywhere; (3) access via a wide variety of devices (phone, tablet, etc) regardless of the videoconferencing platform; and (4) identification of the most correct and efficient procedures and paths for effective development of a VMTB that can represent an interhospital network and community model.

Primary Endpoints

As stated above, the main objectives are the feasibility and implementation of the VMTB program and acceptance of the VMTB model. Accordingly, feasibility measures include the following: (1) technical failures, defined as the inability to connect institutions; (2) technical problems, defined as equipment malfunction; (3) percentage of planned VMTB cases completed; and (4) duration of VMTB case presentations. A crucial aspect is the organization of all steps necessary to a VMTB, such as identification of participating health professionals, creation of working groups, intergroup communication, interpersonal relations, empowerment of boards, and implementation of the validated clinical pathways. The degree of adhesion of the participants to the VMTB will be measured using survey methods validated in accordance with the Delphi methodology. Each match's degree of confidence will be measured using a 5-point Likert scale where higher scores represent more positive responses.

Secondary Endpoints

Secondary outcomes include data on the use of the VMTB program and its effectiveness in providing access to quality and equitable cancer care, including timely and appropriate review of the multidisciplinary assessment of each case. Timely evaluation should occur within 2 weeks of the initial consultation request. Adequate multidisciplinary evaluation requires correspondence between all current oncology specialties/services and those recommended for each type of cancer in accordance with national and international guidelines (Italian Medical Oncology Association, European Society for Medical Oncology, and the National Comprehensive Cancer Network). Discussions and recommendations on each patient's diagnosis and treatment will need to be in accordance with validated methods (Delphi or Grade) and their adherence to evidence-based medicine, national and international guidelines, or the availability of practice-changing data obtained from recently published controlled trials.

Population and Enrollment

Participation in the project will be extended, in a nonprejudicial manner, to all the centers and professionals involved in a process with subsequent steps. The VMTB will be divided in accordance with disease types, including gynecologic cancers, urologic disease, thoracic neoplasms, and gastrointestinal tumors. Patient inclusion criteria are as follows: any patients with solid malignancy, age > 18 years, written informed consent, and processing of personal health information. Exclusion criteria are life expectancy of less than 6 months, Eastern Cooperative Oncology Group performance status > 3, and absence of informed consent and privacy. A crucial recommendation for the case presenters is to admit initially complex clinical cases, and once the VMTB is functional, to expand the presentation to all possible cases.

Definition of Models of Care

Bulk Consulting Service

The standard method for treating cancer involves a series of specialists, one at a time. This method is least efficient as it often takes weeks or even months outside of large comprehensive cancer centers to complete visits with all consultants involved. This approach usually does not translate into the correct choice of the treatment plan. This approach may result in a nonguideline strategy or, equally negatively, the appropriate treatment sequence may be wrong. Each specialist uses his/her usual methodology throughout the patient care process. Patient satisfaction is low, as the patient travels to multiple locations multiple times and over a long time.

Centralized Model of Multidisciplinary Intervention (Tumor Boards)

An MTB can be a useful structure to offer integrated multi-specialist assistance. If patients present prospectively, different specialists may reach a consensus on the treatment plan and its sequence before initiating any treatment. The timeliness of care may not be solved with this approach, as patients still have to make multiple visits for an extended time.

Role of Telemedicine

One of the difficulties of the current case preparation process is that the information is typically contained in heterogeneous or isolated hospital databases or source systems (electronic or paper medical records, laboratory information systems, image archives, and reporting systems). The data must be collected from each network and compiled in a presentable format in anticipation of a tumor board. Professionals generally assemble this information distinctly from each other. This path creates potential communication errors, missing or duplicated information, or not using the most current information. These, and other potential workflow inefficiencies, often lead to an

increase in team workload. They can also extend the time it takes to determine which treatment plan is most appropriate for a patient. The structural and functional components associated with tumor boards may also contribute to conflicting evidence and opinions regarding the impact of tumor boards on patient care or improvement in outcomes. Telemedicine has proved particularly useful for conducting multidisciplinary meetings and a solution to the downsides of standard model workflows.

Work Teams/Analysis Units

VMTB members and their attendance at meetings depend on several factors, including the hospital's size and the type of cancer. In general, the health professionals eligible to participate as members of VMTB are medical oncologists, radiation oncologists, surgeons, radiologists, pathologists, molecular biologists, organ or branch specialists, nurse specialists, nuclear medicine specialists, doctors of palliative medicine, general practitioners, experts in palliative care, pharmacists, and expert psychologists. Various professionals with a background in related health disciplines, such as genetic consultants, nutritionists, and plastic surgeons, may also be solicited. Finally, there may also be experts specialized in other fields relevant to the site of the tumor. Within VMTBs, identified leaders coordinate the organization of clinical services and management. Members have the level of expertise and specialization required by the MTB in question.

Core Groups

The core groups discuss organization and implementation strategies of each VMTB. As a minimum, the core group includes a surgeon oncologist, a radiotherapist oncologist, a medical oncologist, a radiologist, and a pathologist, and a team/case manager. The core team should include any other crucial professional figure in accordance with the type of disease. There will, therefore, be a core group for each type of cancer.

Extended Groups and Participation

In accordance with the previous statement, the VMTB may include more participants of the same categories as indicated above, who can actively participate in the discussion and drafting of each case's minutes. Many other interested individuals can participate through organized communication. All VMTB members must include and schedule time in their work plans to prepare for and attend scheduled meetings. Core members are present for discussion of all cases where their input is required. The VMTB maintains an attendance register. Extended members and nonmembers participate in patients' cases that are relevant to them.

Leadership

A leader/chairperson of the VMTB and a replacement (for whenever required) need to be identified. The MTB president is responsible for organizing and running the MTB meetings. They prepare and agree over an agenda with the VMTB coordinator; ensure that the meeting agenda is appropriate and take action if not appropriate; ensure that all relevant cases are discussed and prioritized if necessary; ensure that all team members are included in the discussions; ensure that conversations are focused and relevant; ensure good communication and an environment conducive to discussion; promote evidence-based and patient-centered recommendations; ensure that the eligibility for recruitment of relevant clinical trials is considered; ensure that the patient's current discussion and treatment/care plan recommendations are complete before discussion on the next patient begins; provide recordings of relevant demographic and clinical data; ensure that recommendations are clearly summarized, recorded, and passed on to the patient, family doctor, and clinical team within a locally agreed time period; and ensure that it is clear who will take subsequent action after the meeting while also ensuring that the meeting is recorded.

Team Governance

Organizational support for VMTB meetings and membership are based on the premise that VMTB is the model adopted to provide effective and high-quality cancer care, with adequate funding/resources in terms of people, time, equipment, and facilities for VMTB meetings to operate effectively. Participants examine the annual assessments of MTBs and intervene on the problems that have emerged by taking appropriate improvement action.

The purpose of the VMTB and the expected results are clearly defined locally. The policies, guidelines, or protocols agree to evaluate how the MTB functions, who are the main members and extended members, the roles of the members, how members should work together, how changes in clinical practice are to be managed, and how postmeeting communications take place (ie, among patients, general practitioners, and other clinical colleagues). VMTB policies, guidelines, and protocols are reviewed at least annually. Systems are put in place for recording MTB recommendations with respect to actual treatment and warn the VMTB if treatment recommendations are not adopted, along with the underlying reasons. The VMTB regularly has the opportunity to review and take action on the experience gained in these cases and ensure that the MTB is alerted in case of serious adverse events of treatment and unexpected events/death. The MTB regularly has the opportunity to review and act on the experience gained in these cases.

Clinical Decision-making

A set of minimum agreed upon information is provided during the meeting; that is, information that the VMTB needs to make informed recommendations, including diagnostic data (pathology and radiology), clinical information (comorbidities, psychosocial needs, and specialist and palliative care), and the patient's medical history, points of view, and preferences. It is important that all data collected locally is digitized upon collection. VMTB considers all treatment options clinically appropriate for a patient, even those that cannot be offered or delivered locally. Case presenters have to clarify which patients should be discussed, the clinical issues to be addressed, what information must be available for the discussion to be efficacious, and when to refer a patient to another MTB.

The MTB has access to a list of all current and relevant clinical trials (including enrollment criteria) and considers patients' eligibility for appropriate clinical trials as part of the decision-making process. Current standard treatment protocols

are used whenever appropriate. The patient's demographic profile and comorbidities are always considered. Psychosocial and supportive issues and patient palliative care are always considered. Patient views, preferences, and needs are an integral part of information during decision-making.

The clinical decision-making process translates into clear recommendations on the treatment/care plan resulting from the meeting. These recommendations ought to be evidence-based, patient-centered, in line with standard treatment protocols, or with a documented deviation. If a recommendation cannot be made owing to incomplete data or if new data become available at a later stage, it should be possible to report the patient's case to the MTB for further discussion. MTBs collect social and clinical demographics. They review these data periodically to reflect on equal access to active treatments and other aspects of the clinical journey, care, and experience of health care professionals.

Virtualization and Cloud-Based Sharing

One of the difficulties of the current MTB management process is the retrieval of clinical information, which is usually found in heterogeneous hospital databases, often difficult to access, or in closed-source systems (eg, electronic medical records, laboratory information systems, image archiving and communication systems, and paper-based medical records). The data must be collected by each system and compiled in a reproducible format, in anticipation of an MTB. Doctors generally assemble this information distinctly from each other. This creates difficulties such as potential communication errors, omitted or duplicated information, or failure to use the most up-to-date information. These, and other potential inefficiencies in workflow caused by the current process of the VMTB, often lead to an increased burden on the MTB. They can also extend the time it takes to determine which treatment plan is most appropriate for a patient. The structural and functional components associated with VMTB may also contribute to conflicting evidence and opinions regarding the impact of VMTB on patient care and improvement of outcomes.

It is increasingly evident that HITs can help transform current data collection processes into more efficient and effective ones by providing the right tools.

Several HIT solutions have been analyzed in the scientific literature to improve patient data management and the workflow associated with multidisciplinary access and use. However, each of them often addresses a specific aspect of the process or deals only with 1 particular application area. Information technology solutions and strategies should easily overcome many of the difficulties of accessing, collecting, organizing, and presenting information for MTBs. In this perspective and in light of the epochal changes that the COVID-19 pandemic induces in the organizational and clinical governance processes, it is advantageous and timely to place HIT systems oriented to virtualization of meetings and cloud-based sharing of clinical information. These systems, which are already active in various research fields and medical/scientific training can now be remodeled and integrated, serving as the solution to MTB's efficiency and efficacy bias already described.

Data Collection

Clinical data will be completely anonymized and will include patients' characteristics, including demographics and disease characteristics when including oncologic and medical history, planned treatment, and clinical outcomes observed during treatments. Feasibility data related to the VMTB will record technical breakdowns and accidents, barriers to participation, pitfalls in discussion, number and type of completed planned cases, average duration of case submission, and customer satisfaction. Effectiveness relative to VMTB will consider cases that meet appropriate multidisciplinary assessment, the average time from the consultation request to the presentation of cases, and the number and percentage of cases with timely assessment within 14 days.

The data acquisition sources (ie, the ability to acquire relevant information in a timely manner) are available to the VMTB. Key information that directly affects decisions (staging, performance status, and comorbidities) is gathered by the VMTB. The data collected during the meetings are analyzed and returned to the participants to support the knowledge and learning process. The participants in internal and external audits of processes, results, and reviews audit the data (eg, to confirm that treatment recommendations correspond to current best practices and to consider recruiting test personnel), taking action to alter the practice where necessary. VMTBs consider and evaluate clinical outcome data as they become available; for example, through peer reviews and clinical target groups.

Statistical Analysis

Statistical analyses will include descriptive statistics and comparisons made using the chi-square test or the Fisher exact test and Wilcoxon 2-sample test, as appropriate. A P value of <.05 will be considered significant.

Ethics and Dissemination

This study was approved by the Ethical Commission Palermo 1, Policlinic Paolo Giaccone, University of Palermo, Italy (n°06/2020; June 24, 2020). Additional approval will be obtained from the participating organizations or oncology units accordingly to current regulations released by the Italian Agency for Medicine.

Results

In the real world, face-to-face MTB boards are often poorly attended by many health care professionals. Several reasons may explain poor adherence to MTB such as lack of time, personal activity in several hospitals, emergencies, or familial and personal issues such as vacations. These aspects represent barriers to review all tumor cases in many hospitals or adequate participation in the MTB. Too often, these issues prevent tumor boards from reviewing all the hospital's cancer cases or attaining full multidisciplinary participation on each case.

New cloud-based platforms are specifically designed to facilitate VMTB functioning and therefore overcome some of the problems detected in the past, such as asynchronous participation in case discussion often limited to written chats, as previously reported [20]. On the other hand, VMTBs allow synchronous

participation of as many participants as needed from different places. A particularly important aspect of VMTB concerns handling of patient data in consideration of privacy laws and regulations. Therefore, any web-based system used for VMTB must assure anonymity and secure handling of sensitive data. Many platforms currently available for web-based meetings have several built-in features if used adequately. Other possible concerns include reimbursement, interruption of workflow, and efficiency.

VMTB present several advantages since participating physicians may attend the real-time web-based meetings from any location, using a wide range of devices such as cellphones, tablets, and personal computers. VMTB-based networks may allow health professionals to participate even if they work from places distant from high-volume referral centers. These meetings also represent a unique opportunity to share cases with MTB at larger institutions or an effective teaching tool for students, residents, and newer health care professionals.

The participating hospitals were able to handle thrice as many patients through the tumor board process. Furthermore, although the number of tumor board cases tripled, they saw a higher level of participation across specialties than they did with the physical tumor board meetings. The virtual tumor board solution also gathers key statistics about each case, which will allow administrators to monitor key metrics, including improvements in time from diagnosis to treatment and the impact on patient outcomes.

Discussion

Barriers

Swedish health care professionals who participated in 7 national VMTBs responded to a questionnaire that assessed key enabling factors, barriers, and opportunities for MTM development. Conventional content analysis was performed to identify thematic categories on the basis of free-text responses. Participants' perspectives could be assigned into 3 categories: a national arena with potential for comprehensive knowledge and collaboration, prerequisites for decision-making, and organization and responsibilities. These categories consisted of 9 subcategories that referred to, for example, collective competence, resources, clinical research, case discussion, meeting climate, patient-related information, MTB potential, referrals, and technical insufficiencies [24].

A study at the Dana-Farber Cancer Institute, presented at the American Society of Clinical Oncology Annual Meeting (May 29-31, 2020), showed that physicians who are more adherent to tumor board participation are more likely to be in an academic setting, have a PhD, or navigate fewer pathways.

Tumor board preparation and session conductance need significant amount of time spent by physicians, and face-to-face MTB are usually very burdensome, often causing MTBs to fail to review all cases. Even if MTBs within high-volume centers are time-consuming and sometimes considered fastidious duty, overloaded oncologists may have difficulties in taking pace with the overwhelming increase in biomolecular knowledge. Therefore, precision medicine MTBs represent an efficient platform to stay informed and receive high-level consultations.

Conclusions

The need for newer and fast tools to implement tumor boards is mandatory. The COVID-19 pandemic has boosted the use of virtual platforms for meetings, advisory boards, congresses, and tumor boards worldwide. However, studies reporting data on specifically designed VMTBs are very few in the medical literature.

A study carried out at Georgetown University modeled their virtual molecular tumor boards to assess the genetic makeup, previous treatment history, and other factors for 1725 patients with cancer [25]. The team compared VMTB outcomes with reviews by 5 gastrointestinal oncologists who performed tumor board duties in a conventional manner. The time spent assessing appropriate trials was noted, and the results were compared to those obtained virtually. From 2014 to 2017, researchers increased the number of patients reviewed from 46 to 622. VMTB allowed patient assessment for participation in 2000 clinical trials, use of 1000 agents, and more than 200 genetic profiles suitable for innovative treatments. Patients with pancreatic cancer represented only 5% of cases. Pishavaian et al [26] recently reported the development of a scalable, cloud-based, molecular VMTB platform, which allowed generating a treatment plan for 1725 patients, who were referred by advocacy organizations. Treatment decisions were generated in a few days on the basis of their genetic profile and a biomarker/treatment association in accordance with previous medical history, updated guidelines, and eligibility criteria for trial enrollment. This platform included a knowledge-based scoring model, rules engine, an asynchronous virtual chat room, and a reporting tool to elaborate shared and consensus reports especially for off-label treatment or clinical trial enrollment.

Conflicts of Interest

LB, RB, DP, and VG received honoraria from Roche Pharma for participation in advisory boards or as speakers. VS received honoraria from Astellas for participation in advisory boards or as speakers.

References

1. Patt DA, Bernstam EV, Mandel JC, Kreda DA, Warner JL. More Medicine, Fewer Clicks: How Informatics Can Actually Help Your Practice. Am Soc Clin Oncol Educ Book 2017;37:450-459 [FREE Full text] [doi: 10.1200/EDBK_174891] [Medline: 28561658]

2. Taylor AD, Micheel CM, Anderson IA, Levy MA, Lovly CM. The Path(way) Less Traveled: A Pathway-Oriented Approach to Providing Information about Precision Cancer Medicine on My Cancer Genome. Transl Oncol 2016 Apr;9(2):163-165 [FREE Full text] [doi: 10.1016/j.tranon.2016.03.001] [Medline: 27084433]
3. Rosell L, Wihl J, Nilbert M, Malmström M. Health Professionals' Views on Key Enabling Factors and Barriers of National Multidisciplinary Team Meetings in Cancer Care: A Qualitative Study. J Multidiscip Healthc 2020;13:179-186 [FREE Full text] [doi: 10.2147/JMDH.S240140] [Medline: 32103978]
4. Shao J, Rodrigues M, Corter AL, Baxter NN. Multidisciplinary care of breast cancer patients: a scoping review of multidisciplinary styles, processes, and outcomes. Curr Oncol 2019 Jun;26(3):e385-e397 [FREE Full text] [doi: 10.3747/co.26.4713] [Medline: 31285683]
5. Specchia ML, Frisicale EM, Carini E, Di Pilla A, Cappa D, Barbara A, et al. The impact of tumor board on cancer care: evidence from an umbrella review. BMC Health Serv Res 2020 Jan 31;20(1):73 [FREE Full text] [doi: 10.1186/s12913-020-4930-3] [Medline: 32005232]
6. Basta YL, Baur OL, van Dieren S, Klinkenbijl JHG, Fockens P, Tytgat KMAJ. Is there a Benefit of Multidisciplinary Cancer Team Meetings for Patients with Gastrointestinal Malignancies? Ann Surg Oncol 2016 Aug;23(8):2430-2437 [FREE Full text] [doi: 10.1245/s10434-016-5178-3] [Medline: 27002814]
7. Soukup T, Lamb B, Arora S, Darzi A, Sevdalis N, Green J. Successful strategies in implementing a multidisciplinary team working in the care of patients with cancer: an overview and synthesis of the available literature. J Multidiscip Healthc 2018;11:49-61 [FREE Full text] [doi: 10.2147/JMDH.S117945] [Medline: 29403284]
8. Iyer NG, Chua MLK. Multidisciplinary team meetings - challenges of implementation science. Nat Rev Clin Oncol 2019 Apr;16(4):205-206. [doi: 10.1038/s41571-018-0148-2] [Medline: 30552396]
9. Rosell L, Wihl J, Hagberg O, Ohlsson B, Nilbert M. Function, information, and contributions: An evaluation of national multidisciplinary team meetings for rare cancers. Rare Tumors 2019;11:2036361319841696 [FREE Full text] [doi: 10.1177/2036361319841696] [Medline: 31105919]
10. Krupinski E, Comas M, Gallego L, GISMAR Group. A New Software Platform to Improve Multidisciplinary Tumor Board Workflows and User Satisfaction: A Pilot Study. J Pathol Inform 2018;9:26 [FREE Full text] [doi: 10.4103/jpi.jpi_16_18] [Medline: 30167341]
11. Harris J, Taylor C, Sevdalis N, Jalil R, Green JS. Development and testing of the cancer multidisciplinary team meeting observational tool (MDT-MOT). Int J Qual Health Care 2016 Jun;28(3):332-338 [FREE Full text] [doi: 10.1093/intqhc/mzw030] [Medline: 27084499]
12. Wakeam E, Odell D, Samson P. Measuring the quality of multi-disciplinary thoracic oncology care. J Thorac Dis 2019 Mar;11(Suppl 4):S562-S565 [FREE Full text] [doi: 10.21037/jtd.2019.02.72] [Medline: 31032074]
13. Nic Giolla Easpaig B, Arnolda G, Tran Y, Bierbaum M, Lamprell K, Delaney GP, et al. What is multidisciplinary cancer care like in practice? a protocol for a mixed-method study to characterise ambulatory oncology services in the Australian public sector. BMJ Open 2019 Oct 10;9(10):e031179 [FREE Full text] [doi: 10.1136/bmjopen-2019-031179] [Medline: 31601594]
14. Lamb BW, Jalil RT, Sevdalis N, Vincent C, Green JSA. Strategies to improve the efficiency and utility of multidisciplinary team meetings in urology cancer care: a survey study. BMC Health Serv Res 2014 Sep 08;14:377 [FREE Full text] [doi: 10.1186/1472-6963-14-377] [Medline: 25196248]
15. Osarogiagbon R, Freeman R, Krasna M. Implementing effective and sustainable multidisciplinary clinical thoracic oncology programs. Transl Lung Cancer Res 2015 Aug;4(4):448-455 [FREE Full text] [doi: 10.3978/j.issn.2218-6751.2015.07.05] [Medline: 26380186]
16. Salami AC, Barden GM, Castillo DL, Hanna M, Petersen NJ, Davila JA, et al. Establishment of a Regional Virtual Tumor Board Program to Improve the Process of Care for Patients With Hepatocellular Carcinoma. J Oncol Pract 2015 Jan;11(1):e66-e74 [FREE Full text] [doi: 10.1200/JOP.2014.000679] [Medline: 25466708]
17. Pillay B, Wootten AC, Crowe H, Corcoran N, Tran B, Bowden P, et al. The impact of multidisciplinary team meetings on patient assessment, management and outcomes in oncology settings: A systematic review of the literature. Cancer Treat Rev 2016 Jan;42:56-72. [doi: 10.1016/j.ctrv.2015.11.007] [Medline: 26643552]
18. Taylor C, Atkins L, Richardson A, Tarrant R, Ramirez A. Measuring the quality of MDT working: an observational approach. BMC Cancer 2012 May 29;12:202 [FREE Full text] [doi: 10.1186/1471-2407-12-202] [Medline: 22642614]
19. van Huizen LS, Dijkstra P, Halmos GB, van den Hoek JGM, van der Laan KT, Wijers OB, et al. Does multidisciplinary videoconferencing between a head-and-neck cancer centre and its partner hospital add value to their patient care and decision-making? A mixed-method evaluation. BMJ Open 2019 Nov 07;9(11):e028609 [FREE Full text] [doi: 10.1136/bmjopen-2018-028609] [Medline: 31699717]
20. Munro AJ, Swartzman S. What is a virtual multidisciplinary team (vMDT)? Br J Cancer 2013 Jun 25;108(12):2433-2441 [FREE Full text] [doi: 10.1038/bjc.2013.231] [Medline: 23756866]
21. Shea CM, Teal R, Haynes-Maslow L, McIntyre M, Weiner BJ, Wheeler SB, et al. Assessing the feasibility of a virtual tumor board program: a case study. J Healthc Manag 2014;59(3):177-193 [FREE Full text] [Medline: 24988672]

22. Taylor C, Brown K, Lamb B, Harris J, Sevdalis N, Green JSA. Developing and testing TEAM (Team Evaluation and Assessment Measure), a self-assessment tool to improve cancer multidisciplinary teamwork. Ann Surg Oncol 2012 Dec;19(13):4019-4027. [doi: 10.1245/s10434-012-2493-1] [Medline: 22820934]
23. Stevenson MM, Irwin T, Lowry T, Ahmed MZ, Walden TL, Watson M, et al. Development of a virtual multidisciplinary lung cancer tumor board in a community setting. J Oncol Pract 2013 May;9(3):e77-e80 [FREE Full text] [doi: 10.1200/JOP.2013.000882] [Medline: 23942505]
24. Rosell L, Wihl J, Nilbert M, Malmström M. Health Professionals' Views on Key Enabling Factors and Barriers of National Multidisciplinary Team Meetings in Cancer Care: A Qualitative Study. J Multidiscip Healthc 2020;13:179-186 [FREE Full text] [doi: 10.2147/JMDH.S240140] [Medline: 32103978]
25. Madhavan S, Blais EM, Bender RJ, Chung VM, Hendifar AE, Mikhail S, et al. A cloud-based virtual tumor board to facilitate treatment recommendations for patients with advanced cancers. JCO 2018 May 20;36(15_suppl):6508-6508. [doi: 10.1200/jco.2018.36.15_suppl.6508]
26. Pishvaian M, Blais E, Bender R, Rao S, Boca S, Chung V, et al. A virtual molecular tumor board to improve efficiency and scalability of delivering precision oncology to physicians and their patients. JAMIA Open 2019 Dec;2(4):505-515 [FREE Full text] [doi: 10.1093/jamiaopen/ooz045] [Medline: 32025647]

Abbreviations

HIT: health information technology
MTB: multidisciplinary tumor board
VTMB: virtual multidisciplinary tumor board

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Protocol

Using Electronically Delivered Therapy and Brain Imaging to Understand Obsessive-Compulsive Disorder Pathophysiology: Protocol for a Pilot Study

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Abstract

Background: Obsessive-compulsive disorder (OCD) is a debilitating and prevalent anxiety disorder. Although the basal ganglia and frontal cortex are the brain regions that are most commonly hypothesized to be involved in OCD, the exact pathophysiology is unknown. By observing the effects of proven treatments on brain activation levels, the cause of OCD can be better understood. Currently, the gold standard treatment for OCD is cognitive behavioral therapy (CBT) with exposure and response prevention. However, this is often temporally and geographically inaccessible, time consuming, and costly. Fortunately, CBT can be effectively delivered using the internet (electronically delivered CBT [e-CBT]) because of its structured nature, thus addressing these barriers.

Objective: The aims of this study are to implement an e-CBT program for OCD and to observe its effects on brain activation levels using functional magnetic resonance imaging (MRI). It is hypothesized that brain activation levels in the basal ganglia and frontal cortex will decrease after treatment.

Methods: Individuals with OCD will be offered a 16-week e-CBT program with exposure and response prevention mirroring in-person CBT content and administered through a secure web-based platform. The efficacy of the treatment will be evaluated using clinically validated symptomology questionnaires at baseline, at week 8, and after treatment (week 16). Using functional MRI at baseline and after treatment, brain activation levels will be assessed in the resting state and while exposed to anxiety-inducing images (eg, dirty dishes if cleanliness is an obsession). The effects of treatment on brain activation levels and the correlation between symptom changes and activation levels will be analyzed.

Results: The study received initial ethics approval in December 2020, and participant recruitment began in January 2021. Participant recruitment has been conducted through social media advertisements, physical advertisements, and physician referrals. To date, 5 participants have been recruited. Data collection is expected to conclude by January 2022, and data analysis is expected to be completed by February 2022.

Conclusions: The findings from this study can further our understanding of the causation of OCD and help develop more effective treatments for this disorder.

Trial Registration: ClinicalTrials.gov NCT04630197; https://clinicaltrials.gov/ct2/show/NCT04630197.

International Registered Report Identifier (IRRID): PRR1-10.2196/30726

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KEYWORDS

mental health; obsessive-compulsive disorder; cognitive behavioral therapy; exposure ritual prevention; electronic; functional magnetic resonance imaging; eHealth; brain imaging

Introduction

Background

Obsessive-compulsive disorder (OCD) is a debilitating anxiety disorder that can manifest in a multitude of ways in individuals. The 1-year prevalence of OCD in Canada is estimated to be 1%, with approximately 3% of the population developing OCD at some point in their lifetime [1,2]. Although OCD is a relatively widespread disorder, there have been no conclusive results to date regarding its etiology [3,4]. By understanding the pathophysiology of OCD better, more targeted treatments can be developed, leading to higher effectiveness in symptom reduction.

OCD is categorized as having obsessions and compulsions that an individual is unable to control. These obsessions, uncontrollable thoughts, impulses, and ideas are found to be disturbing and anxiety-inducing by the individual. These obsessive thoughts and/or feelings typically manifest in the impaired control of mental activities, thoughts related to uncertainty, sex, violence, or contamination [5]. The differentiation between obsessive thoughts and common worries is that obsessive thoughts tend to be more unrealistic and involve more imagery than common worries [6]. Moreover, individuals are often embarrassed by their obsessive and intrusive thoughts and can be reluctant to share these thoughts with their health care provider [7]. Individuals with OCD often combat their obsessive thoughts with compulsive, uncontrollable behaviors. These repetitive behaviors or cognitive acts are intended to reduce the individual's anxiety. Common compulsions include hand washing, and checking and rigid maintenance of order and organization. Common cognitive acts include counting numbers, praying, and repeating words or phrases over and over. Much as with their obsessive thoughts, individuals with OCD are commonly embarrassed by their compulsions and recognize that they are irrational but are still unable to refrain from them. Although obsessions can occur exclusively without compulsions, it is more likely that they co-occur [8]. Individuals with OCD may also use neutralizations, which are repeated thought processes that help prevent, cancel, or reverse the feared consequences and distresses caused by their obsession [9,10]. Individuals with OCD often present with a concern that their thoughts will lead to negative consequences for themselves and/or others. An additional common trait in individuals with OCD is thought-action fusion, the belief that thinking of an event increases the probability of its occurrence and that a thought is a moral equivalent of the physical act [11,12].

Cognitive behavioral theories explain the etiology of OCD, with obsessive behaviors serving as a distraction from unpleasant thoughts [10]. It is theorized that abnormal obsessions are caused by problematic reactions to feelings of elevated responsibility, leaving the individual feeling a need to always be competent to avoid criticism. The compulsive behaviors then serve as an avoidance tactic [9,13]. These compulsions reinforce maladaptive behaviors and eventually develop to outlast the cause of the anxiety-inducing thought [14]. By using these theories and observing the effect of treatment on cognitive anxiety processes at a neural level, we can understand the etiology of OCD better.

Cognitive behavioral therapy (CBT) with exposure and response prevention (ERP) is regarded as the first-line treatment for OCD [15-20]. CBT targets thoughts and cognition, the central components of OCD [20,21]. The structure of CBT for OCD is similar to that of CBT for depression or anxiety, with the addition of ERP being the biggest difference [22-24]. Although CBT is a frontline treatment, it is costly, time consuming, and often inaccessible. Therefore, more accessible and efficient interventions must be developed without sacrificing the quality of care. Fortunately, web-based mental health interventions have become increasingly popular, and the electronically delivered CBT (e-CBT) is a feasible option [25]. Research suggests that e-CBT is an effective and feasible intervention for OCD, with results comparable with those of in-person treatment [25-30]. However, e-CBT is often implemented in nonscalable and nonsecure formats. Moreover, the efficacy of CBT, along with new and innovative treatments, can be drastically improved if we understand better how treatment affects neural anxiety processing and cognitive functioning [16-21].

The most implicated regions of the brain associated with OCD are the basal ganglia and frontal cortex. These regions are involved in motor control and cognitive functioning tasks, including abstract reasoning, planning, decision-making, and inhibition [31-33]. More specifically, the basal ganglia play a large part in selecting movements that have positive effects [34]. In the case of OCD, it is hypothesized that this could play a part in the compulsive behaviors of OCD (eg, hand washing if cleanliness is an obsession). The frontal cortex is involved in reward processing, impulse control, and emotional control, among others [35]. If we learn that treatment can alter a patient's anxiety processing at a neural level, more specific treatments targeting these brain regions can be developed. Research suggests that in patients with OCD, the basal ganglia and frontal cortex are hyperactive at rest, becoming further activated while in anxiety-inducing situations [13,15,33,36-43]. These studies also suggest that successful treatment may result in a partial reversal of this hyperactivation [13,15,33,36-43]. However, more work is needed to make definitive conclusions on whether activation levels decrease following successful treatment.

By measuring brain activation levels while exposed to neutral and anxiety-inducing stimuli pre- and posttreatment, the

suspected regions involved in OCD pathology (basal ganglia and frontal cortex) can be observed. These findings can help explain whether effective treatment results in changes in activation levels, whether symptom improvement is correlated to changes in activation levels, and if there are any treatment response identifiers. If anxiety processing in patients with OCD can be understood better, more targeted treatments altering these specific parts of cognition can be developed. It is currently unknown whether e-CBT can produce these effects.

Objectives

This study will use a 16-week e-CBT with an ERP program to evaluate the effects of treatment on activation levels in the basal ganglia and frontal cortex. Previous findings suggest that CBT may partially reduce the hyperactivation commonly observed in OCD. It is hypothesized that successful treatment will decrease activation levels in the basal ganglia and frontal cortex when comparing pre- and posttreatment levels in patients with OCD with controls. This study will aim to address the following questions:

1. Does successful treatment result in changes in brain activation levels in regions involved in neural anxiety processing at the core of OCD pathology?
2. Is there a correlation between changes in symptom severity and changes in brain activation levels after treatment in patients with OCD?
3. What is the efficacy of this e-CBT program compared with control in improving symptoms, quality of life, and levels of functioning in patients with OCD?
4. What is the feasibility and user experience of this e-CBT program from a patient perspective?

Methods

Design

A nonrandomized pilot study design will be used with all participants receiving 16 weekly sessions of e-CBT. Functional magnetic resonance imaging (fMRI) will be conducted at baseline and posttreatment to evaluate activation level changes in the basal ganglia and frontal cortex. Clinically validated symptomology questionnaires will be used to evaluate treatment efficacy. In addition, qualitative interviews will be conducted to gather personal demographic information as well as information regarding participant experience while using the web-based psychotherapy clinic. The pilot study has been registered on the ClinicalTrials.gov Protocol Registration and Results System (NCT04630197). In addition, ethics approval has been obtained from the Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board (HSREB; file number 6031276).

Participants

Participants (n=10) will be recruited from family medicine and psychiatric clinics at Queen's University and Kingston Health Sciences Centre sites (Hotel Dieu Hospital and Kingston General Hospital) in Kingston, Ontario, Canada. In addition, local and social media advertisements will be used. Participants will be enrolled in the study based on referrals from outpatient clinics and family doctors as well as self-referrals. Those invited and interested in participating will have the study protocol explained and an evaluation done by a psychiatrist on the research team through a secured video appointment. Participants will be evaluated for a diagnosis of OCD based on the *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition* [44]. After a diagnosis of OCD is confirmed and the participant is given written and verbal instructions on how to participate in the study, informed consent will be obtained.

The inclusion criteria include the following: between the ages of 18 and 65 years at the start of the study, a diagnosis of OCD according to the *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition* criteria, competence to consent to participate, ability to speak and read English, and consistent and reliable access to the internet. Exclusion criteria include the following: having any metal implants or additional factors deemed not safe for an MRI scan, active psychosis, acute mania, severe alcohol or substance use disorder, and/or active suicidal or homicidal ideation. In addition, if a participant is currently receiving another form of psychotherapy, they will be excluded from the study.

Therapy

Weekly sessions of e-CBT will be conducted through the Online Psychotherapy Tool (OPTT; OPTT Inc), a secure, web- and cloud-based mental health care delivery platform. These web-based sessions will consist of approximately 30 slides and interactive therapist videos, with 16 modules in total (1 module per week). The content and format of these web-based sessions will mirror in-person CBT for OCD. The connection between thoughts, behaviors, emotions, physical reactions, and the environment will be a focus. Moreover, mindfulness, body scanning, self-care, goal setting, thinking errors, the 5-part model, and thought records will be employed as techniques for participants. ERP will be incorporated into the e-CBT program as this is the first-line route of treatment. Slides will highlight different topics each week and include general information, an overview of skills, and homework on that topic. The homework included in each session will be submitted through OPTT and reviewed by therapists, with personalized feedback provided within 3 days of submission. Weekly homework submission for feedback will be mandatory before being eligible for the next session. After each completion of the e-CBT program, participants will be interviewed to investigate their experience using OPTT and their perceptions of how the treatment went. OPTT can be accessed from a variety of devices (ie, desktop computers, laptops, cell phones, and tablets) and internet browsers.

Imaging

All imaging will occur at the Queen's University MRI Facility in Kingston, Ontario, Canada, using a Siemens 3.0 Tesla whole-body MRI scanner with a standard coil. Scans will occur at baseline (pretreatment) and after week 16 (posttreatment). During scanning, participants will lie on the scanning table on their backs, with their heads resting on a foam pad to reduce movement. Scanning appointments will take approximately 1 hour per session.

Anatomical reference images will be captured initially. After this, fMRI scans will occur while participants are shown neutral images and anxiety-inducing images (eg, dirty dishes if cleanliness is an anxiety-inducing concept for a specific participant). The frontal cortex and basal ganglia will be the focus of the imaging procedures as their activation level changes during neural anxiety processing are of interest. These images will be standardized pictures from the International Affective Picture System [45]. This large database allows for the selection of images that relate to a variety of obsessions representative of each participant (ie, contamination, sexual thought intrusion, and fear of harm). Each set of pictures will be individually tailored to each participant. These images will be selected ahead of time by a psychiatrist on the research team and will be related to the participant's anxieties. Participants will be shown a total of 40 images (20 neutral and 20 anxiety inducing; R=0.5) during the fMRI sessions. There will be four fMRI runs that occur in the following sequence:

1. 5 neutral images (30 seconds per image, 5 seconds break between), 1-minute break, 5 anxiety-inducing images (30 seconds per image, 5 seconds break between), 1-minute break.
2. 5 new anxiety-inducing images (30 seconds per image, 5 seconds break between), 1-minute break, 5 new neutral images (30 seconds per image, 5 seconds break between), 1-minute break.
3. 5 new anxiety-inducing images (30 seconds per image, 5 seconds break between), 1-minute break, 5 new neutral images (30 seconds per image, 5 seconds break between), 1-minute break.
4. 5 neutral images (30 seconds per image, 5 seconds break between), 1-minute break, 5 anxiety-inducing images (30 seconds per image, 5 seconds break between).

The images will be shown in sets (groups of 5 images) as opposed to intermingled, in the hope of producing a more sustained emotional state and allowing for more distinct readings. The ordering of the image sets repeats halfway through (back to back of the anxiety-inducing images in the example above) to control for participants becoming accustomed to image ordering. This ordering will be changed for every participant (ie, the next participant would receive back-to-back sets of the neutral imaging in runs 2 and 3) to counterbalance the imaging sets. Participants will be prompted to imagine themselves in the situations described in the images. The images will appear on a screen that will be reflected into the scanner for participants to view. A 0.5% blood oxygen level–dependent (BOLD) signal difference between conditions ($P<10^{-6}$) will be considered a detectable change (eff=0.005).

Anatomical reference images will be captured with the phase-encoding direction collected sagittally from anterior to posterior. These images will be captured with T1-weighted high-resolution magnetization-prepared rapid acquisition gradient-echo (MPRAGE) images with 0.8×0.8×0.8 mm^3 isotropic voxels. These images will use a 256 mm field of view (FOV), 2500 ms repetition time (TR), 2.22 ms echo time (TE), 8-degree flip angle, and a 320×320 mm matrix resolution. Following this, T2*-weighted gradient-echo echo-planar imaging (GE-EPI) with 3.0 mm 3.0×3.0×3.0 mm^3 isotropic voxels will be used for the stimuli-exposed image acquisitions in an anterior-to-posterior direction. These images will use a 192 mm FOV, 2500 ms TR, 28.4 ms TE, 90-degree flip angle, and a 64×64 mm matrix resolution. A multiband acceleration factor of 2 will be used, with 170 volumes being captured. Following the GE-EPI imaging, two short spin-echo field map scans will be captured from anterior to posterior and then posterior to anterior. These images will use a 192 mm FOV, 8000 ms TR, 66.0 ms TE, 90-degree flip angle, 180-degree refocus flip angle, and a 64×64 mm matrix resolution. All images will use a bandwidth of 1500 Hz.

The GE-EPI fMRI data will be mapped to a nondistorted set of gradient-echo images from the same participant to undistort the images. Next, the nondistorted gradient-echo images will be mapped onto the T1-weighted MPRAGE image. Finally, the T1-weighted MPRAGE will be mapped to the Montreal Neurological Institute standardized brain template. In doing this, the GE-EPI fMRI data will be mapped to the Montreal Neurological Institute template with maximum accuracy.

Training

All therapists will be research assistants trained in psychotherapy delivery and supervised by a psychiatrist on the research team who has extensive experience in electronically delivered psychotherapy. All therapists are taught the standard care pathway, the aim, and the content of each therapeutic session. Moreover, they will be provided with sample homework from a previous patient and will be asked to provide feedback as practice. Feedback templates will vary between sessions, and therapists will personalize each template for each patients' homework. Before feedback is submitted to the participant, it will be read, edited, and approved by a psychiatrist on the research team. Training will occur through webinars and exercises with feedback.

Outcomes

The primary outcome measure will be changes in activation levels of the basal ganglia and frontal cortex. This will be collected through detectable changes in BOLD values from the fMRI scans at baseline and after treatment (week 16). The secondary outcomes will be changes in symptom severity, quality of life, and functioning. Changes in symptom severity will be evaluated using clinical symptomatology questionnaires (Yale-Brown Obsessive-Compulsive Scale and Obsessive-Compulsive Inventory, Revised) [46,47]. Changes in quality of life will be measured using the Quality of Life and Enjoyment Questionnaire [48]. Changes in levels of functioning will be measured using the Sheehan Disability Scale [49]. All questionnaires will be collected directly through OPTT at baseline, after session 8, and after treatment (week 16).

Compliance

As with all mental health disorders, treatment compliance is always an area of focus when designing interventions. Participants will have the importance of treatment compliance explained to them during the informed consent process, and participants will need to submit their homework assignments through OPTT before gaining access to their next treatment

session. From a previous meta-analysis conducted, the estimated completion rate from in-person psychotherapy is approximately 75% [50]. Additional meta-analyses found treatment adherence for web-based psychotherapy to be between 61% and 66%, with no significant difference with in-person psychotherapy [51-53]. A study investigating the efficacy of a 10-session e-CBT program for OCD had a mean completion of 7.28 sessions [54]. Previous research using OPTT indicated participants completed >8 sessions on average, with over half the participants completing all sessions. In a previous project using e-CBT for patients with generalized anxiety disorder, 90% of participants completed 10-12 weeks of the 12-week program, with over 75% of participants being retained for a 12-month follow-up [55].

Analysis

For the fMRI data (primary outcome), a 0.5% (eff=0.005) change in BOLD hemodynamic response function will be considered a detectable signal variation between conditions ($P>10^{-6}$). An estimated paradigm of expected BOLD response will be created, and the correlation between the real and expected signals will be calculated to detect noise using a general linear model:

$$S = \beta X + e \quad \textbf{(1)}$$

Where, S is the time-series data, β is the value for each pattern, X is the set of time-series patterns, and e is the residual.

The general linear model will provide a β value for each term in the basis set and a T value for each β. The BOLD contrast between conditions and scanning periods (ie, baseline and posttreatment) will be evaluated using one- and two-sample *t* tests, assuming a normal distribution. Realignment parameter regressors for the testing conditions will be implemented [56,57]. The effects at each condition will enter a group analysis using a random-effects model [58]. A group-level comparison will be used with small volume corrections performed for multiple comparisons using the Gaussian random field theory. Missing data points can be accounted for in the analysis with usable questionnaires and fMRI data using the linear model.

For questionnaire scores (secondary outcomes), a linear regression analysis will be used to identify variables associated with the outcome measures while controlling for demographic variables (ie, age, sex, and gender). Repeated measures of analysis of variance will be conducted to determine changes between periods (ie, baseline, week 8, and posttreatment) questionnaire scores. Greenhouse-Geisser adjustment for F-statistics and Bonferroni corrections for multiple comparisons will be used. Using the Pearson correlation coefficient, the correlation between the questionnaire score and the BOLD response will be evaluated. Data outliers will be defined as SD 3.29 away from the mean on scores.

Skew and kurtosis will be analyzed assuming a normal distribution in the questionnaire and fMRI data at all collection time points. Age, gender, and sex variables will be considered in knowledge creation and translation.

Ethics and Privacy

The pilot study has received approval from the Queen's University HSREB. Only the care providers involved in the care of the participants will have access to their information. Participants will only be identifiable by an identification number on the OPTT platform, and hard copies of consent forms with participant identity will be stored securely on site and will be destroyed 5 years after study completion. Only anonymized data will be provided to the analysis team members. OPTT is compliant with the Health Insurance Portability and Accountability Act, Personal Information Protection and Electronic Documents Act, and Service Organization Control–2. In addition, all servers and databases will be hosted in the Amazon Web Service Canada cloud infrastructure, which is managed by Medstack to assure all provincial and federal privacy and security regulations are met. OPTT will only collect anonymized metadata to improve its service quality and provide advanced analytics to the research team. OPTT will encrypt all data, and no employee will have direct access to patient data. All encrypted backups will be kept in the S3 storage dedicated to Queen's University.

Results

The pilot study is currently being conducted at Queen's University by the members of the research team. This pilot study is a nonrandomized, open-label study, with a plan for an expanded randomized controlled trial in the future. The pilot study received ethics approval from the Queen's University HSREB in December 2020, and the recruitment of participants began in January 2021. To date, 5 participants have been seen for initial assessments and enrolled in the study. Data collection is anticipated to begin in June 2021, with collection and analyses concluding by January and February 2022, respectively. All reporting of this study has been and will be in accordance with the GUIDance for the rEporting of intervention Development (GUIDED) and Template for Intervention Description and Replication (TIDieR) reporting checklists and guides (Multimedia Appendices 1 and 2).

Discussion

This trial can contribute to creating more effective treatments for OCD in the future. However, to do this, we must understand the pathophysiology and etiology of this debilitating and prevalent condition. Currently, there is no conclusive information on the pathophysiology and etiology of OCD. Although CBT with ERP is currently the frontline psychotherapy for OCD, the efficacy of this treatment, along with those of new and innovative ones, can be improved drastically if we understand better how treatment affects neural anxiety processing and cognitive functioning. By measuring brain activation levels during exposure to neutral and anxiety-inducing stimuli pre- and posttreatment, we can observe how the suspected regions involved in OCD pathology (basal ganglia and frontal cortex) change following treatment. This can enlighten us on various aspects of OCD, including whether effective treatment results in changes to activation levels, whether symptom improvement is correlated to changes in activation levels, and if there are any identifiers for brain activation levels for responders and nonresponders to treatment. If how patients with OCD process anxiety-inducing stimuli (ie,

dirty dishes if cleanliness is a patient's obsession) can be understood better, more targeted treatments can be given to specifically alter these parts of a person's cognition.

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Authors' Contributions

CS developed the project as part of their master's thesis project (ie, literature review and protocol development). NM contributed to the development of the electronically delivered cognitive behavioral therapy (e-CBT) modules. TS is a thesis committee member and provided expertise in the functional magnetic resonance imaging protocol development. RM is a cosupervisor for CS and provided their expertise in methodology and clinical trial development. NA is a cosupervisor for CS and provided their expertise and guidance in methodology and clinical trial development. In addition, NA contributed to the development of the e-CBT modules and provided overall management and supervision of the web-based psychotherapy program.

Conflicts of Interest

NA is a cofounder of the care delivery platform used in this study (Online Psychotherapy Tool [OPTT]) and has ownership stakes in OPTT Inc. RM has received consulting and speaking honoraria from AbbVie, Allergan, Eisai, Janssen, KYE, Lallemand, Lundbeck, Otsuka, and Sunovion, and research grants from CAN-BIND, Canadian Institutes of Health Research, Janssen, Lallemand, Lundbeck, Nubiyota, OBI, and Ontario Mental Health Foundation.

Multimedia Appendix 1
GUIDED (Guidance for the Reporting of Intervention Development) report checklist.
[PDF File (Adobe PDF File), 68 KB - resprot_v10i9e30726_app1.pdf]

Multimedia Appendix 2
TIDieR (Template for Intervention Description and Replication) report checklist.
[PDF File (Adobe PDF File), 97 KB - resprot_v10i9e30726_app2.pdf]

References

1. Osland S, Arnold PD, Pringsheim T. The prevalence of diagnosed obsessive compulsive disorder and associated comorbidities: A population-based Canadian study. Psychiatry Res 2018 Oct;268:137-142. [doi: 10.1016/j.psychres.2018.07.018] [Medline: 30025284]
2. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry 2005 Jun;62(6):593-602. [doi: 10.1001/archpsyc.62.6.593] [Medline: 15939837]
3. Pauls DL. The genetics of obsessive-compulsive disorder: a review. Dialogues Clin Neurosci 2010;12(2):149-163 [FREE Full text] [Medline: 20623920]
4. Sternberger LG, Burns GL. Compulsive activity checklist and the maudsley obsessional-compulsive inventory: Psychometric properties of two measures of obsessive-compulsive disorder. Behav Ther 1990;21(1):117-127. [doi: 10.1016/s0005-7894(05)80193-5]
5. Stuker PB, Adams HE, editors. Obsessive-compulsive disorders. In: Comprehensive Handbook of Psychopathology. Boston: Springer; 1993:129-144.
6. Comer JS, Kendall PC, Franklin ME, Hudson JL, Pimentel SS. Obsessing/worrying about the overlap between obsessive-compulsive disorder and generalized anxiety disorder in youth. Clin Psychol Rev 2004 Oct;24(6):663-683. [doi: 10.1016/j.cpr.2004.04.004] [Medline: 15385093]
7. Newth S, Rachman S. The concealment of obsessions. Behav Res Ther 2001 Apr;39(4):457-464. [doi: 10.1016/s0005-7967(00)00006-1] [Medline: 11280343]
8. Foa EB, Kozak MJ, Goodman WK, Hollander E, Jenike MA, Rasmussen SA. DSM-IV field trial: obsessive-compulsive disorder. Am J Psychiatry 1995 Jan;152(1):90-96. [doi: 10.1176/ajp.152.1.90] [Medline: 7802127]
9. Rachman S. A cognitive theory of obsessions. Behav Res Ther 1997 Sep;35(9):793-802. [doi: 10.1016/s0005-7967(97)00040-5] [Medline: 9299799]
10. Salkovskis PM. Obsessional-compulsive problems: a cognitive-behavioural analysis. Behav Res Ther 1985;23(5):571-583. [doi: 10.1016/0005-7967(85)90105-6] [Medline: 4051930]
11. Lawrence PJ, Williams TI. Pathways to inflated responsibility beliefs in adolescent obsessive-compulsive disorder: a preliminary investigation. Behav Cogn Psychother 2011 Mar;39(2):229-234. [doi: 10.1017/S1352465810000810] [Medline: 21092378]

12. Rachman S. Obsessions, responsibility and guilt. Behav Res Ther 1993 Feb;31(2):149-154. [doi: 10.1016/0005-7967(93)90066-4] [Medline: 8442740]
13. Saxena S, Rauch SL. Functional neuroimaging and the neuroanatomy of obsessive-compulsive disorder. Psychiatr Clin North Am 2000 Sep;23(3):563-586. [doi: 10.1016/s0193-953x(05)70181-7] [Medline: 10986728]
14. Saxena S, Bota RG, Brody AL. Brain-behavior relationships in obsessive-compulsive disorder. Semin Clin Neuropsychiatry 2001 Apr;6(2):82-101. [doi: 10.1053/scnp.2001.21833] [Medline: 11296309]
15. Schwartz JM. Neuroanatomical aspects of cognitive-behavioural therapy response in obsessive-compulsive disorder. An evolving perspective on brain and behaviour. Br J Psychiatry Suppl 1998(35):38-44. [Medline: 9829025]
16. Bandelow B, Michaelis S, Wedekind D. Treatment of anxiety disorders. Dialogues Clin Neurosci 2017 Jun;19(2):93-107 [FREE Full text] [Medline: 28867934]
17. National Institute of Mental Health. Obsessive-compulsive disorder: When unwanted thoughts or repetitive behaviors take over. NIH 2020:1. [doi: 10.1037/e620122011-001]
18. Hunsley J, Elliott K, Therrien Z. The efficacy and effectiveness of psychological treatments for mood, anxiety, and related disorders. Can Psychol/Psychologie canadienne 2014;55(3):161-176. [doi: 10.1037/a0036933]
19. National Institute for Health and Care Excellence. Obsessive-compulsive disorder and body dysmorphic disorder: treatment. Clinical Guidelines 2005:1. [doi: 10.1016/b978-008044701-8/50012-7]
20. Beck A, Rush A, Shaw B, Emergy G. Cognitive Therapy of Depression. New York: Guilford Press; 1987:1-425.
21. Margraf J, Barlow DH, Clark DM, Telch MJ. Psychological treatment of panic: work in progress on outcome, active ingredients, and follow-up. Behav Res Ther 1993 Jan;31(1):1-8. [doi: 10.1016/0005-7967(93)90036-t] [Medline: 8093337]
22. Whittal ML, Thordarson DS, McLean PD. Treatment of obsessive-compulsive disorder: cognitive behavior therapy vs. exposure and response prevention. Behav Res Ther 2005 Dec;43(12):1559-1576. [doi: 10.1016/j.brat.2004.11.012] [Medline: 15913543]
23. Wilhelm S, Steketee G. Cognitive Therapy for Obsessive-Compulsive Disorder: A Guide for Professionals. Oakland, CA: New Harbinger Publications; 2005:1-240.
24. Storch EA, Merlo LJ. Obsessive-compulsive disorder: strategies for using CBT and pharmacotherapy. J Fam Pract 2006 Apr;55(4):329-333. [Medline: 16608672]
25. Wootton BM, Titov N, Dear BF, Spence J, Andrews G, Johnston L, et al. An Internet administered treatment program for obsessive-compulsive disorder: a feasibility study. J Anxiety Disord 2011 Dec;25(8):1102-1107. [doi: 10.1016/j.janxdis.2011.07.009] [Medline: 21899983]
26. Matsumoto K, Sutoh C, Asano K, Seki Y, Urao Y, Yokoo M, et al. Internet-based cognitive behavioral therapy with real-time therapist support via videoconference for patients with obsessive-compulsive disorder, panic disorder, and social anxiety disorder: pilot single-arm trial. J Med Internet Res 2018 Dec 17;20(12):e12091 [FREE Full text] [doi: 10.2196/12091] [Medline: 30559094]
27. Patel SR, Wheaton MG, Andersson E, Rück C, Schmidt AB, La Lima CN, et al. Acceptability, feasibility, and effectiveness of internet-based cognitive-behavioral therapy for obsessive-compulsive disorder in New York. Behav Ther 2018 Jul;49(4):631-641 [FREE Full text] [doi: 10.1016/j.beth.2017.09.003] [Medline: 29937263]
28. Herbst N, Voderholzer U, Thiel N, Schaub R, Knaevelsrud C, Stracke S, et al. No talking, just writing! Efficacy of an internet-based cognitive behavioral therapy with exposure and response prevention in obsessive compulsive disorder. Psychother Psychosom 2014;83(3):165-175. [doi: 10.1159/000357570] [Medline: 24732962]
29. Andersson E, Enander J, Andrén P, Hedman E, Ljótsson B, Hursti T, et al. Internet-based cognitive behaviour therapy for obsessive-compulsive disorder: a randomized controlled trial. Psychol Med 2012 Oct;42(10):2193-2203 [FREE Full text] [doi: 10.1017/S0033291712000244] [Medline: 22348650]
30. Mahoney AE, Mackenzie A, Williams AD, Smith J, Andrews G. Internet cognitive behavioural treatment for obsessive compulsive disorder: A randomised controlled trial. Behav Res Ther 2014 Dec;63:99-106. [doi: 10.1016/j.brat.2014.09.012] [Medline: 25461784]
31. Rauch SL, Dougherty DD, Shin LM, Alpert NM, Manzo P, Leahy L, et al. Neural correlates of factor-analyzed OCD symptom dimensions: A PET study. CNS spectr 2014 Nov 07;3(7):37-43. [doi: 10.1017/s1092852900006167]
32. Rosenberg DR, Keshavan MS. A.E. Bennett Research Award. Toward a neurodevelopmental model of obsessive--compulsive disorder. Biol Psychiatry 1998 May 01;43(9):623-640. [doi: 10.1016/s0006-3223(97)00443-5] [Medline: 9582996]
33. Saxena S, Brody AL, Schwartz JM, Baxter LR. Neuroimaging and frontal-subcortical circuitry in obsessive-compulsive disorder. Br J Psychiatry Suppl 1998(35):26-37. [Medline: 9829024]
34. Nelson AB, Kreitzer AC. Reassessing models of basal ganglia function and dysfunction. Annu Rev Neurosci 2014;37:117-135 [FREE Full text] [doi: 10.1146/annurev-neuro-071013-013916] [Medline: 25032493]
35. Tamminga CA, Buchsbaum MS. Frontal cortex function. Am J Psychiatry 2004 Dec;161(12):2178. [doi: 10.1176/appi.ajp.161.12.2178] [Medline: 15569885]
36. Zhong Z, Yang X, Cao R, Li P, Li Z, Lv L, et al. Abnormalities of white matter microstructure in unmedicated patients with obsessive-compulsive disorder: Changes after cognitive behavioral therapy. Brain Behav 2019 Feb;9(2):e01201 [FREE Full text] [doi: 10.1002/brb3.1201] [Medline: 30623612]

37. Whiteside SP, Port JD, Abramowitz JS. A meta-analysis of functional neuroimaging in obsessive-compulsive disorder. Psychiatry Res 2004 Nov 15;132(1):69-79. [doi: 10.1016/j.pscychresns.2004.07.001] [Medline: 15546704]
38. Pato MT, Pato CN, Pauls DL. Recent findings in the genetics of OCD. J Clin Psychiatry 2002;63 Suppl 6:30-33. [Medline: 12027117]
39. Pauls DL, Alsobrook JP. The inheritance of obsessive-compulsive disorder. Child Adolesc Psychiatr Clin N Am 1999 Jul;8(3):481-96, viii. [Medline: 10442227]
40. Taylor S, Coles ME, Abramowitz JS, Wu KD, Olatunji BO, Timpano KR, et al. How are dysfunctional beliefs related to obsessive-compulsive symptoms? J Cogn Psychother 2010 Aug 01;24(3):165-176. [doi: 10.1891/0889-8391.24.3.165]
41. Beutel ME, Stark R, Pan H, Silbersweig D, Dietrich S. Changes of brain activation pre- post short-term psychodynamic inpatient psychotherapy: an fMRI study of panic disorder patients. Psychiatry Res 2010 Nov 30;184(2):96-104. [doi: 10.1016/j.pscychresns.2010.06.005] [Medline: 20933374]
42. Steiger VR, Brühl AB, Weidt S, Delsignore A, Rufer M, Jäncke L, et al. Pattern of structural brain changes in social anxiety disorder after cognitive behavioral group therapy: a longitudinal multimodal MRI study. Mol Psychiatry 2017 Aug;22(8):1164-1171. [doi: 10.1038/mp.2016.217] [Medline: 27922605]
43. Norman LJ, Mannella KA, Yang H, Angstadt M, Abelson JL, Himle JA, et al. Treatment-specific associations between brain activation and symptom reduction in OCD following CBT: a randomized FMRI trial. Am J Psychiatry 2021 Jan 01;178(1):39-47. [doi: 10.1176/appi.ajp.2020.19080886] [Medline: 32854533]
44. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5 Ed. Arlington, VA: American Psychiatric Association; 2013:1-991.
45. Lang P, Bradley M, Cuthbert B. International affective picture system (IAPS): Affective ratings of pictures and instruction manual. Technical Report A-8. University of Florida, Gainesville, FL 2008:1. [doi: 10.1037/t66667-000]
46. Goodman WK, Price LH, Rasmussen SA, Mazure C, Delgado P, Heninger GR, et al. The Yale-Brown Obsessive Compulsive Scale. II. Validity. Arch Gen Psychiatry 1989 Nov;46(11):1012-1016. [doi: 10.1001/archpsyc.1989.01810110054008] [Medline: 2510699]
47. Abramowitz JS, Deacon BJ. Psychometric properties and construct validity of the Obsessive-Compulsive Inventory--Revised: Replication and extension with a clinical sample. J Anxiety Disord 2006;20(8):1016-1035. [doi: 10.1016/j.janxdis.2006.03.001] [Medline: 16621437]
48. Endicott J, Nee J, Harrison W, Blumenthal R. Quality of Life Enjoyment and Satisfaction Questionnaire: a new measure. Psychopharmacol Bull 1993;29(2):321-326. [Medline: 8290681]
49. Leon AC, Olfson M, Portera L, Farber L, Sheehan DV. Assessing psychiatric impairment in primary care with the Sheehan Disability Scale. Int J Psychiatry Med 1997;27(2):93-105. [Medline: 9565717]
50. Swift JK, Greenberg RP. A treatment by disorder meta-analysis of dropout from psychotherapy. J Psychother Integr 2014;24(3):193-207. [doi: 10.1037/a0037512]
51. Andrews G, Basu A, Cuijpers P, Craske M, McEvoy P, English C, et al. Computer therapy for the anxiety and depression disorders is effective, acceptable and practical health care: An updated meta-analysis. J Anx Disord 2018 Apr;55:70-78. [doi: 10.1016/j.janxdis.2018.01.001]
52. Etzelmueller A, Vis C, Karyotaki E, Baumeister H, Titov N, Berking M, et al. Effects of internet-based cognitive behavioral therapy in routine care for adults in treatment for depression and anxiety: systematic review and meta-analysis. J Med Internet Res 2020 Aug 31;22(8):e18100. [doi: 10.2196/18100]
53. Guo S, Deng W, Wang H, Liu J, Liu X, Yang X, et al. The efficacy of internet-based cognitive behavioural therapy for social anxiety disorder: A systematic review and meta-analysis. Clin Psychol Psychother 2020 Nov 10;28(3):656-668. [doi: 10.1002/cpp.2528]
54. Andersson E, Enander J, Andrén P, Hedman E, Ljótsson B, Hursti T, et al. Internet-based cognitive behaviour therapy for obsessive–compulsive disorder: a randomized controlled trial. Psychol Med 2012 Feb 21;42(10):2193-2203. [doi: 10.1017/s0033291712000244]
55. ALAVI N, HIRJI A. The efficacy of powerpoint-based CBT delivered through email. J Psychiat Pract 2020;26(2):89-100. [doi: 10.1097/pra.0000000000000455]
56. Andersson JL, Ashburner J, Friston K. A global estimator unbiased by local changes. Neuroimage 2001 Jun;13(6 Pt 1):1193-1206. [doi: 10.1006/nimg.2001.0763] [Medline: 11352625]
57. Desjardins AE, Kiehl KA, Liddle PF. Removal of confounding effects of global signal in functional MRI analyses. Neuroimage 2001 Apr;13(4):751-758. [doi: 10.1006/nimg.2000.0719] [Medline: 11305902]
58. Worsley KJ, Liao CH, Aston J, Petre V, Duncan GH, Morales F, et al. A general statistical analysis for fMRI data. Neuroimage 2002 Jan;15(1):1-15. [doi: 10.1006/nimg.2001.0933] [Medline: 11771969]

Abbreviations

BOLD: blood oxygen level–dependent
CBT: cognitive behavioral therapy
e-CBT: electronically delivered cognitive behavioral therapy

ERP: exposure and response prevention
fMRI: functional magnetic resonance imaging
FOV: field of view
GE-EPI: gradient-echo echo-planar imaging
GUIDED: GUIDance for the rEporting of intervention Development
HSREB: Health Sciences and Affiliated Teaching Hospitals Research Ethics Board
MPRAGE: magnetization-prepared rapid acquisition gradient-echo
OCD: obsessive-compulsive disorder
OPTT: Online Psychotherapy Tool
TE: echo time
TIDieR: Template for Intervention Description and Replication
TR: repetition time

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Protocol

Co-Development of a Web-Based Hub (eSocial-hub) to Combat Social Isolation and Loneliness in Francophone and Anglophone Older People in the Linguistic Minority Context (Quebec, Manitoba, and New Brunswick): Protocol for a Mixed Methods Interventional Study

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Abstract

Background: The first wave of the COVID-19 pandemic has severely hit Canadian nursing facilities (81% of deaths). To this toll, public health measures (eg, visitation restriction) have subsequently deepened the social isolation and loneliness of residents in nursing facilities (NFs), especially those in linguistic minority settings: Anglophone institutions in Quebec and Francophone institutions outside Quebec. However, very few COVID-19 initiatives targeting these populations specifically have been documented. Given the limited number of NFs serving linguistic minorities in Canadian populations, families and loved ones often live far from these facilities, sometimes even in other provinces. This context places the digital solutions as particularly relevant for the present COVID-19 pandemic as well as in the post–COVID-19 era.

Objective: This project aims to co-develop a virtual community of practice through a web-based platform (eSocial-hub) to combat social isolation and loneliness among the older people in linguistic minority settings in Canada.

Methods: An interventional study using a sequential mixed methods design will be conducted. Four purposely selected NFs will be included, 2 among facilities in Manitoba and 2 in New Brunswick; and 2 Anglophone NFs in Quebec will serve as knowledge users. The development of eSocial-hub will include an experimental 4-month phase involving the following end users: (1) older people (n=3 per NF), (2) families of the participating older people (n=3 per NF), and (3) frontline staff (nurse and health care aid; n=2 per NF).

Results: Activities and solutions aiming at reducing social isolation and loneliness will be implemented and then evaluated with the project stakeholders, and the best practices generated. The assessment will be conducted using indicators derived from the 5 domains of the Consolidated Framework for Implementation Research. The project will be led by an interdisciplinary team and will involve a multisectoral partnership.

Conclusions: The project will develop a promising and generalizable solution that uses virtual technology to help reduce social isolation and loneliness among the older people.

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KEYWORDS

older people; nursing facility; nursing home; long-term care home; linguistic minority; digital health; COVID-19; social isolation; loneliness; older adults; development; isolation; minority; community

Introduction

Background

As vaccination for COVID-19 is ongoing worldwide, the third wave of the pandemic continues to surge. Canadian older adults in nursing facilities (NFs) paid the highest toll in terms of COVID-19 mortality, with 81% of deaths (first wave) versus 42% for all Organisation for Economic Co-operation and Development (OECD) countries [1]. This burden is compounded by the social isolation and loneliness endured by older people in NFs [2] as a consequence of public health measures that limit contact with professionals, family members, and caregivers. These unanticipated collateral effects increase vulnerability among older people [3] and continue to impact NF residents. This is particularly alarming in linguistic minorities, and poses a major challenge for managers and families, urging for innovative solutions—in this case, digital technologies. This approach is not only encouraged but also a necessity in light of its enormous potential to improve social capital and address the social isolation and loneliness of older people living in NFs. The literature contended that in addition to combatting social isolation and loneliness, video interactions increase learning effectiveness through the use of images [4], stimulate cognitive activity [5], and promote the transmission of knowledge [6].

Burden of Social Isolation and Loneliness

Social isolation consists of reduced social contacts and loneliness (the subjective feeling of isolation); it represents a serious public health threat for older people [7] living in NFs. Social isolation and loneliness affect up to 72% of NF residents [8,9]; thus, there is a mounting concern in considering social isolation and loneliness as a determinant of the health and well-being among older people [10]. Owing to the *ageing tsunami* especially in high-income countries including Canada, costs of NFs and provision of care to older people are of the fastest-growing areas of governments' spendings [11]. Additionally, the role of nurses, especially those working in NFs, has gained significant extension over the last decades [12] to deal with a broad range of care or services, namely (1) postacute care requiring rehabilitation and recovery, (2) terminal phases of an illness, or (3) management of (multiple) chronic conditions including cognitive or functional impairments [11]. Though the number of nurses in NFs has grown recently, evidence from a systematic review has unveiled nurse staffing issues in some of these facilities with nurses spending between 3.1 and 4.8 hours on each resident on ordinary days [11]. Undoubtedly, the COVID-19 pandemic has heightened this burden, and activities to counter social isolation and loneliness have taken a hit.

Besides the associated extra budget (eg, US $6.7 billion to Medicare costs [13]), social isolation and loneliness are associated with premature mortality [14], somatic diseases such as cardiovascular disease or obesity [15,16], or psychological issues including depression or anxiety [17]. The extreme vulnerability of older people is exacerbating the current COVID-19 crisis. For example, Francophone older people (≥65 years) in Manitoba are older than their Anglophone counterparts [18]. The majority of older people fear admission to NFs [19], some are either widowed, under guardianship, or have identified as sexual minorities (lesbian, gay, bisexual, transgender, questioning, or 2-spirited [LGBTQ2S+]) [20]. Furthermore, according to the Canadian Institute for Health Information, 87% of older adults in the country have some form of cognitive impairment, 69% have dementia, 50% experience behavioral problems, and 31% have depression [21]. As a previous study [11] highlighted that care outcomes targeted in NFs include changes and maintenance of a status and health condition–monitoring, with 2 unique dimensions of quality: quality of care and quality of life. Older people who are isolated or are experiencing cognitive decline may experience anxiety or behavioral problems (eg, agitation and withdrawal) during an outbreak or during lockdown [22]. Under normal circumstances, owing to the progressive collaborative culture, almost all (82%) older people in NFs benefit from their families' involvement in visiting and in activities of daily living such as hygiene care and emotional and social support [21-23]. For instance, in Canada, at least 10 hours per week are devoted by one-fifth of families to their institutionalized loved ones [24]. Families' role is of utmost importance in promoting and maintaining the social capital as the best source of ideas and knowledge [25] and for resolving social isolation and loneliness [26].

Apart from public health measures as one of the causes of social isolation and loneliness in older people, a dearth of health care workers over the successive waves contributes to the toll. Approximately 20% of Quebec's health care workers were infected with COVID-19 during the first wave [27]. NFs are understaffed and their exhausted personnel are living in fear owing to the high risk of becoming infected and infecting others. They operate under protocols that reduce previously observed physical interactions. Although NFs are a primary setting for recurrent disease outbreaks (eg, influenza), they are the least computerized segment of the Canadian health care [28]. While older people are often perceived as resistant to information and communication technology (ICT), surveys have noted a sharp increase (>40 per cent) in the use of ICT among this population since the 1990s [29].

Social Isolation and Loneliness in Older Adults From Linguistic Minorities

As a numerical minority, the needs and realities of NFs for older adults from linguistic and cultural minority communities were given little consideration in the establishment of measures aimed at countering the effects of the COVID-19 pandemic. Additionally, older adults in linguistic NFs often live geographically far from their families, even in different jurisdictions. Francophones outside Quebec weight 3.5% and Anglophones in Quebec 7.5% [30]. Very few NFs serve older people who belong to these linguistic minority groups, and their residents generally live far from their families, sometimes even in other provinces. Compounding this issue, the COVID-19 pandemic has revealed how public institutions and governments in multiple jurisdictions throughout Canada are failing to meet their linguistic obligations [31], which impedes timely access to information. Health systems did not demonstrate a strong surge capacity to address the pandemic of COVID-19 or its impact such as social isolation and loneliness, which could be more difficult for institutionalized older adults from linguistic and cultural minorities where even adults experience challenges in accessing the health care system [32]. The activities once offered by NFs to combat social isolation and loneliness (eg, outings) were even found to be effective [33], including the conventional ICT platforms (Skype, FaceTime, etc) currently offered by NFs to connect older adults with their families [34].

Nevertheless, the response to the pandemic (both the first wave and the third wave currently underway) has led to the successful implementation of some interventions (broadcasting video activities to patients in their rooms [35], video calling to bring together families and the institutionalized older people [36], and phone-based video calling, text messaging, or voicemail messaging [37]). Our project will capitalize on these practices, focusing on digital approaches to address social isolation and loneliness in anglophone minorities in Quebec and francophone minorities in NFs in Manitoba and New Brunswick.

Basically, our proposed web-based app, eSocial-hub, will allow interactive audio-video exchanges between the institutionalized older adults and their families. Some features such as autoresponse, à la carte ringing systems, and imaging pop off are intended to be tested. On the other hand, eSocial-hub will be designed to support socializing, fun, and educative activities.

Purpose of the Project

This project aims to co-develop, implement, and assess a virtual hub (eSocial-hub), in partnership with end users at 4 NFs that serve Anglophone and Francophone older adults in minority settings. eSocial-hub will be a web-based digital platform, synchronized among the participating NFs to promote mainly the connection of institutionalized older people with their families and their frontline workers.

Objective 1

Our first objective is to identify and evaluate practices and lived experiences with families, residents, managers and frontline workers in using web-based apps to optimize older people's resilience and combat social isolation and loneliness during the COVID-19 pandemic.

Objective 2

Our second objective is to co-develop eSocial-hub with older people, families, and professionals with a user-centered approach.

Objective 3

Our third objective is to implement and assess the community of practice's eSocial-hub with older people, families, caregivers, and professionals in communicating and sharing resources (eg, entertainment activities, evidence-based findings, and chatting).

Methods

Methods Overview

This interventional study will be conducted in a minority community setting using a sequential mixed (qualitative/quantitative) design [38]. A collaborative approach will be used to involve end-users (managers, older adults, families, and frontline workers) in co-developing eSocial-hub. Four NFs in minority language/cultural settings, purposely selected, will be included: 1 in Manitoba (Résidence Despins) and 2 in New Brunswick (Manoir Edith B. Pinet Inc and Résidences Lucien Saindon). The 2 Anglophone NFs in Quebec (Jeffery Hale and Saint Brigid's Home) will serve as knowledge users. The study will exclude older adults with terminal illnesses but will include those living with mild to moderate cognitive impairment.

eSocial-hub Features

eSocial-hub includes voice/video calls, text messing, voice-mailing, and autoresponse features. Because it is developed for older people, a viable precaution has been made to eliminate any technicality and provide an information technology (IT)–lay environment that usually hinders IT product use. eSocial-hub will support families and their institutionalized loved ones in their daily communication needs, prompted either by the former or the latter or by frontline workers. eSocial-hub is designed to be interoperable between exploitation systems and uploadable on cell phones, tablet devices, as well as laptops. The platform will be host by the University of Ottawa's IT infrastructure with biweekly maintenance by its IT's staff.

As a communication based-system, eSocial-hub is an internet-based app that adds to the running cost paid by the project budget. The study team is distinct with the developers of the platform as well as the funder. Its role toward the system being evaluated is to inform the developer on the expected features and finally evaluate its effectiveness. The project will be carried out in 3 phases.

Inventory of Interventions in Digital Technologies (Phase 1: June 1 to July 30, 2021)

This phase will involve several steps. During step 1, an inventory of interventions that use digital technologies to reduce the harms of isolation and loneliness in residents during the COVID-19 pandemic will be conducted. The study sample will include participants in the NFs as well as families. Therefore, we will select the chief executive officer and 2 other major program managers (nursing chief and social worker), 3 in each

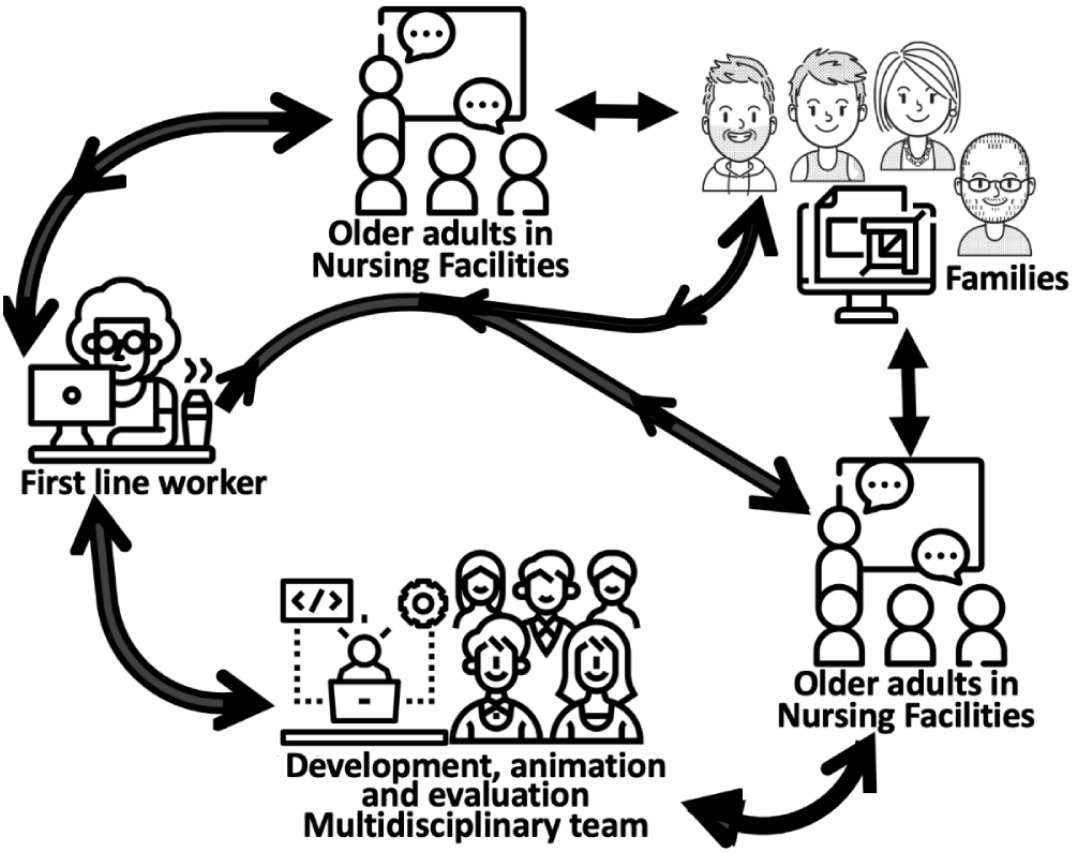
NF (n=12) for a semistructured interviews. We also plan to select frontline workers including nurses (n=12) and health care aides (n=12). Step 2 will explore lived experiences in maintaining social connections and social capital between families and their older residents. Thus, 1 focus group per site (n=4), completed with a short structured survey of families (n=80), will be performed through Lime Survey. Using data collected in Phase 1, a deliberative workshop will then be held with stakeholders (4 older adults, 4 families/caregivers, 4 managers, and 4 frontline staff) to validate appropriate strategies, implementation modalities, and success indicators on the basis of the 5 domains of the Consolidated Framework for Implementation Research (CFIR) [39] (Phase 3), integrating sex, gender, and LGBTQ2S+ [40], social and linguistic justice, and cultural and racial diversity factors. The study will include participants from these diverse groups as much as possible; alternatively, at least half the participants will be men and the other half will be women. Activities will take place in both languages: French for older people in Francophone NFs and English for those residing in Quebec NFs.

eSocial-hub Co-Development Trial (Phase 2: August 5 to October 30, 2021)

Participants who consent to continue with Phase 2 will be asked to renew their written consent. For new participants, written consent will be solicited. Based on feedback from the participating NF concerning their experiences with digital technology, the co-development team will build eSocial-hub to share promising evidence-based practices. One day will be devoted to train the participants to use the platform. This process will take place during a 3-month pilot phase. Consenting families and their loved older adults will be involved in an experimental group comprising 2 expert older adults per NF (n=8), 2 families or caregivers per NF (n=8), and 1 frontline worker (1 health care aid or 1 nurse) per NF (n=4). They will use a device (tablet, laptop or desktop computer) connected to the internet. In a departure from traditional approaches, testing of eSocial-hub will be conducted using a virtual *Hackerspace* to complement the data collected from the experimental group. *Hackerspace* will be a chat platform open to friends of older people, NF users, older people's associations, and interested members of the public.

The deliberative workshop and the interviews will be conducted entirely on the internet. eSocial-hub will be designed and validated by a software developer, following the DMAIC (Define, Measure, Analyze, Improve, and Control) approach [41]. The DMAIC cycle will optimize the efficiency of eSocial-hub, improve its user-friendliness, and enhance its features' functionality on the basis of the modus operandi of eSocial-hub (Figure 1). The following indicators will be measured: results optimization, aesthetics, ergonomics, operational reliability, and durability [42]. User feedback (complaints, comments, and observations) will be compiled consecutively during this trial in the form of text messages and audio messages. These will be analyzed biweekly with personalized follow-ups by the research team, as needed.

Figure 1. Modus operandi of the eSocial-hub.



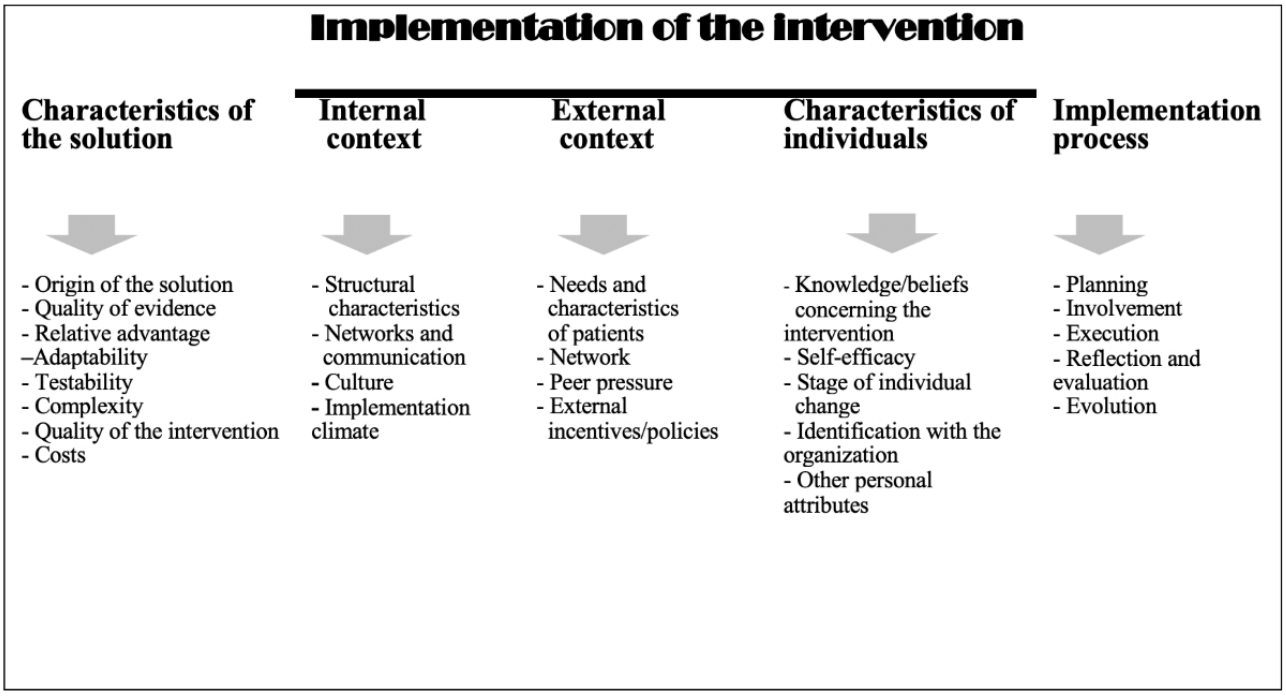
Content of eSocial-hub

This will be defined by the deliberative workshop. However, in addition to the chat and audiovisual features used to connect older people and their families or frontline workers (or to connect 3 types of users simultaneously), the eSocial-hub will provide an outlet to share activities in real time. Furthermore, entertainment activities will be offered by several nursing students who will be trained in audiovisual facilitation/presentation by our partner, La Liberté, Manitoba's sole French-language newspaper. Students' participation in the project will allow them to achieve their personal and professional development objectives.

eSocial-hub Trial Assessment Strategy (Phase 3: October 10 to November 5, 2021)

The assessment will analyze indicators defined by consensus during the deliberative workshop, in accordance with the 5 CFIR domains (Figure 2), and integrate patient-partner and diversity factors (cultural, sex, gender, and LGBTQ2S+, and linguistic justice). The CFIR's metatheoretical framework draws on concepts from multiple theories and models [39] based on expert consensus. It includes five components: (1) the characteristics of the intervention, (2) the external context, (3) the internal context, (4) the characteristics of the individuals, and (5) the implementation process. Figure 2 presents the various constructs and factors that will be considered for each component to optimize and evaluate the eSocial-hub's implementation. We will use the indicators to develop a structured survey questionnaire, using a 6-point Likert scale (to prevent an average response bias [43]). The questionnaire will be administered before and after the trial.

Figure 2. Main components of the CFIR and corresponding constructs (adapted from [44]).



The final questionnaire items will be validated through a modified Delphi process [45]. Six end-users (3 families and 3 older adults) and 5 experts will be consulted to obtain a consensus on the indicators to be considered. The survey will consist of two sections: the first set of questions on the personal and professional characteristics of the respondents (age group, gender, role, type of organization, time in the organization, involvement in the intervention) and a second section on the proposed CFIR indicators. For each of the indicators, the respondents will have to indicate its degree of importance for the implementation of the innovation on a 6-point Likert scale (1=not important to 6=very important). Analyses will be performed to calculate the median and interquartile range for each indicator. Indicators with a score of 5 or 6 and an interquartile range of ≤1 will be retained as consensus. Indicators with a score of 4 or less and an interquartile range of ≤1 will be excluded. The second round of surveys will be conducted with the same respondents to assess indicators that did not have a consensus for retention or exclusion in the first round. For this second survey, the score given by the respondent in the first round as well as the median score obtained will be presented, and then the respondent will be asked to change their score if they wish to reach a consensus. If there is no consensus on certain indicators following this second round, a third round may be conducted. Respondents will have 1 week to complete each round of the survey and a reminder will be sent to them after 3 days.

Finally, using a utilization-focused evaluation approach [46], our team will coordinate the monitoring of the trial phase at mid-project (August 2021) and at the end of the project (December 2021) and conduct follow-up interviews with the trial participants to further explore some of the quantitative results. The use of mixed methods will allow for a more detailed analysis of the implementation process, taking into account the local context and dynamics. The findings will be shared during

a web-based meeting with the NF teams, and their feedback will be incorporated into the final evaluation report and a peer-reviewed paper presenting the results. The complementary expertise of the team members in implementation science and evaluation, digital technologies (MPG), nursing and long-term care (IB), public health (DS), psychology (JR and NJCB), health economics (ENT), sociology and health services organization (AA), and organizational studies (SC) will enrich the analyses from multiple perspectives. This cohesive research team has been involved in research collaborations since 2015 and completed and published numerous projects [47-55]. Much of their recent work [52,54,55] is closely related to this project.

Data Analysis

The quantitative analysis will be descriptive. Data will also be subjected to a bivariate analysis (analysis of variance or *t* test, as appropriate). In the event of a non-Gaussian distribution, the Mann–Whitney test will be used, with $P<.05$ considered significant. The qualitative analysis will involve data from focus groups and individual interviews. Verbatims will be transcribed and imported into N-Vivo 12 analysis software. Inductive thematic analysis will be carried out by at least 2 coresearchers independently working to develop preliminary coding structures to organize the data thematically (IB and JR) [56] to understand the meaning of the participants' experience [57]. Coding in 2 phases will refine the relationship among categories to be explored to facilitate the raising of the analytical level from categorical to thematic for meaningful interpretations of the data. Emerging themes will be defined by consensus by the research team [58]. Rigor credibility will be achieved by obtaining data from all stakeholders and investigator triangulation [59]. For its multi-site feature, we intend to achieve the transferability of the findings by providing a clear description of the participants, settings, and research process [60]. We will achieve confirmability through data triangulation and researcher reflexivity [59]. Finally, quantitative and qualitative data will be triangulated [61].

Results

This study was funded in April 2021. We plan to start active enrollment, and data collection will start on June 1, 2021. The project was granted ethical approval from the ethical committee for research of the University of Saint-Boniface and the University of Moncton (2021-085). This project is intended to end by February 2022. As of December 2021, we will have concluded the project evaluation. Early winter 2022 is the anticipated period to disseminate nationally and internationally the results generated.

Discussion

Social isolation and loneliness are prominent topical issues since the onset of the first wave of the COVID-19 pandemic. Best practices for the use of web-based apps will optimize institutionalized resilience among older people in combatting isolation and loneliness. Furthermore, the development of eSocial-hub using a user-centered approach is innovative to prove a concept and pave the way for health policymakers based on its added value, namely for older people in the context of the linguistic minority.

This project stems directly from a need felt and expressed by the participating NFs that are partnering with the 3 universities involved in this project. It is clear that NFs have been overwhelmed by the effects of COVID-19. They remain a weak link in our system, subject to recurring outbreaks (eg, seasonal illnesses). We expect to validate the eSocial-hub concept as a means to combat social isolation and loneliness. This issue will persist in the post–COVID-19 era, considering that NF may find it necessary to continue imposing certain restrictions, namely physical access to NF. This ensures the pertinence of a virtual solution. During eSocial-hub's testing phase, the expected outcomes include, in addition to the objective of combatting social isolation and loneliness, the use of digital tools (eg, iPad and laptop computer) that subsequently help stimulate and develop learning and cognitive activity in older adults. eSocial-hub, in addition to connecting families and caregivers with their older members, will allow for secure communications with staff, including live interactions and support a web-based professional community of practice as well as services and entertainment activities that were previously offered in person (eg, religious services, music, entertainment, lectures, and bingo sessions).

Inaugural entertainment activities will be offered by nursing students of the Université de Saint-Boniface after receiving training in facilitating and presenting audiovisual media from our partner, the La Liberté newspaper (the only French-language publication in Manitoba).

The results of this project will be published in a peer-reviewed open-access journal for public dissemination. We intend to participate in at least 1 colloquium or conference. These knowledge dissemination activities will raise awareness among co-researchers and decision-makers concerning the positive effects of the web-based hub on social isolation and loneliness (and therefore the quality of life) among older people in linguistic and cultural minority communities in the context of the COVID-19 pandemic.

The anticipated potential challenges pertain to the limited availability of managers and frontline staff in the event of COVID-19 outbreaks.

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Conflicts of Interest

None declared.

References

1. Pandemic Experience in the Long-Term Care Sector: How Does Canada Compare With Other Countries? Canadian Institute for Health Information. 2020. URL: https://www.cihi.ca/sites/default/files/document/covid-19-rapid-response-long-term-care-snapshot-en.pdf [accessed 2021-08-31]
2. Armitage R, Nellums LB. COVID-19 and the consequences of isolating the elderly. Lancet Public Health 2020 May;5(5):e256 [FREE Full text] [doi: 10.1016/S2468-2667(20)30061-X] [Medline: 32199471]
3. Banerjee D, D'Cruz M, Sathyanarayana Rao T. Coronavirus disease 2019 and the elderly: Focus on psychosocial well-being, agism, and abuse prevention – An advocacy review. J Geriatr Ment Health 2020;7(1):4-10. [doi: 10.4103/jgmh.jgmh_16_20]
4. Paivio A, Csapo K. Picture superiority in free recall: Imagery or dual coding? Cogn Psychol 1973 Sep;5(2):176-206. [doi: 10.1016/0010-0285(73)90032-7]
5. Kisielius J, Sternthal B. Detecting and Explaining Vividness Effects in Attitudinal Judgments. J Mark Res 2018 Dec 13;21(1):54-64. [doi: 10.1177/002224378402100106]
6. Houts PS, Doak CC, Doak LG, Loscalzo MJ. The role of pictures in improving health communication: a review of research on attention, comprehension, recall, and adherence. Patient Educ Couns 2006 May;61(2):173-190. [doi: 10.1016/j.pec.2005.05.004] [Medline: 16122896]
7. Wenger GC, Davies R, Shahtahmasebi S, Scott A. Social Isolation and Loneliness in Old Age: Review and Model Refinement. Ageing Soc 2008 Nov 14;16(3):333-358. [doi: 10.1017/s0144686x00003457]
8. Zhou Z, Mao F, Zhang W, Towne SD, Wang P, Fang Y. The Association Between Loneliness and Cognitive Impairment among Older Men and Women in China: A Nationwide Longitudinal Study. Int J Environ Res Public Health 2019 Aug 12;16(16):2877 [FREE Full text] [doi: 10.3390/ijerph16162877] [Medline: 31408955]
9. Prieto-Flores M, Forjaz MJ, Fernandez-Mayoralas G, Rojo-Perez F, Martinez-Martin P. Factors associated with loneliness of noninstitutionalized and institutionalized older adults. J Aging Health 2011 Mar;23(1):177-194. [doi: 10.1177/0898264310382658] [Medline: 20881107]
10. Linehan T, Bottery S, Kaye A. 2030 vision: the best - and worst - futures for older people in the UK. Social Welfare. 2014. URL: http://wwwilcukorguk/indexphp/publications/publication_details/2030_ [accessed 2021-08-31]
11. Spilsbury K, Hewitt C, Stirk L, Bowman C. The relationship between nurse staffing and quality of care in nursing homes: a systematic review. Int J Nurs Stud 2011 Jul;48(6):732-750. [doi: 10.1016/j.ijnurstu.2011.02.014] [Medline: 21397229]
12. Daly W, Carnwell R. Nursing roles and levels of practice: a framework for differentiating between elementary, specialist and advancing nursing practice. J Clin Nurs 2003 Mar;12(2):158-167. [doi: 10.1046/j.1365-2702.2003.00690.x] [Medline: 12603547]
13. Flowers L, Houser A, Noel-Miller C, AARP Public Policy Institue, Shaw J, Bhattacharya J, et al. Medicare Spends More on Socially Isolated Older Adults. AARP Public Policy Insittute. 2017. URL: https://www.aarp.org/ppi/info-2017/medicare-spends-more-on-socially-isolated-older-adults.html [accessed 2021-08-31]
14. Rico-Uribe LA, Caballero FF, Martín-María N, Cabello M, Ayuso-Mateos JL, Miret M. Association of loneliness with all-cause mortality: A meta-analysis. PLoS One 2018;13(1):e0190033 [FREE Full text] [doi: 10.1371/journal.pone.0190033] [Medline: 29300743]
15. National Academies of Sciences, Engineering, and Medicine. Social Isolation and Loneliness in Older Adults. Washington, DC: The National Academies Press; 2020.
16. Shankar A, McMunn A, Banks J, Steptoe A. Loneliness, social isolation, and behavioral and biological health indicators in older adults. Health Psychol 2011 Jul;30(4):377-385. [doi: 10.1037/a0022826] [Medline: 21534675]
17. Evans IE, Martyr A, Collins R, Brayne C, Clare L. Social Isolation and Cognitive Function in Later Life: A Systematic Review and Meta-Analysis. J Alzheimers Dis 2019;70(s1):S119-S144 [FREE Full text] [doi: 10.3233/JAD-180501] [Medline: 30372678]
18. Chartier MJ, Finlayson G, Prior H, Mcgowan KL, Chen H, Walld R, et al. Are there mental health differences between francophone and non-francophone populations in manitoba? Can J Psychiatry 2014 Jul;59(7):366-375 [FREE Full text] [doi: 10.1177/070674371405900704] [Medline: 25007420]
19. Brownie S, Horstmanshof L, Garbutt R. Factors that impact residents' transition and psychological adjustment to long-term aged care: a systematic literature review. Int J Nurs Stud 2014 Dec;51(12):1654-1666. [doi: 10.1016/j.ijnurstu.2014.04.011] [Medline: 24813582]

20. Armstrong P, Boscart V, Donner G, Ducharme F, Estabrooks C, Flood C, et al. Rétablir la confiance : La COVID-19 et l'avenir des soins de longue durée. Royal Society of Canada. URL: https://rsc-src.ca/fr/r%C3%A9tablir_la_confiance_la_covid-19_et_l_avenir_des_soins_de_longue_dur%C3%A9e [accessed 2021-08-31]
21. Dementia in long-term care. Canadian Institute for Health Information. URL: https://www.cihi.ca/en/dementia-in-canada/dementia-care-across-the-health-system/dementia-in-long-term-care [accessed 2021-08-31]
22. OECD. Fit Mind, Fit Job: From Evidence to Practice in Mental Health and Work. In: Mental Health and Work. Paris: OECD; 2015.
23. Bangerter LR, Van Haitsma K, Heid AR, Abbott K. "Make Me Feel at Ease and at Home": Differential Care Preferences of Nursing Home Residents. Gerontologist 2016 Aug;56(4):702-713 [FREE Full text] [doi: 10.1093/geront/gnv026] [Medline: 26035895]
24. Turcotte M, Sawaya C. Senior care: Differences by type of housing. Statistics Canada. URL: https://www150.statcan.gc.ca/n1/pub/75-006-x/2015001/article/14142-eng.htm [accessed 2021-08-31]
25. Shippee TP, Hong H, Henning-Smith C, Kane RL. Longitudinal Changes in Nursing Home Resident-Reported Quality of Life: The Role of Facility Characteristics. Res Aging 2015 Aug;37(6):555-580. [doi: 10.1177/0164027514545975] [Medline: 25651583]
26. Gritzner C. The CASPE Patient Satisfaction System. In: Measurement of patients' satisfaction with their care. London: Royal College of Physicians of London; 1993.
27. Boutros M. Le personnel de la santé hypothéqué. Le Devoir. 2020. URL: https://www.ledevoir.com/societe/sante/581140/coronavirus-le-personnel-de-la-sante-hypotheque [accessed 2021-08-31]
28. Sondage national des infirmières et infirmiers du Canada 2020 : Utilisation des technologies de santé numériques au travail. Inforoute Santé du Canada. URL: https://www.infoway-inforoute.ca/fr/component/edocman/resources/reports/benefits-evaluation/3813-sondage-national-des-infirmieres-et-infirmiers-du-canada-2020-utilisation-des-technologies-de-sante-numeriques-au-travail?Itemid=189 [accessed 2021-08-31]
29. Xie B. Improving older adults' e-health literacy through computer training using NIH online resources. Libr Inf Sci Res 2012 Jan 01;34(1):63-71 [FREE Full text] [doi: 10.1016/j.lisr.2011.07.006] [Medline: 22639488]
30. Update of the 2016 Census language data. Statistics Canada. URL: https://www12.statcan.gc.ca/census-recensement/2016/ref/lang/lang-note-eng.cfm [accessed 2021-08-31]
31. Chouinard S, Normand M. Talk COVID to Me: Language Rights and Canadian Government Responses to the Pandemic. Can J Pol Sci 2020 Apr 28;53(2):259-264. [doi: 10.1017/s0008423920000359]
32. de Moissac D, Bowen S. Impact of Language Barriers on Quality of Care and Patient Safety for Official Language Minority Francophones in Canada. J Patient Exp 2019 Mar;6(1):24-32 [FREE Full text] [doi: 10.1177/2374373518769008] [Medline: 31236448]
33. Theurer K, Mortenson WB, Stone R, Suto M, Timonen V, Rozanova J. The need for a social revolution in residential care. J Aging Stud 2015 Dec;35:201-210 [FREE Full text] [doi: 10.1016/j.jaging.2015.08.011] [Medline: 26568229]
34. Chen YR, Schulz PJ. The Effect of Information Communication Technology Interventions on Reducing Social Isolation in the Elderly: A Systematic Review. J Med Internet Res 2016 Jan 28;18(1):e18 [FREE Full text] [doi: 10.2196/jmir.4596] [Medline: 26822073]
35. Abbasi J. Social Isolation-the Other COVID-19 Threat in Nursing Homes. JAMA 2020 Aug 18;324(7):619-620. [doi: 10.1001/jama.2020.13484] [Medline: 32692848]
36. Mo S, Shi J. The Psychological Consequences of the COVID-19 on Residents and Staff in Nursing Homes. Work Aging Retire 2020 Oct;6(4):254-259 [FREE Full text] [doi: 10.1093/workar/waaa021] [Medline: 34192005]
37. Gilbert GL. COVID-19 in a Sydney nursing home: a case study and lessons learnt. Med J Aust 2020 Nov;213(9):393-396.e1 [FREE Full text] [doi: 10.5694/mja2.50817] [Medline: 33037646]
38. Onwuegbuzie A, Collins K. A Typology of Mixed Methods Sampling Designs in Social Science Research. TQR 2015 Jan 15:218-316. [doi: 10.46743/2160-3715/2007.1638]
39. Damschroder LJ, Aron DC, Keith RE, Kirsh SR, Alexander JA, Lowery JC. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. Implement Sci 2009 Aug 07;4:50 [FREE Full text] [doi: 10.1186/1748-5908-4-50] [Medline: 19664226]
40. What a Difference Sex and Gender Make: A Gender, Sex and Health Research Casebook. Canadian Institutes of Health Research. URL: https://cihr-irsc.gc.ca/e/44734.html [accessed 2021-08-31]
41. Jacobs F, Chase R. Loose Leaf for Operations and Supply Chain Management: The Core. Toronto, ON: McGraw-Hill Education; 2016.
42. Spooner M, Bendavid Y, Bourenane H, Marcotte S. Introduction à la gestion des opérations: Viser l'excellence opérationnelle. Québec, QC: Presses de l'Université du Québec; 2014.
43. Gritzner C. The CASPE Patient Satisfaction System. In: Measurement of patients' satisfaction with their care. London: Royal College of Physicians of London; 1993.
44. CFIR constructs. Consolidated Framework for Implementation Research. URL: https://cfirguide.org/constructs/ [accessed 2020-05-05]

45. Custer R, Scarcella J, Stewart B. The Modified Delphi Technique--A Rotational Modification. J Vocat Tech Educ 1999;15(2):50-58.
46. Patton MQ. Essentials of Utilization-Focused Evaluation. Thousand Oaks, CA: Sage Publications; 2011.
47. Beogo I, Huang N, Gagnon M, Amendah DD. Out-of-pocket expenditure and its determinants in the context of private healthcare sector expansion in sub-Saharan Africa urban cities: evidence from household survey in Ouagadougou, Burkina Faso. BMC Res Notes 2016 Jan 21;9:34 [FREE Full text] [doi: 10.1186/s13104-016-1846-4] [Medline: 26795567]
48. Beogo I, Liu C, Dlamini CP, Gagnon M. Registered Nurse to Bachelor of Science in Nursing: nesting a fast-track to traditional generic program, teachings from nursing education in Burkina Faso. BMC Nurs 2015;14:66 [FREE Full text] [doi: 10.1186/s12912-015-0118-2] [Medline: 26633940]
49. Beogo I, Mendez Rojas B, Gagnon M. Determinants and materno-fetal outcomes related to cesarean section delivery in private and public hospitals in low- and middle-income countries: a systematic review and meta-analysis protocol. Syst Rev 2017 Jan 14;6(1):5 [FREE Full text] [doi: 10.1186/s13643-016-0402-6] [Medline: 28088214]
50. Beogo I, Rojas BM, Gagnon M, Liu C. Psychometric evaluation of the French version of the Clinical Nursing Competence Questionnaire (CNCQ-22): A cross-sectional study in nursing education in Burkina Faso. Nurse Educ Today 2016 Oct;45:173-178. [doi: 10.1016/j.nedt.2016.08.007] [Medline: 27529835]
51. Beogo I, Van LP. A Systematic Review of eHealth Interventions for Healthy Aging: Status of Progress. Proceedings of the International Conference on Information and Communication Technologies for Ageing Well and e-Health - ICT4AWE 2016:122-126. [doi: 10.5220/0005910001220126]
52. Buyl R, Beogo I, Fobelets M, Deletroz C, Van Landuyt P, Dequanter S, et al. e-Health interventions for healthy aging: a systematic review. Syst Rev 2020 Jun 03;9(1):128 [FREE Full text] [doi: 10.1186/s13643-020-01385-8] [Medline: 32493515]
53. Gagnon MP, Beogo I, Buyl R. e-Health Interventions for Healthy Aging: A Systematic Review Protocol. Stud Health Technol Inform 2016;225:954-955. [Medline: 27332428]
54. Tchouaket Nguemeleu E, Beogo I, Sia D, Kilpatrick K, Séguin C, Baillot A, et al. Economic analysis of healthcare-associated infection prevention and control interventions in medical and surgical units: systematic review using a discounting approach. J Hosp Infect 2020 Oct;106(1):134-154 [FREE Full text] [doi: 10.1016/j.jhin.2020.07.004] [Medline: 32652215]
55. Tchouaket EN, Beogo I, Sia D, Kilpatrick K, Séguin C, Baillot A, et al. Protocol for a systematic review of economic analyses of nosocomial infection prevention and control interventions in OECD hospitals. BMJ Open 2020 Jul 14;10(7):e037765 [FREE Full text] [doi: 10.1136/bmjopen-2020-037765] [Medline: 32665392]
56. Graneheim U, Lundman B. Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness. Nurse Educ Today 2004 Mar;24(2):105-112. [doi: 10.1016/j.nedt.2003.10.001] [Medline: 14769454]
57. Krippendorff K. Content Analysis An Introduction to Its Methodology (3rd edition). Thousand Oaks, CA: Sage Publications; 2013.
58. Paillé P, Mucchielli A. L'analyse qualitative en sciences humaines et sociales. Paris: Colin; 2012.
59. Lincoln YS, Guba EG, Pilotta JJ. Naturalistic inquiry. Int J Intercult Relat 1985 Jan;9(4):438-439. [doi: 10.1016/0147-1767(85)90062-8]
60. Creswell J, Poth C. Qualitative Inquiry and Research Design: Choosing Among Five Approaches. Thousand Oaks, CA: Sage Publications; 2013.
61. Onwuegbuzie A, Collins K. A Typology of Mixed Methods Sampling Designs in Social Science Research. TQR 2015 Jan 15;12(2):281-316. [doi: 10.46743/2160-3715/2007.1638]

Abbreviations

CFIR: Consolidated Framework for Implementation Research
DMAIC: Define, Measure, Analyze, Improve, and Control
ICT: information and communication technology
NF: nursing facility
OECD: Organisation for Economic Co-operation and Development

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Protocol

Conversational Agents for Health and Well-being Across the Life Course: Protocol for an Evidence Map

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Abstract

Background: Conversational agents, which we defined as computer programs that are designed to simulate two-way human conversation by using language and are potentially supplemented with nonlanguage modalities, offer promising avenues for health interventions for different populations across the life course. There is a lack of open-access and user-friendly resources for identifying research trends and gaps and pinpointing expertise across international centers.

Objective: Our aim is to provide an overview of all relevant evidence on conversational agents for health and well-being across the life course. Specifically, our objectives are to identify, categorize, and synthesize—through visual formats and a searchable database—primary studies and reviews in this research field.

Methods: An evidence map was selected as the type of literature review to be conducted, as it optimally corresponded to our aim. We systematically searched 8 databases (MEDLINE; CINAHL; Web of Science; Scopus; the Cochrane, ACM, IEEE, and Joanna Briggs Institute databases; and Google Scholar). We will perform backward citation searching on all included studies. The first stage of a double-stage screening procedure, which was based on abstracts and titles only, was conducted by using predetermined eligibility criteria for primary studies and reviews. An operational screening procedure was developed for streamlined and consistent screening across the team. Double data extraction will be performed with previously piloted data collection forms. We will appraise systematic reviews by using A Measurement Tool to Assess Systematic Reviews (AMSTAR) 2. Primary studies and reviews will be assessed separately in the analysis. Data will be synthesized through descriptive statistics, bivariate statistics, and subgroup analysis (if appropriate) and through high-level maps such as scatter and bubble charts. The development of the searchable database will be informed by the research questions and data extraction forms.

Results: As of April 2021, the literature search in the eight databases was concluded, yielding a total of 16,351 records. The first stage of screening, which was based on abstracts and titles only, resulted in the selection of 1282 records of primary studies and 151 records of reviews. These will be subjected to second-stage screening. A glossary with operational definitions for supporting the study selection and data extraction stages was drafted. The anticipated completion date is October 2021.

Conclusions: Our wider definition of a conversational agent and the broad scope of our evidence map will explicate trends and gaps in this field of research. Additionally, our evidence map and searchable database of studies will help researchers to avoid

fragmented research efforts and wasteful redundancies. Finally, as part of the Harnessing the Power of Conversational e-Coaches for Health and Well-being Through Swiss-Portuguese Collaboration project, our work will also inform the development of an international taxonomy on conversational agents for health and well-being, thereby contributing to terminology standardization and categorization.

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KEYWORDS

artificial intelligence; conversational agent; chatbot; virtual assistant; relational agent; virtual humans; e-coach; intervention; health; well-being

Introduction

In 2016, noncommunicable diseases (NCDs) accounted for 40.5 million deaths worldwide, which corresponded to 71% of deaths worldwide. The top 4 NCDs are cardiovascular diseases, cancers, diabetes, and chronic lung diseases [1]. NCDs can be prevented by adopting a healthy lifestyle. For example, a European multicohort study, which was conducted from 1991 to 2006 and included 116,043 people who were free of major NCDs at baseline, suggested that various healthy lifestyle profiles yield gains in life years without major NCDs, including type 2 diabetes, coronary heart disease, stroke, cancer, asthma, and chronic obstructive pulmonary disease [2].

Changing and sustaining health behaviors, which are integral to both the prevention and self-management of NCDs, are known to be challenging and resource intensive [3]. Digitalization and automation remove time and place restrictions, thereby broadening access to lifestyle and self-management interventions in a potentially cost-effective manner. For example, full economic evaluations of interventions that use the internet, mobile devices, or computers for the prevention and control of type 2 diabetes have demonstrated high cost-effectiveness, even though they were not fully automated [4].

The European Blueprint on Digital Transformation of Health and Care for the Ageing Society reflects a common vision that key stakeholders have on the role of innovation in changing health and care provision among older populations [5]. The priority topics encompassed by this policy vision are disease prevention, personalized health and care, and digital tools for citizen empowerment and person-centered care. A total of 12 blueprint personas have been created based on the health and care needs of people across the life course, ranging from children to persons aged ≥80 years [5].

Digital technology that mimics human communication is suitable for different age populations and populations with different literacy levels and is arguably more engaging for long-term use. A scan of this landscape has revealed a considerable body of scientific literature, although no agreements have emerged on the definition of so-called conversational agents. For instance, some authors consider conversational agents to be software capable of natural language processing [6]. However, others have used broader definitions that encompass agents that use predefined text options as inputs but exclude embodied agents that use nonverbal communication [7].

For the purpose of our review, we defined conversational agents as computer programs that are designed to simulate two-way human conversation by using language (speech or text) and are potentially supplemented with nonlanguage modalities. We believe that conversational agents for health and well-being should be further characterized according to the health intervention (eg, target population, design, the entity on which the intervention is carried out, and duration), the agent (eg, embodiment, role, and delivery channel), and the conversation (eg, input and output options, dialogue engine, and sentiment detection). We derived these ideas from literature [7-11], the international classification of health interventions [12], our interdisciplinary experience [13-16], and discussions within the research team.

This study is part of the Harnessing the Power of Conversational e-Coaches for Health and Well-being Through Swiss-Portuguese Collaboration (eCCo) project [17], which encompasses an evidence map and the subsequent development of an international taxonomy on conversational agents for health and well-being via a scientific consensus method that will be informed by our literature review. In addition to this purpose, the evidence map independently serves a much-needed research endeavor—fostering collaboration in the field through an open-access resource. In their review on conversational interfaces for health, Xing et al [18] highlighted the need to improve collaboration among stakeholders in research and patent activities. To our knowledge, there is no open, searchable database on conversational agents for health—a resource that could foster collaboration by pinpointing expertise across international centers and networks. Such collaboration can help with tackling research fragmentation and duplication.

Our aim is to provide an overview of all relevant evidence on conversational agents for health and well-being across the life course. Specifically, our objectives are to identify, categorize, and synthesize primary studies and reviews on this topic by focusing on the following research questions:

- What is the nature of literature on conversational agents for health and well-being (eg, information source, research group, and study characteristics)?
- What are the characteristics of health interventions based on conversational agents (eg, setting, target population, intervention target, duration, and frequency)?
- What are the characteristics of the automated conversations conducted in health interventions (eg, interaction input and output and dialogue engine)?

- What are the characteristics of the agents used in health interventions (eg, embodiment, emotions, role, and delivery channel)?

Methods

Evidence Map

An evidence map is "a systematic search of a broad field to identify gaps in knowledge and/or future research needs that presents results in a user-friendly format, often a visual figure or graph, or a searchable database" [19]. These reviews typically encompass different types of studies, such as reviews and primary studies. They rely on a systematic search strategy, conducting screening based on explicit eligibility criteria, and conducting data extraction in a structured format. Critical appraisal may be performed, but it is not required [19].

Searching

Keyword Selection and Initial Database Query

To comprehensively identify relevant keywords, we resorted to using a purposive sample of 13 literature reviews [6,7,9,10,18,20-29] and a review protocol [30] related to conversational agents for health and well-being. A total of 318 keywords were extracted. The removal of duplicates resulted in 220 keywords.

Keywords were categorized into tentative domains and tested in MEDLINE; we resorted to using PubMed as the interface. The search process was documented and iteratively optimized [31] to yield a compromise between feasibility and completeness. This led to the choice of using the following two final keyword domains: K1 (variations of conversational agent–related terms) and K2 (variations of health-related and well-being–related terms). We expanded the K1 domain by including all variations and combinations of the terms *agent* (ie, *bot*, *robot*, *assistant*, *coach*, *companion*, *system*, *avatar*, and *entity program*) and *conversational* (ie, *talking*, *voice*, *communication*, *social*, *dialogue*, and *utterance*). We also included terms in the K1 domain related to popular commercial conversational agents, such as *Google Home*, *Google Assistant*, *Cortana*, *Alexa*, and *Siri*.

The search strategy encompassed (when applicable) plural forms of keywords and variations at the end of keywords, which were indicated with the wildcard asterisk (ie, "*"). We accounted for variations in the middle of phrases and hyphenation by using similar vocabulary (eg, *talk bot* and *talkative bot*, *ecoach* and *e-coach*, etc). We ended up with 265 keywords for the K1 domain and 13 keywords for the K2 domain.

There was ambiguity between the terms *Amazon Alexa assistant* and *alexa fluor compounds*. Therefore, a third keyword domain was developed (K3), which consisted of variations of *alexa fluor compounds* to be excluded from the search query. This domain limited the number of irrelevant results through the use of database syntax.

The search string for the search conducted on MEDLINE via PubMed is depicted in Multimedia Appendix 1. The search was restricted to titles and abstracts only.

Database Selection

Initially, we listed the data sources used by the aforementioned sample of studies [6,7,9,10,18,20-30]. This led to a set of the following nine potentially useful scientific literature databases: MEDLINE; CINAHL; Web of Science; Scopus; the Cochrane, ACM, IEEE, and Joanna Briggs Institute (JBI) databases; and Google Scholar. These were then analyzed in terms of their coverage and suitability.

Both ACM and IEEE publish computer science conference proceedings, and these were relevant to our evidence map and supplemented our health data sources. Although Scopus and Web of Science cover most journal publications from ACM and IEEE, their indexing of conference proceedings is poorer [32]. Therefore, from a coverage standpoint, it would make sense to retain these databases.

In terms of the search quality of the data sources, the work of Gusenbauer and Haddaway [33] endorsed the choice of using MEDLINE, CINAHL, Web of Science, Scopus, Cochrane, and ACM. These authors did not consider Google Scholar to be an appropriate principal search system, since it does not allow for the use of Boolean queries and does not provide consistent results over time [33].

After taking both coverage and search qualities into account, we decided to retain Google Scholar and ACM in the final list of databases. When compared to Scopus and Web of Science, Google Scholar is still the most far-reaching source [34]. Scopus and Web of Science exhibit indexing lags and may miss the latest publications, unlike Google Scholar [35,36]. However, we discarded IEEE from the list on the grounds of its limited search capabilities, as we were unable to search this database for all the proposed keywords.

The decision to exclude grey literature was dictated by our available resources. A definition of grey literature was put forward during the 1997 International Conference on Grey Literature in Luxembourg and was expanded in 2004 (in New York) as "information produced on all levels of government, academics, business and industry in print and electronic formats, but which is not controlled by commercial publishers, i.e. where publishing is not the primary activity of the producing body" [37]. Recently, Garousi et al [38] proposed a wider definition for grey literature in the software engineering field and grouped grey literature into 3 tiers according to expertise (ie, the established knowledge of the content producer) and outlet control (ie, content production in conformance with explicit and transparent criteria). The tiers encompass content from blogs, tweets, and news articles; presentations, and government reports. Regardless of the definition, grey literature would add to the predictably extensive amount of formal literature and was deemed to be of uncertain value in light of the review's aim. Grey literature would also require additional resources for analysis.

Testing the Query on the Remaining Databases

The PubMed search query was used in CINAHL (via EBSCO [Elton B. Stephens Company]); Web of Science; Scopus; and the Cochrane (via EBSCO), ACM, and JBI databases; minor adjustments were made [31]. The restriction to a title and

abstract search was maintained in these databases, with the exception of the JBI database, which does not allow for such searches.

The Google Scholar query, which is presented in Multimedia Appendix 1, comprised short forms of the K1 and K2 domain terms. This search was limited to literature published from 2020 onward and those without patents and citations. The search results were sorted by relevance. As recommended by Haddaway et al [39], we retrieved only the first 300 results.

Citation Searching

We will conduct a backward citation search by manually searching the reference lists of all articles included in the evidence map. Forward citation searching by using a citation index to identify studies that cite included articles [40] was deemed unfeasible in light of the project resources.

Selection of Studies

Rayyan (Rayyan Systems Inc)—a collaborative web application—was used to streamline the selection of studies [41]. It supports the screening and coding of studies, documents reviewers' decisions by using tags, and allows for the organization of records via filters.

Teams of 2 researchers will independently screen retrieved records by using predetermined eligibility criteria for primary studies and reviews, which are detailed in Textboxes 1 and 2. Meeting all of the inclusion criteria will be a requirement for an article to be selected for the evidence map. Selected articles must also not meet any of the exclusion criteria.

Textbox 1. Eligibility criteria for primary studies on conversational agents for health and well-being.

Inclusion criteria

- Primary studies that focus on persons of all ages regardless of their health status
- Presenting a computer program that is able to simulate two-way human conversation for a health-related purpose or general well-being–related purpose by using language (speech or text) and is potentially supplemented with nonlanguage modalities, regardless of the input and output options
- Reporting the design, development, evaluation, or implementation of conversational agents regardless of the involvement of human users and study design

Exclusion criteria

- Articles focused solely on caregivers, health care professionals, or the education of health care professionals or students
- Articles that do not concomitantly report information on the following three components: the health intervention, the agent, and the conversational capabilities (eg, articles focused on individual features only, such as speech recognition)
- Agents without automated conversational capabilities (eg, Wizard of Oz tool)
- Press articles
- Unavailable full text
- Articles written in languages other than English, Italian, French, Portuguese, and Spanish
- Commentaries, opinion papers, position papers, study protocols, or any article not presenting primary research (eg, discussing the intention to develop a conversational agent)
- Conference abstracts

Textbox 2. Eligibility criteria for reviews on conversational agents for health and well-being.

Inclusion criteria

- All review designs that focus on primary studies on human participants regardless of their health status
- Reviews comprised of studies that present a computer program that is able to simulate human conversation for a health-related purpose or general well-being–related purpose by using language and is potentially supplemented with nonlanguage modalities, regardless of the input and output options
- Reporting the design, development, evaluation, implementation, or funding of conversational agents regardless of the involvement of human users and study design

Exclusion criteria

- Reviews that include conversational agents for the education of health care professionals or students or another nonhealth purpose
- Reviews including studies on nonconversational agents or those without automated conversational capabilities (eg, Wizard of Oz tool)
- Review protocols
- Unavailable full text
- Articles written in languages other than English, Italian, French, Portuguese, and Spanish

The screening procedure was piloted at the commencement of this stage; we used a set of primary studies and reviews. In the first stage, we reviewed the titles and abstracts of retrieved records. Discrepancies in inclusion and exclusion decisions were resolved by a third reviewer. In the second stage we will focus on the full-text review of the records selected in the first stage. Discrepancies in inclusion and exclusion decisions at this stage will be resolved by discussion between the reviewer pairs, and if a consensus is not reached, a third researcher will be involved.

Data Extraction

Data collection forms for primary studies and reviews were designed using Microsoft Excel spreadsheets. In addition to general information such as article ID numbers (unique identifiers), titles, and aims, we will extract information related to our research questions. Moreover, we will extract definitions of conversational agents if they are provided. The forms will be piloted with a set of primary studies and reviews to ensure that they capture relevant information comprehensively. Multimedia Appendix 2 presents variables that were preliminarily included in the Excel spreadsheet.

Teams of 2 researchers will independently extract data from included records. Potential discrepancies will be resolved via consultation with a third researcher.

Critical Appraisal

As previously explained, critical appraisal is recommended for evidence maps but is not mandatory [19]. Therefore, based on project resources, we will conduct the critical appraisal of systematic reviews, but this will not be done for the anticipated large number of primary studies. A Measurement Tool to Assess Systematic Reviews (AMSTAR) 2—a revised 16-item version of AMSTAR—will be used to evaluate the quality of included systematic reviews [42]. AMSTAR 2 takes longer to apply than AMSTAR; however, both have higher levels of interrater reliability compared to those of similar tools, such as the Risk of Bias Assessment Tool for Systematic Reviews (ROBIS) [43]. Compared to the ROBIS, AMSTAR 2 is easier to apply. Further, guidance on using AMSTAR 2 is clearer and simpler, which promotes its use by nonexperienced reviewers [44].

Data Synthesis

We will assess primary and secondary studies separately in the analysis. Each data set will be subjected to a descriptive analysis to summarize the characteristics of included studies. This will be guided by our research questions. The bivariate exploration of data will be conducted, as appropriate. Subgroup analyses will be conducted, if feasible.

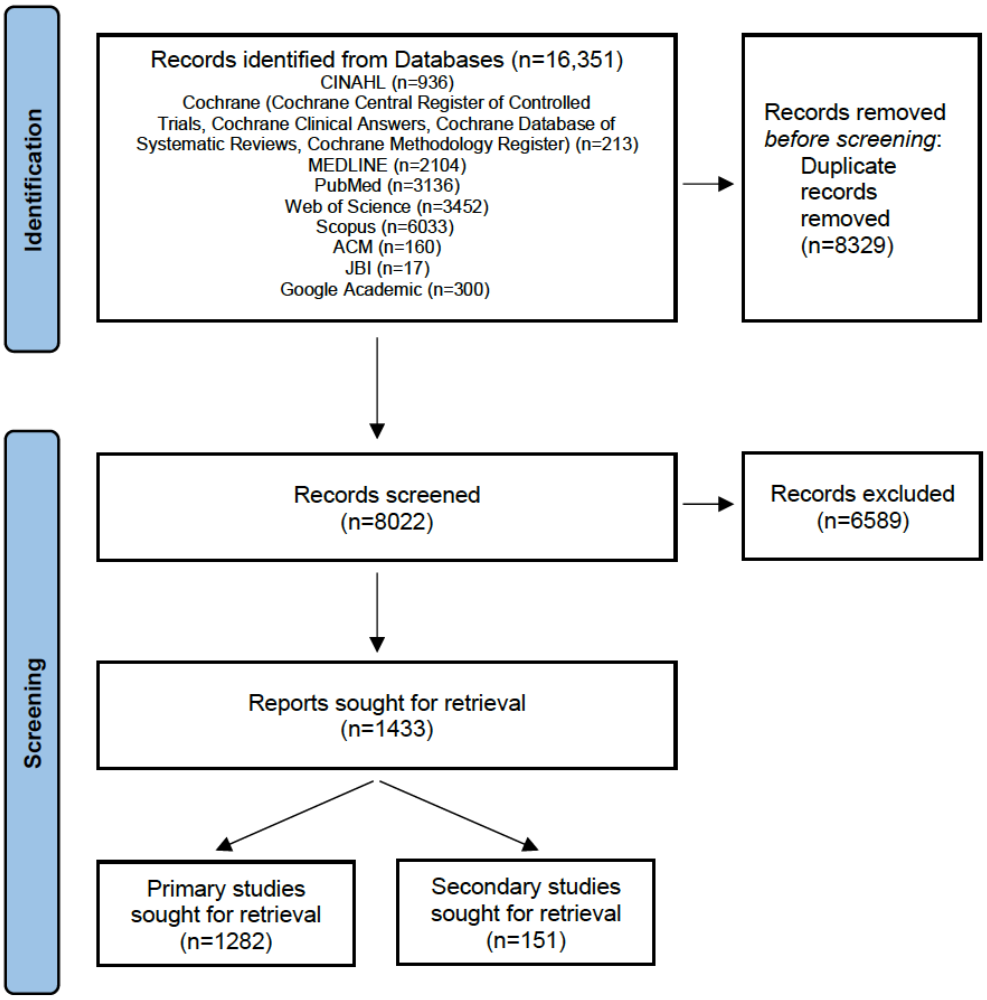
High-level maps, such as scatter charts and bubble charts, will be used to depict results and illustrate research trends and gaps. The development of the searchable database will be informed by the research questions and data extraction forms.

Results

The literature search in MEDLINE; CINAHL; Web of Science; Scopus; the Cochrane, ACM, IEEE, and JBI databases; and Google Scholar was conducted between November 11 and November 19, 2020. A total of 16,351 records were identified and exported to Rayyan. The removal of duplicates yielded 8022 records, which were subjected to screening (Figure 1).

As of April 2021, we produced an operational procedure to support screening (aided by Rayyan) to ensure consistency and reduce the amount of errors. We also drafted a glossary with operational definitions to support the study selection and data extraction procedures. This is regarded as a living document, which will be updated as our work progresses (Multimedia Appendix 3; the glossary is currently based on 5 publications [7,45-48]). Moreover, we concluded the first the stage of screening, as depicted in Figure 1.

Figure 1. A PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart of the literature search and selection procedures (first stage of screening) [49]. JBI: Joanna Briggs Institute.



Discussion

Our work aims to provide an overview of all relevant evidence on conversational agents for health and well-being across the life course. The evidence and gap map is a type of literature review that is particularly suited for this aim. As White et al [50] put it, "[evidence and gap maps] usually show what evidence is there, not what the evidence says." By following the same systematic approach as a systematic review, we aim to offer a wider picture of the research landscape by including both primary studies and meta-research. To the best of our knowledge, published reviews on conversational agents, such as those of Car et al [7] and Chattopadhyay et al [27], have only included primary studies. Therefore, we add to current knowledge by extending the scope of existing reviews. As for other evidence maps, the novelty of our evidence synthesis comes from its breadth (ie, summarizing all reviews and primary studies on the topic without collating effects or effect sizes), while the strength of the scoping reviews comes from their depth (ie, typically a narrower scope and direction of effect) [50]. Another aspect regarding the broader scope of our work is our definition of a conversational agent, which comprises not only chatbots but also agents with physical or web-based embodiments, such as robots or anthropomorphic web-based agents.

The number of reviews that were preliminarily uncovered by our review also suggests that it may appropriate to conduct an umbrella review of meta-research in the future. This will help those aspiring to conduct a review in this field to avoid wasteful redundancies. The number of reviews we uncovered raises the issue of the degree of overlap and the incremental value of these publications. Recently, Tugwell et al [51] elaborated on the replication of systematic reviews. In addition to direct replication, which involves repetition for verifying results, these authors put forward the concept of conceptual replication, in which a research question is broadened or narrowed to ascertain different intervention types, settings, outcomes, or study designs [51]. The data extraction of the included reviews in our work will clarify whether these reviews performed conceptual replication or undesirable repetition, which has been coined as *research waste* [51]. We envisage that the open, searchable database that will be developed in the data synthesis stage will help researchers to avoid future research waste by highlighting published reviews.

Another methodological consideration is the role of bias and its influence on the evidence map results. For instance, we addressed bias in the selection of studies through a multifold

procedure [52]. First, we detailed the research questions and the inclusion and exclusion criteria to avoid inconsistent application. Second, we developed a glossary of operational definitions to reduce discrepancies in the interpretation of key terms. Third, per the review protocol, two independent reviewers will screen and extract data, and a third reviewer will be involved when discrepancies cannot be resolved by consensus. Other procedures specified in the protocol include presenting a PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram for results, pilot testing the several steps of the review method (searching, selection of studies, data extraction and critical appraisal), and having workflows subsumed in the evidence map.

The evidence and gap map relies on a framework for detailing its dimensions, which will be operationalized by using row and column headings [50]. The eCCo project will tackle this issue by pursuing an integrated approach based on the interdependency of its two core activities, as follows: (1) producing an evidence map on conversational agents in health and well-being and (2) consensualizing a taxonomy on the topic. The matrix for the data extraction (Multimedia Appendix 2) was informed by the first draft of this taxonomy, and the evidence map will allow for the identification of international experts who will be involved in the consensus conference. Further, the results of the evidence map will be used to fine-tune the taxonomy draft before the draft is subjected to the scrutiny of international experts. Our research project is in line with the work of Bittner et al [53], who used an empirical-to-conceptual approach for the development of a taxonomy for conversational agents and drew upon a literature review to identify new subsets of objects. We identified a set of taxonomies in the field, albeit none were health specific [8,9]. The foci of all these taxonomies are design options that do not detail the aspects of the health intervention. Guidelines for reporting on digital health interventions [54,55] have recommended the specification of intervention components and modes of delivery (eg, specifying who delivers the intervention, who receives the intervention, how often the intervention is delivered, the intervention duration, the format of the intervention, and the context in which the intervention is delivered). These requirements were considered when first drafting the eCCo taxonomy.

None of the above-mentioned taxonomies used a scientific consensus process to standardize terminology and categories of conversational agents. This is a limitation that we are addressing via the eCCo project.

In spite of its clear strengths, the review will not be without limitations. Integral to evidence maps is the fact that study outcomes are not extracted to ascertain effects. Moreover, the fact that we will not appraise the quality of primary studies means that we cannot pinpoint research gaps for areas with high volumes of potentially poor-quality studies. Another limitation is that research gaps do not necessarily translate to research needs; when prioritizing research needs, one should consider aspects such as relevance and potential impact. Nonetheless, synthesizing evidence on health-focused conversational agents will facilitate the prioritization of strategic research by commissioners.

In addition to fostering collaboration, we envisage that the open, searchable database will also contribute to bridging the translational gap by, for instance, identifying projects with a higher technology readiness level. Such projects can more easily reach the market via partnerships with the business sector.

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Authors' Contributions

MPG, LA, and EM designed the study. The remaining authors contributed to iteratively conceiving the study in more detail. MPG, HRH, MEK, CB, JB, and IBF prepared the protocol, and revisions were made by the remaining authors. HRH and MEK conducted the literature searches. All authors except MPG executed the first stage of screening.

Conflicts of Interest

None declared.

Multimedia Appendix 1
MEDLINE and Google Scholar search.
[PDF File (Adobe PDF File), 75 KB - resprot_v10i9e26680_app1.pdf]

Multimedia Appendix 2
Preliminary data extraction form.
[PDF File (Adobe PDF File), 85 KB - resprot_v10i9e26680_app2.pdf]

Multimedia Appendix 3
Operational definitions.
[PDF File (Adobe PDF File), 119 KB - resprot_v10i9e26680_app3.pdf]

References

1. Noncommunicable diseases: mortality. World Health Organization. URL: https://www.who.int/gho/ncd/mortality_morbidity/en/ [accessed 2021-07-14]
2. Nyberg ST, Singh-Manoux A, Pentti J, Madsen IEH, Sabia S, Alfredsson L, et al. Association of healthy lifestyle with years lived without major chronic diseases. JAMA Intern Med 2020 May 01;180(5):760-768 [FREE Full text] [doi: 10.1001/jamainternmed.2020.0618] [Medline: 32250383]
3. Kelly MP, Barker M. Why is changing health-related behaviour so difficult? Public Health 2016 Jul;136:109-116 [FREE Full text] [doi: 10.1016/j.puhe.2016.03.030] [Medline: 27184821]
4. Rinaldi G, Hijazi A, Haghparast-Bidgoli H. Cost and cost-effectiveness of mHealth interventions for the prevention and control of type 2 diabetes mellitus: A systematic review. Diabetes Res Clin Pract 2020 Apr;162:108084. [doi: 10.1016/j.diabres.2020.108084] [Medline: 32061819]
5. Blueprint for a digital transformation of health and care in an ageing society. European Commission. 2017. URL: https://ec.europa.eu/digital-single-market/en/blueprint-digital-transformation-health-and-care-ageing-society [accessed 2021-01-24]
6. Laranjo L, Dunn AG, Tong HL, Kocaballi AB, Chen J, Bashir R, et al. Conversational agents in healthcare: a systematic review. J Am Med Inform Assoc 2018 Sep 01;25(9):1248-1258 [FREE Full text] [doi: 10.1093/jamia/ocy072] [Medline: 30010941]
7. Car TL, Dhinagaran DA, Kyaw BM, Kowatsch T, Joty S, Theng Y, et al. Conversational agents in health care: Scoping review and conceptual analysis. J Med Internet Res 2020 Aug 07;22(8):e17158 [FREE Full text] [doi: 10.2196/17158] [Medline: 32763886]
8. Diederich S, Brendel AB, Kolbe L. Towards a taxonomy of platforms for conversational agent design. 2019 Presented at: Internationale Tagung Wirtschaftsinformatik; February 2019; Siegen, Germany.
9. Montenegro JLZ, da Costa CA, da Rosa Righi R. Survey of conversational agents in health. Expert Syst Appl 2019 Sep;129:56-67. [doi: 10.1016/j.eswa.2019.03.054]
10. Kocaballi AB, Berkovsky S, Quiroz JC, Laranjo L, Tong HL, Rezazadegan D, et al. The personalization of conversational agents in health care: Systematic review. J Med Internet Res 2019 Nov 07;21(11):e15360 [FREE Full text] [doi: 10.2196/15360] [Medline: 31697237]
11. Burden D, Savin-Baden M. What are virtual humans? In: Virtual Humans: Today and Tomorrow. Boca Raton, Florida: Chapman and Hall/CRC Press; 2019.
12. International Classification of Health Interventions (ICHI). World Health Organization. URL: https://www.who.int/standards/classifications/international-classification-of-health-interventions [accessed 2021-06-14]
13. Angelini L, Mugellini E, Abou KO, Boqué N, Del Bas J, Röcke C, et al. The Nestore e-Coach: Accompanying older adults through a personalized pathway to wellbeing. 2019 Jun Presented at: PETRA '19: The 12th PErvasive Technologies Related to Assistive Environments Conference; June 5-7, 2019; Rhodes, Greece p. 620-628. [doi: 10.1145/3316782.3322763]
14. El Kamali M, Angelini L, Caon M, Andreoni G, Khaled OA, Mugellini E. Towards the NESTORE e-coach: A tangible and embodied conversational agent for older adults. 2018 Oct Presented at: UbiComp '18: The 2018 ACM International Joint Conference on Pervasive and Ubiquitous Computing; October 8-12, 2018; Singapore, Singapore p. 1656-1663. [doi: 10.1145/3267305.3274188]
15. Félix IB, Guerreiro MP, Cavaco A, Cláudio AP, Mendes A, Balsa J, et al. Development of a complex intervention to improve adherence to antidiabetic medication in older people using an anthropomorphic virtual assistant software. Front Pharmacol 2019;10:680 [FREE Full text] [doi: 10.3389/fphar.2019.00680] [Medline: 31281256]
16. Guerreiro MP, Félix IB, Balsa J, Carmo MB, Henriques MA, Cavaco A, et al. Contribution of an intelligent virtual assistant to healthy ageing in idults with type 2 diabetes. In: Mendes D, Fonseca C, Lopes M, García-Alonso J, Murillo J, editors. Exploring the Role of ICTs in Healthy Aging. Hershey, Pennsylvania: IGI Global; 2020.
17. Harnessing the power of conversational e-coaches for health and well-being through Swiss-Portuguese Collaboration. eCCo. URL: https://ecco.esel.pt/ [accessed 2021-07-15]
18. Xing Z, Yu F, Du J, Walker JS, Paulson CB, Mani NS, et al. Conversational interfaces for health: Bibliometric analysis of grants, publications, and patents. J Med Internet Res 2019 Nov 18;21(11):e14672 [FREE Full text] [doi: 10.2196/14672] [Medline: 31738171]
19. Miake-Lye IM, Hempel S, Shanman R, Shekelle PG. What is an evidence map? A systematic review of published evidence maps and their definitions, methods, and products. Syst Rev 2016 Feb 10;5:28 [FREE Full text] [doi: 10.1186/s13643-016-0204-x] [Medline: 26864942]
20. Kamali ME, Angelini L, Caon M, Carrino F, Rocke C, Guye S, et al. Virtual coaches for older adults' wellbeing: A systematic review. IEEE Access 2020;8:101884-101902. [doi: 10.1109/access.2020.2996404]
21. Pereira J, Díaz Ó. Using health chatbots for behavior change: A mapping study. J Med Syst 2019 Apr 04;43(5):135. [doi: 10.1007/s10916-019-1237-1] [Medline: 30949846]

22. Vaidyam AN, Wisniewski H, Halamka JD, Kashavan MS, Torous JB. Chatbots and conversational agents in mental health: A review of the psychiatric landscape. Can J Psychiatry 2019 Jul;64(7):456-464. [doi: 10.1177/0706743719828977] [Medline: 30897957]
23. Ma T, Chattopadhyay D, Sharifi H. Virtual humans in health-related interventions: A meta-analysis. 2019 May Presented at: CHI '19: CHI Conference on Human Factors in Computing Systems; May 4-9, 2019; Glasgow, Scotland p. 1-6. [doi: 10.1145/3290607.3312853]
24. Tropea P, Schlieter H, Sterpi I, Judica E, Gand K, Caprino M, et al. Rehabilitation, the great absentee of virtual coaching in medical care: Scoping review. J Med Internet Res 2019 Oct 01;21(10):e12805 [FREE Full text] [doi: 10.2196/12805] [Medline: 31573902]
25. Provoost S, Lau HM, Ruwaard J, Riper H. Embodied conversational agents in clinical psychology: A scoping review. J Med Internet Res 2017 May 09;19(5):e151 [FREE Full text] [doi: 10.2196/jmir.6553] [Medline: 28487267]
26. Schachner T, Keller R, Wangenheim FV. Artificial intelligence-based conversational agents for chronic conditions: Systematic literature review. J Med Internet Res 2020 Sep 14;22(9):e20701 [FREE Full text] [doi: 10.2196/20701] [Medline: 32924957]
27. Chattopadhyay D, Ma T, Sharifi H, Martyn-Nemeth P. Computer-controlled virtual humans in patient-facing systems: Systematic review and meta-analysis. J Med Internet Res 2020 Jul 30;22(7):e18839 [FREE Full text] [doi: 10.2196/18839] [Medline: 32729837]
28. Bibault JE, Chaix B, Nectoux P, Pienkowsky A, Guillemasse A, Brouard B. Healthcare ex machina: Are conversational agents ready for prime time in oncology? Clin Transl Radiat Oncol 2019 Apr 04;16:55-59 [FREE Full text] [doi: 10.1016/j.ctro.2019.04.002] [Medline: 31008379]
29. Hoermann S, McCabe KL, Milne DN, Calvo RA. Application of synchronous text-based dialogue systems in mental health interventions: Systematic review. J Med Internet Res 2017 Jul 21;19(8):e267 [FREE Full text] [doi: 10.2196/jmir.7023] [Medline: 28784594]
30. de Cock C, Milne-Ives M, van Velthoven MH, Alturkistani A, Lam C, Meinert E. Effectiveness of conversational agents (virtual assistants) in health care: Protocol for a systematic review. JMIR Res Protoc 2020 Mar 09;9(3):e16934 [FREE Full text] [doi: 10.2196/16934] [Medline: 32149717]
31. Bramer WM, de Jonge GB, Rethlefsen ML, Mast F, Kleijnen J. A systematic approach to searching: an efficient and complete method to develop literature searches. J Med Libr Assoc 2018 Oct;106(4):531-541 [FREE Full text] [doi: 10.5195/jmla.2018.283] [Medline: 30271302]
32. Bar-Ilan J. Tale of Three Databases: The Implication of Coverage Demonstrated for a Sample Query. Front Res Metr Anal 2018 Feb 20;3:6. [doi: 10.3389/frma.2018.00006]
33. Gusenbauer M, Haddaway NR. Which academic search systems are suitable for systematic reviews or meta-analyses? Evaluating retrieval qualities of Google Scholar, PubMed, and 26 other resources. Res Synth Methods 2020 Mar;11(2):181-217 [FREE Full text] [doi: 10.1002/jrsm.1378] [Medline: 31614060]
34. Martín-Martín A, Orduna-Malea E, Delgado López-Cózar E. Coverage of highly-cited documents in Google Scholar, Web of Science, and Scopus: a multidisciplinary comparison. Scientometrics 2018 Jun 26;116(3):2175-2188. [doi: 10.1007/s11192-018-2820-9]
35. Moed HF, Bar-Ilan J, Halevi G. A new methodology for comparing Google Scholar and Scopus. J Informetr 2016 May;10(2):533-551. [doi: 10.1016/j.joi.2016.04.017]
36. Haustein S, Bowman T, Costas R. When is an article actually published? An analysis of online availability, publication, and indexation dates. arXiv Preprint posted online on May 4, 2015. [FREE Full text]
37. Lefebvre C, Glanville J, Briscoe S, Littlewood A, Marshall C, Metzendorf MI, et al. Chapter 4: Searching for and selecting studies. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al, editors. Cochrane Handbook for Systematic Reviews of Interventions version 6.2. Chichester, United Kingdom: John Wiley & Sons; 2019.
38. Garousi V, Felderer M, Mäntylä MV. Guidelines for including grey literature and conducting multivocal literature reviews in software engineering. Inf Softw Technol 2019 Feb;106:101-121. [doi: 10.1016/j.infsof.2018.09.006]
39. Haddaway NR, Collins AM, Coughlin D, Kirk S. The role of Google Scholar in evidence reviews and its applicability to grey literature searching. PLoS One 2015;10(9):e0138237. [doi: 10.1371/journal.pone.0138237] [Medline: 26379270]
40. Briscoe S, Bethel A, Rogers M. Conduct and reporting of citation searching in Cochrane systematic reviews: A cross-sectional study. Res Synth Methods 2020 Mar;11(2):169-180 [FREE Full text] [doi: 10.1002/jrsm.1355] [Medline: 31127978]
41. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. Syst Rev 2016 Dec 05;5(1):210 [FREE Full text] [doi: 10.1186/s13643-016-0384-4] [Medline: 27919275]
42. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ 2017 Dec 21;358:j4008 [FREE Full text] [doi: 10.1136/bmj.j4008] [Medline: 28935701]
43. Gates M, Gates A, Duarte G, Cary M, Becker M, Prediger B, et al. Quality and risk of bias appraisals of systematic reviews are inconsistent across reviewers and centers. J Clin Epidemiol 2020 Sep;125:9-15 [FREE Full text] [doi: 10.1016/j.jclinepi.2020.04.026] [Medline: 32416337]

44. Pieper D, Puljak L, González-Lorenzo M, Minozzi S. Minor differences were found between AMSTAR 2 and ROBIS in the assessment of systematic reviews including both randomized and nonrandomized studies. J Clin Epidemiol 2019 Apr;108:26-33. [doi: 10.1016/j.jclinepi.2018.12.004] [Medline: 30543911]
45. Bickmore TW, Picard RW. Establishing and maintaining long-term human-computer relationships. ACM Trans Comput Hum Interact 2005 Jun;12(2):293-327. [doi: 10.1145/1067860.1067867]
46. de Antonio A, Aylett R, Ballin D. Intelligent virtual agents. 2001 Presented at: Third International Workshop on Intelligent Virtual Agents; September 10-11, 2001; Madrid, Spain. [doi: 10.1007/3-540-44812-8]
47. El Kamali M, Angelini L, Caon M, Khaled OA, Mugellini E, Dulack N, et al. NESTORE: Mobile chatbot and tangible vocal assistant to support older adults' wellbeing. 2020 Presented at: CUI '20: 2nd Conference on Conversational User Interfaces; July 22-24, 2020; Bilbao, Spain p. 1-3. [doi: 10.1145/3405755.3406167]
48. Poole DL, Mackworth AK. Artificial Intelligence: Foundations of Computational Agents, 2nd Edition. Cambridge, United Kingdom: Cambridge University Press; 2017.
49. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ 2021;372. [doi: 10.1136/bmj.n71] [Medline: 33782057]
50. White H, Albers B, Gaarder M, Kornør H, Littell J, Marshall Z, et al. Guidance for producing a Campbell evidence and gap map. Campbell Syst Rev 2020 Nov 19;16(4):e1125. [doi: 10.1002/cl2.1125]
51. Tugwell P, Welch VA, Karunananthan S, Maxwell LJ, Akl EA, Avey MT, et al. When to replicate systematic reviews of interventions: consensus checklist. BMJ 2020 Sep 15;370:m2864. [doi: 10.1136/bmj.m2864] [Medline: 32933948]
52. Drucker AM, Fleming P, Chan A. Research techniques made simple: Assessing risk of bias in systematic reviews. J Invest Dermatol 2016 Nov;136(11):e109-e114 [FREE Full text] [doi: 10.1016/j.jid.2016.08.021] [Medline: 27772550]
53. Bittner EAC, Oeste-Reiß S, Leimeister JM. Where is the bot in our team? Toward a taxonomy of design option combinations for conversational agents in collaborative work. 2019 Presented at: 52nd Hawaii International Conference on System Sciences; January 8-11, 2019; Maui, Hawaii, USA. [doi: 10.24251/hicss.2019.035]
54. Agarwal S, LeFevre AE, Lee J, L'Engle K, Mehl G, Sinha C, WHO mHealth Technical Evidence Review Group. Guidelines for reporting of health interventions using mobile phones: mobile health (mHealth) evidence reporting and assessment (mERA) checklist. BMJ 2016 Mar 17;352:i1174. [doi: 10.1136/bmj.i1174] [Medline: 26988021]
55. Eysenbach G, CONSORT-EHEALTH Group. CONSORT-EHEALTH: improving and standardizing evaluation reports of Web-based and mobile health interventions. J Med Internet Res 2011 Dec 31;13(4):e126 [FREE Full text] [doi: 10.2196/jmir.1923] [Medline: 22209829]

Abbreviations

AMSTAR: A Measurement Tool to Assess Systematic Reviews
EBSCO: Elton B. Stephens Company
eCCo: Harnessing the Power of Conversational e-Coaches for Health and Well-being Through Swiss-Portuguese Collaboration
JBI: Joanna Briggs Institute
NCD: noncommunicable disease
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
ROBIS: Risk of Bias Assessment Tool for Systematic Reviews

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Protocol

An App-Based Surveillance System for Undergraduate Students' Mental Health During the COVID-19 Pandemic: Protocol for a Prospective Cohort Study

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Abstract

Background: The COVID-19 pandemic is a public health emergency that poses challenges to the mental health of approximately 1.4 million university students in Canada. Preliminary evidence has shown that the COVID-19 pandemic had a detrimental impact on undergraduate student mental health and well-being; however, existing data are predominantly limited to cross-sectional survey-based studies. Owing to the evolving nature of the pandemic, longer-term prospective surveillance efforts are needed to better anticipate risk and protective factors during a pandemic.

Objective: The overarching aim of this study is to use a mobile (primarily smartphone-based) surveillance system to identify risk and protective factors for undergraduate students' mental health. Factors will be identified from weekly self-report data (eg, affect and living accommodation) and device sensor data (eg, physical activity and device usage) to prospectively predict self-reported mental health and service utilization.

Methods: Undergraduate students at Western University (London, Ontario, Canada), will be recruited via email to complete an internet-based baseline questionnaire with the option to participate in the study on a weekly basis, using the Student Pandemic Experience (SPE) mobile app for Android/iOS. The app collects sensor samples (eg, GPS coordinates and steps) and self-reported weekly mental health and wellness surveys. Student participants can opt in to link their mobile data with campus-based administrative data capturing health service utilization. Risk and protective factors that predict mental health outcomes are expected to be estimated from (1) cross-sectional associations among students' characteristics (eg, demographics) and key psychosocial factors (eg, affect, stress, and social connection), and behaviors (eg, physical activity and device usage) and (2) longitudinal associations between psychosocial and behavioral factors and campus-based health service utilization.

Results: Data collection began November 9, 2020, and will be ongoing through to at least October 31, 2021. Retention from the baseline survey (N=427) to app sign-up was 74% (315/427), with 175-215 (55%-68%) app participants actively responding to weekly surveys. From November 9, 2020, to August 8, 2021, a total of 4851 responses to the app surveys and 25,985 sensor

samples (consisting of up to 68 individual data items each; eg, GPS coordinates and steps) were collected from the 315 participants who signed up for the app.

Conclusions: The results of this real-world longitudinal cohort study of undergraduate students' mental health based on questionnaires and mobile sensor metrics is expected to show psychosocial and behavioral patterns associated with both positive and negative mental health–related states during pandemic conditions at a relatively large, public, and residential Canadian university campus. The results can be used to support decision-makers and students during the ongoing COVID-19 pandemic and similar future events. For comparable settings, new interventions (digital or otherwise) might be designed using these findings as an evidence base.

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KEYWORDS

undergraduate; mental health; smartphone; app; COVID-19; postsecondary institutions; mobile apps; mHealth; mobile health

Introduction

There are approximately 1.4 million students enrolled at Canadian universities [1], and more than 50% of students report feeling overwhelmed, lonely, anxious, and depressed during typical periods of study [2]. The presence of mental health concerns places a demand on campus mental health services, which has only escalated as students cope with the psychological effects of the COVID-19 pandemic [3,4]. Since the start of the pandemic, undergraduate students have faced abrupt campus-based restrictions, displacement from on-campus living and learning environments, increased financial uncertainty, and unprecedented shifts to web-based learning. Further, the necessary physical distancing policies have diminished opportunity for social connection, which is important for coping, particularly during a public health crisis [5]. Preliminary data on undergraduate students have shown detrimental impacts on mental health and psychological well-being [4,6-8]. For example, over 100,000 postsecondary students from across Canada participated in a web-based Statistics Canada–sponsored questionnaire about the impacts of the COVID-19 pandemic. In Spring 2020, students reported significant concern about the pandemic affecting their academic performance, the disruption of their studies, loss of work, and increased concerns about their financial stability [9,10]. As the pandemic progressed to 2021, research involving undergraduates in the United States, Canada, and China continued to show that undergraduate students were experiencing a multitude of difficulties related to their well-being (eg, financial situation and food security) and particularly their mental health (eg, depression and anxiety) as a result of the pandemic [2,3,7-14].

However, notwithstanding some published studies [15-18], the existing knowledge on undergraduate student mental health relies primarily on cross-sectional survey-based research. Owing to the rapidly evolving nature of the pandemic, public health restrictions, and the current vaccine rollout, research is needed to examine the dynamic changes in student mental health. Earlier recommendations for the psychological management of COVID-19 urged widespread surveillance efforts [19], which are critical in anticipating the forthcoming mental health needs for students on campus [20]. Following this, studies that successfully used mobile surveillance systems to examine student mental health during the pandemic are now emerging [17,18].

However, to the best of our knowledge, none of these studies have been performed at a Canadian university and linked to campus-based administrative mental health utilization data. As such, there is a unique opportunity and immediate need to use a mobile surveillance system to identify the personal and contextual risk and protective factors, which might prospectively predict mental health among Canadian undergraduate students, further contributing to the international results emerging in this area. This protocol describes a study that integrates 3 separate data sources—self-reported survey responses, mobile sensor data, and campus-based health administrative data—to identify indicators associated with student mental health. This method of data acquisition based on our designed software will aid in devising strategies to support vulnerable student groups and potentially mitigate the adverse effects of COVID-19 and other future pandemics.

The specific aims of this study are to estimate cross-sectional associations among student characteristics (eg, living accommodation, previous on-campus service utilization, and demographics such as gender/sex), key psychosocial factors (eg, affect, stress, coping, and social support), and behaviors (eg, physical activity, sleep, and device usage) during the pandemic. This study will identify factors associated with student mental health and coping responses during the pandemic. Additionally, longitudinal associations between key psychosocial (eg, affect, stress, coping, and social support) and behavioral factors (eg, physical activity, sleep, and device usage) during the pandemic and key health service utilization outcomes (eg, frequency of visits, diagnoses, and treatments) will be estimated. We anticipate that the estimation of the previously described cross-sectional and longitudinal associations will allow for the identification of indicators of mental health and coping responses during the COVID-19 pandemic for new interventions, and may facilitate a prospective prediction of mental health outcomes by using machine learning methods.

Methods

App Development

Members of this research group (CB, MAB, and DJL) implemented a new software suite called Ecological Momentary

Assessment eXtensions 1 (EMAX1) in 2019, which consisted of a server and customizable mobile app for surveys and device sensor data collection. Previous software in this area tend to rely on uploads of large data batches. One example is StudentLife, which was used for research on university student mental health since 2014 [21] and remains in successful use as of 2021 [18]. In comparison, EMAX opts for more restrained and transaction-based data collection to manage ethical complexities around the collection of personal and potentially identifiable data on a university campus [22]. In addition to StudentLife, software comparable to EMAX has existed for some time, such as (but not limited to) Funf (2011) [23], Mobilyze (2011) [24], and Beiwe (2016) [25]. EMAX further contributes to this space as an up-to-date solution which is expected to be open-sourced/improved [22] for general smartphone-based EMA-type research.

EMAX1 was used to facilitate the development of a compact, digitized version of an existing study called Smart Healthy Campus (SHC). SHC investigated overviews of undergraduate mental health by using long internet-based questionnaires. EMAX1 was used as a cost-effective, customizable software solution to eliminate the disadvantages of using long questionnaires while adding the capability to collect a range of mobile device sensor readings and explore how they might relate to undergraduate students' mental health profiles. The EMAX1-based "Smart Healthy Campus" app was published on Android/iOS. A publication on the preliminary SHC formative work was accepted during this protocol submission [26].

For the current study the EMAX1 software was repurposed and upgraded to accommodate the pandemic context. Specifically, the EMAX2 upgrade was implemented to accommodate new surveys focusing on the pandemic, background data collection events, and additional sensor items (described in Textbox 1). As EMAX2 was developed, a new Android/iOS app based on it was branded as "Student Pandemic Experience" to match the study name, shown in Figure 1. At the same time, the protocol for Student Pandemic Experience was developed with a comprehensive baseline survey assessing sociodemographic and broad indicators of mental health, and brief weekly follow-up surveys measuring time-varying psychological constructs (eg, affect and health behavior engagement). The SPE study received Health Sciences Research Ethics Board approval from Western University in October 2020 and recruitment began in November 2020 when the iOS version of the SPE app was released. The release of the SPE Android app followed in December 2020. A separate paper to describe the EMAX2 platform in technical detail will be available for September 2021 [22].

For the SPE app, there is a maximum of 68 individual data items that may be recorded by our server when certain events occur, such as a questionnaire response event or background data collection event. Table 1 displays these, although each of the 68 data items are not listed on individual rows for brevity. Individual components of key items (such as GPS coordinates) are included as part of the 68-item total. Some items may not be sent depending on participant permissions for the SPE app. There are differences between Android and iOS, which only allowed certain items to be collected on each platform. The category "Mental Health and Support Resources panel" refers to data collection features of a panel from our EMAX2-based apps, which lists mental health–related services and organizations local to Western University (London, Ontario, Canada), with their weblinks and telephone numbers.

Figure 1. The Student Pandemic Experience (SPE) App.

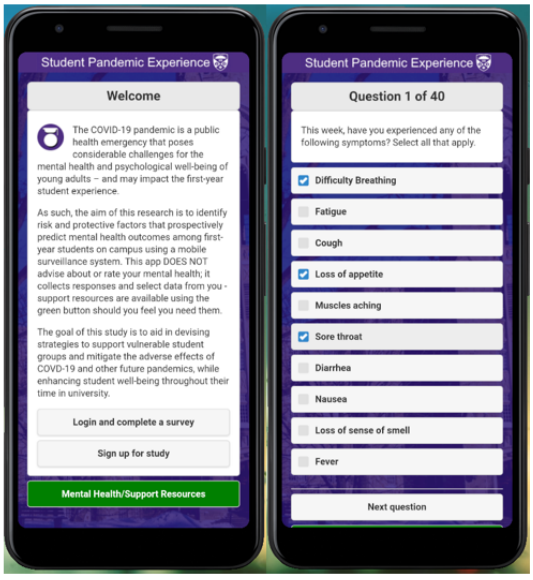

Table 1. A summary of the data collection features of the Ecological Momentary Assessment eXtensions 2nd edition–based Student Pandemic Experience iOS/Android App.

Data collected	Android	iOS
Device and participant characteristics		
Western university email address	✓	✓
Device make/model/platform	✓	✓
Time spent completing the survey	✓	✓
Time spent with the app open	✓	✓
Timestamps of requests	✓	✓
Process names of running apps and time spent executing, idling, RAM usage, and start times	✓	
Detecting the installation of a number of popular apps	✓	✓
Mindfulness minutes		✓
Height/weight (if recorded)		✓
Exercise information (if recorded)		✓
Physical activity and sleep behavior		
Step count information at various times and elevations (including floors ascended or descended)	✓	✓
Apple bedtime information		✓
System sleep time	✓	✓
Imprecise GPS coordinates (latitude, longitude, accuracy, heading, and speed)	✓	✓
Active device usage		
System start time	✓	✓
Central processing unit/individual central processing unit core idle, user, and kernel time	✓	✓
Available RAM/total RAM	✓	✓
SIM Information: call state at current time	✓	✓
Internet connection type (WiFi/data)	✓	✓
Device plugged in or not	✓	✓
Battery level	✓	✓
System up time	✓	✓
Air temperature, ambient light level, humidity, and air pressure	✓	
Amount of free storage space, internal or external	✓	✓
Counts of photos	✓	✓
Mental health and support resources panel with weblinks and telephone numbers		
Time spent with the panel open	✓	✓
Which resource links or phone numbers were selected (records if participants tapped phone numbers or weblinks)	✓	✓
Social activity		
Total contact counts	✓	✓
Family-related contact counts	✓	✓
Friend-related contact counts	✓	✓
Calendar events daily	✓	✓
Calendar events weekly	✓	✓

Study Design

SPE is a longitudinal survey–based prospective cohort study, with data collection based on the purpose-built SPE mobile app, which relies on established smartphone personal sensing capabilities [27]. It is capable of weekly repeat measures, ideally suited to studying time-varying phenomena [28]. The study does share similarities with previous EMA-based smartphone studies [16,21], although this work will have only a weekly

sample rate of self-report surveys, in addition to background sensor data that are collected at multiple points daily.

Setting

The setting is Western University from November 9, 2020, until October 31, 2021. Funds permitting, the study may extend into the Fall 2021 semester, but the study is not expected to continue to 2022. Most participants stated they were living on or near Western University's main campus during the Fall 2020/Winter 2021 semesters; others may be located out of town simply owing to living arrangements. As the baseline survey is internet-based, and additional participation is facilitated through the SPE app, participants may contribute to the study from any location. At the time of writing, some were participating in various countries outside Canada.

Throughout the pandemic, significant outbreak events occurred in residence buildings and in predominantly student living areas in London (Ontario, Canada), similar to other universities [29]. Considering that predominantly student living areas can be COVID-19 hotspots and that restrictive measures changed, we believe this justifies the weekly repeat measures and hourly sensor data collections for this investigation of an overview of undergraduate mental health. Additionally, provincial/university restrictive measures are expected to influence participant location. For instance, Western University's residences were not fully open again in 2021, until February, as Western University delayed opening its residences owing to the provincial lockdown.

Recruitment and Consent

Through campus-wide emailing systems, all Western University undergraduate students were invited via mass email to complete a web-based baseline survey. To complete the baseline survey, a participant had to view and accept the letter of information and consent for the study. After completing the baseline survey, participants received another email with information on the SPE app and Snapchat and quick response codes to download. If participants chose to continue with weekly participation through the SPE app, they were required to view the letter of information again during the sign-up process in the app and were also able to consent for linkage with their records from administrative sources on campus (health and psychological services).

Inclusion and Exclusion Criteria

The initial inclusion criterion was that a participant would be a first-year undergraduate student at Western University; to increase enrollment, in January 2021, this criterion was relaxed to include any undergraduate students. Exclusion criteria were an inability to provide written informed consent or to complete surveys or forms owing to language or cognitive difficulties; students enrolled in graduate or professional programs; or students enrolled and actively participating in the SHC study, which employed a similar version of the software and was initiated prior to the pandemic.

Participant Compensation

Participants will be remunerated for time spent completing surveys. Participants who submitted the internet-based baseline surveys will be compensated with a Can $10 Amazon e-gift card. Participants who complete at least 3 of 4 weekly surveys each month will be compensated with a Can $10 Amazon e-gift card per month. This compensation structure was intended to optimize baseline recruitment and promote participant retention over time.

Baseline Survey

The SPE baseline survey is composed primarily of existing psychometrically tested instruments that demonstrate validity evidence, and takes approximately 30 minutes to complete. It is delivered on the internet through the Qualtrics XM platform. Participants were asked about sociodemographic factors, current living arrangement, physical and mental health history, social support, and COVID-19–related risks. Participants may skip any questions they prefer not to answer. The composition of the baseline survey is outlined below in Textbox 1. Many COVID-19 questions were adapted from The Healthy Minds Network + American College Health Association COVID HMS Survey Items Spring 2020 [30].

Textbox 1. Baseline survey items and questionnaires.

Sociodemographics

- Age
- Sex & gender
- Ethnicity
- Sexual minority status
- Relationship status
- Socioeconomic status

Campus/student data

- Faculty name
- Degree (based on faculty)
- Program year
- Place of residence (on campus in residence, off campus in London, or off campus outside London)
- Classes enrolled in
- Time spent web-based vs in-person learning

Diagnosed mental illness

- Lifetime diagnosis

COVID-19 assessment and history

- Previous diagnosis of COVID-19
- If yes, symptom severity
- If yes, hospitalization
- Engaging in recommended hygiene practices
- COVID-19–related discrimination

Physical activity

- Leisure Time Physical Activity Questionnaire [31]

Perceived social connection

- Social Connectedness Scale 8-items [32]

Depressive symptoms

- Patient Health Questionnaire 9 items [33]

Anxiety symptoms

- Generalized Anxiety Scale, 7-item [34]

Flourishing

- Flourishing Scale, 8-item [35]

Resilience

- Brief Resilience Scale, 6-item [36]

Self-compassion

- Self-Compassion Scale Short Version [37]

Body appreciation

- Body Appreciation Scale-2 [38]

Self-worth

- Contingencies of Self-Worth Scale [39]

Weight bias

- Weight Bias Internalization Scale [40]

Self-objectification

- Self-Objectification Beliefs & Behaviours Scale [41]

SPE App and Weekly Surveys

The SPE app facilitates the distribution of the weekly surveys should participants choose to continue with the study past the baseline survey. An app survey takes approximately 5 minutes to complete each week. Push notifications are sent to participants weekly to remind them to complete a brief report of their psychosocial states and behaviors over the past week. Similar to the baseline survey, they are primarily based on existing validated instruments with some new items for COVID-19. COVID-19–related questions include 2 questions for reporting on COVID-19 symptoms. A notification is set up on the app, so that, if participants report in their questionnaire responses experiencing at least 1 important COVID-19 symptom (such as difficulty breathing, fatigue, cough, loss of appetite, muscles aching, sore throat, diarrhea, nausea, loss of sense of smell, or fever), they are prompted to visit the Ontario government's COVID-19 self-assessment website [42] and be provided with recommendations. Textbox 2 outlines the biweekly assessment items.

The SPE app supports other features in addition to administering the questionnaire. Background data collection occurs every 1, 2, or 3 hours depending on the participant setting. When the app is closed, background data collection stops. The app also includes a "Mental Health Resources" panel that offers various support services relevant to Western University's undergraduate students. If a participant uses this panel, actions including clicking on weblinks or telephone numbers to the services are recorded. The app is designed to collect data from device sensors, such as GPS coordinates, physical steps, and other device and use characteristics (as shown in Table 1). When a participant starts a questionnaire, completes a questionnaire, uses the mental health resource panel, or when the app triggers a background data collection event, based on the participant setting, data are collected through the app. All data are sent over HTTPS and are further encrypted when stored by the app server; GPS coordinates are first encrypted on the device with RSA before being sent over HTTPS.

Textbox 2. Biweekly assessment items.

Mental health symptoms

- Depression Anxiety and Stress Scale [43]

Self-compassion

- 6-item weekly self-compassion items [44]

COVID-19 monitoring

- Symptom monitoring (adapted from Health Canada)
- Pandemic worry
- Impact of pandemic on academics
- Impact of pandemic on mental well-being
- Impact of pandemic on first-year experience

Substance use

- Binge drinking in past 2 weeks
- Use of recreational substances in past 2 weeks

Affect

- Positive and Negative Affective Schedule [45]

Body emotions

- 4-item body self-conscious emotions [46]

COVID-19 monitoring

- Symptom monitoring (adapted from Health Canada)
- Impact of pandemic on first-year experience
- Pandemic worry
- Impact of pandemic on academics
- Impact of pandemic on mental well-being

Dietary restraint

- Restrict food intake to influence shape/weight in past 2 weeks [47]

Physical activity

- Moderate-to-vigorous physical activity in past 2 weeks
- Strength training in past 2 weeks
- Primary reason for exercising

Data Preparation and Analysis

SPSS, R, and Python will be used for data cleaning and analysis of items described in Tables 1 and 2, as required. Additional tools may also be used. The data infrastructure we develop for subsequent publications is expected to support a wide range of analyses, ranging from confirmatory (eg, studying the association between COVID-19 perceptions and mental health utilization) to exploratory (eg, identifying clusters of students with similar psychological profiles). The identification of student clusters based on the psychological profile (derived from questionnaire responses and mobile sensor data) is expected to reveal various mental health–related states, which may range from positive to negative, and predict campus-based mental health utilization. Taken together, this information might then be used to identify students at higher risk and inform decision-making or build evidence-based interventions (digital or otherwise) that may target at-risk individuals, and broadly promote indices of positive mental health and reduce indices of negative mental health.

Initial analyses will use the cross-sectional data to assess univariate and multivariable associations between psychosocial and behavioral factors and outcomes, including health and psychological service utilization. Following this, the longitudinal data will be used to assess these associations and their change over time by applying repeated measures techniques. Statistical

comparisons might include (but will not be limited to) *t* tests, analysis of variance, the Mann–Whitney *U* test, Kruskal–Wallis test, Pearson/Spearman correlation analyses, and linear and multiple regression analyses. This will be followed by exploratory analyses using machine learning methods to identify latent structure in the data and to develop predictive models for mental health outcomes. Additionally, a log of key events related to the COVID-19 pandemic will be compiled during data collection. The log may include items such as on-campus outbreaks and vaccine developments. Potential associations between these events and study data will be explored during analysis. As this is an exploratory study examining a constantly evolving health and social phenomenon, additional research questions and analyses are expected to arise as the study progresses.

Table 2. Data collection summary from November 9, 2020, to August 8, 2021.

Data	Value, n
Participants	315
Survey responses	4851
Sensor samples	25,985

Results

Participation and Data Collection Summary

After 2 months of first year–only recruitment from November 9 to December 31, 2020, a total of 87 first year students were actively participating. To obtain a larger participant group, we amended the study in January 2021 to allow for recruitment of all undergraduate students; a total of 427 completed the baseline survey. In total, 315/427 (74%) students signed up to use the SPE app and 266/315 (84%) completed at least 1 weekly app survey. Recruitment efforts ended in February 2021. From mid-February to April 2021, weekly app usage was in a steady range of 175-215 participants. Regular participation declined over the summer term from May to August 2021, and by August 2021 there were approximately 95 participants still responding to surveys. Data collection, at the time of this writing, was conducted from November 9 to August 8, 2021, and data collection was planned to conclude October 31, 2021. Data collection efforts are summarized below in Table 2. Each participant completed at least 1 survey. Each “sensor sample” consists of all the items in Table 1, although certain values for items may be null owing to participant telephone permissions (they may deny GPS access, for instance) or data simply being unavailable depending on the situation or smartphone model.

The analysis of the survey responses (representative of mental health–related states) and sensor sample data (representative of associated lifestyle/behavior) is not provided in this protocol paper and will be the main component of a subsequent publication.

Demographics

Below, Table 3 outlines key aspects of participant demographics, and Table 4 shows key participant experiences with COVID-19. These results were taken from the SPE internet-based baseline survey. Owing to their length, some data that were collected were omitted from these tables. The full versions of the tables are provided in Multimedia Appendix 1.

Table 3. Participant demographics at baseline. Additionally, as questions can be skipped, sometimes the cells for each item may not add to 100%.

Data	Completed baseline survey and at least 1 app survey (n=266), %	Completed baseline survey only (n=161), %
What is your gender identity?		
Man	22.9	24.9
Woman	75.9	74.5
Trans man	≤5[a]	≤5
Trans woman	≤5	≤5
Gender queer/gender nonconforming	≤5	≤5
Enrollment status		
Full-time	75.2	80.75
Part-time	≤5	≤5
Missing	20	19.3
Enrollment year		
First year	22.2	23.6
Second year	18.8	11.8
Third year	17.7	19.3
Fourth year	14.6	23.6
≥Fifth year	≤5	≤5
Device type		
Android	14.7	22.4
iOS	85.3	77.6
How would you characterize your relationship status?		
Single	56.8	55.9
In a relationship	42.1	41
Married, domestic partnership, engaged	≤5	≤5
Missing	≤5	≤5
Housing situation		
On or off campus non-university housing in London, Ontario	51.5	48.4
On-campus housing	24.4	27.3
Outside of London, Ontario	21.1	21.1
Other	≤5	≤5
Proportion of classes enrolled in primarily web-based learning?		
All classes	81.9	73.7
Some classes	28.1	26.3
Diagnosis for mental health condition		
None	59.4	58.4
Do not know	≤5	≤5
Anxiety	9	6
Bipolar disorder	≤5	≤5
Depression	20	20.5
Eating disorder	≤5	≤5
Neurodevelopmental disorder (eg, attention-deficit/hyperactivity disorder)	≤5	≤5

Data	Completed baseline survey and at least 1 app survey (n=266), %	Completed baseline survey only (n=161), %
Obsessive-compulsive or related disorder (eg, body dysmorphia)	≤5	≤5
Substance use disorder	≤5	≤5
Trauma and stressor related disorders (eg, posttraumatic stress disorder)	≤5	≤5

[a]For privacy reasons, "≤5%" is used in some cells.

Table 4. Experience with COVID-19 at baseline. Additionally, as questions can be skipped, sometimes the cells for each item may not add to 100%.

Data	Completed baseline survey and at least 1 app survey (n=266), %	Completed baseline survey only (n=161), %
Have you had COVID-19?		
Yes (confirmed by a test)	≤5[a]	≤5
Probably (eg, a health care provider told me that I likely had COVID-19, but it was not confirmed by a test)	≤5	≤5
Maybe (eg, I have had symptoms consistent with COVID-19, but it was not confirmed through a test)	7.9	7.5
No (no symptoms or other reason to think I have had it)	89.5	90
How severe were any of the symptoms of COVID-19?[b]		
Severe (eg, difficulty breathing or speaking, low blood pressure, and a high fever of 103°F [39.4°C] or higher)	≤5	≤5
Moderate (eg, some shortness of breath, cough, a fever of 100.4°F [38°C] or higher, or mild [eg, cold-like symptoms])	8.3	6.2
No symptoms (asymptomatic)	≤5	≤5
How likely do you think you will get COVID-19?[c]		
Very likely	≤5	≤5
Likely	≤5	6.2
Somewhat likely	47	42.9
Not at all likely	36.8	41%
To what extent have you been following recommendations for hygiene practices (frequent hand-washing; avoiding touching your eyes, nose, and mouth; and disinfecting surfaces)?		
Not at all following recommendations	≤5%	≤5%
Not closely following recommendations	≤5%	6.2%
Somewhat closely following recommendations	46.2%	46.6%
Very closely following recommendations	49.2%	47.2
To what extent have you been following recommendations for social/physical distancing (maintaining a 6-foot distance between yourself and others in public, avoiding large gatherings, and avoiding nonessential trips outside of home)?		
Not at all following recommendations	≤5	≤5
Not closely following recommendations	≤5	6.8
Somewhat closely following recommendations	46.2	50.9
Very closely following recommendations	49.2	41

[a]For privacy reasons, ≤5% is used in some cells.

[b]Only asked to students who reported having had COVID-19.

[c]May include students that previously disclosed infection.

Discussion

Expected Outcome

This novel and integrated surveillance paradigm will support action to address student mental health during an unprecedented public health crisis. The outcomes of this surveillance study will provide postsecondary institutions with critical data to support evidence-informed planning and decision-making after a pandemic, as well as ongoing resourcing of student mental health supports. Further, the SPE app will be used as a model for the development of other institution-specific tools that combine student-level data, campus-wide administrative data, and longitudinal self-reported data. By examining associations between (1) student characteristics and key psychosocial and behavioral factors and (2) how these factors predict health service utilization, this study will be essential to building capacity at institutions for the early estimation of student mental health concerns, as well as informing the creation of agile and responsive institutional policies during a public health crisis.

Impact

To the best of our knowledge, there are no comparable studies conducted on student mental health at any Canadian institution during a pandemic such as COVID-19. A study from a US Ivy League university on student mental health during the pandemic has been conducted with similar data collection techniques by using a platform that pre-dates our EMAX software [17,18]. Although aspects of the university experience in Canada might be comparable to those at institutions from other studies on student mental health, it still is a nuanced experience that may not be fully represented by other studies in the area. Further, this study will be the first to integrate administrative campus-based mental health utilization data with longitudinal self-report and sensor data on mental health. Therefore, this research is expected to be of particular interest to post-secondary institution stakeholders and policy makers in Canada. In particular, this study has the potential to inform other postsecondary institutions that are considered a residential campus, and thus comparable to Western University. Our results are also expected to provide a foundation on which new evidence-based interventions in lifestyle (digital or otherwise) might be designed to improve student mental health at Canadian institutions, given our combination of mental health–related assessment via questionnaires with its associated sensor data collected from cellphones.

Limitations

There are some limitations to the study. For instance, the data collected during the end of 2020 were limited to first-year students only, and were expanded to all undergraduate students at the beginning of 2021. Additionally, despite our EMAX-based SPE app being able to collect up to 68 values from participants, in practice we will receive less than that number since many items were optional with cellphone permissions. Another potential limitation is that participants might not have always had their cellphones with them during lockdowns, which might impact our results.

Conclusions

Given the absence of longitudinal data on student lifestyle and indicators of mental health during a pandemic in Canada, this study is expected to produce a unique assessment of undergraduates with our mobile surveillance system, which has captured aspects of day-to-day life combined with a significant number of weekly responses. Analysis of these data is expected to yield various mental health-related states associated with academic and pandemic-related events. Our results are expected to be of use for the design of interventions to improve student mental health during a pandemic and to institution stakeholders who may benefit from the results for policy and decision-making.

Acknowledgments

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Conflicts of Interest

None declared.

Multimedia Appendix 1
Full baseline survey demographics - extended Table 5 and 6.
[DOCX File , 25 KB - resprot_v10i9e30504_app1.docx]

References

1. Facts and stats. Universities Canada. URL: https://www.univcan.ca/universities/facts-and-stats/ [accessed 2021-09-13]
2. American College Health Association. American College Health Association National College Health Assessment Spring 2006 Reference Group data report (abridged). J Am Coll Health 2007;55(4):195-206. [doi: 10.3200/JACH.55.4.195-206] [Medline: 17319325]
3. Cao W, Fang Z, Hou G, Han M, Xu X, Dong J, et al. The psychological impact of the COVID-19 epidemic on college students in China. Psychiatry Res 2020 May;287:112934 [FREE Full text] [doi: 10.1016/j.psychres.2020.112934] [Medline: 32229390]

4. Wang X, Hegde S, Son C, Keller B, Smith A, Sasangohar F. Investigating Mental Health of US College Students During the COVID-19 Pandemic: Cross-Sectional Survey Study. J Med Internet Res 2020 Sep 17;22(9):e22817 [FREE Full text] [doi: 10.2196/22817] [Medline: 32897868]
5. Yin-xia B, Gegentuya H, Hu L, Zhen-Hua W, Wen-Rui W, Zhi-Gang NG. Correlation Between Psychological Changes of The Community Crowd and The Social Support in Grave Public Health Event. Nei Moivgol Med J 2005:295-297.
6. Ma Z, Zhao J, Li Y, Chen D, Wang T, Zhang Z, et al. Mental health problems and correlates among 746 217 college students during the coronavirus disease 2019 outbreak in China. Epidemiol Psychiatr Sci 2020 Nov 13;29:e181 [FREE Full text] [doi: 10.1017/S2045796020000931] [Medline: 33185174]
7. Zhai Y, Du X. Addressing collegiate mental health amid COVID-19 pandemic. Psychiatry Res 2020 Jun;288:113003 [FREE Full text] [doi: 10.1016/j.psychres.2020.113003] [Medline: 32315885]
8. Zhai Y, Du X. Mental health care for international Chinese students affected by the COVID-19 outbreak. Lancet Psychiatry 2020 Apr;7(4):e22 [FREE Full text] [doi: 10.1016/S2215-0366(20)30089-4] [Medline: 32199511]
9. Doreleyers A, Knighton T. COVID-19 Pandemic: Academic Impacts on Postsecondary Students in Canada. Statistics Canada 2020 May 14 [FREE Full text]
10. COVID-19 Pandemic: financial impacts on postsecondary students in Canada. Statistics Canada. 2020 May 15. URL: https://www150.statcan.gc.ca/n1/pub/45-28-0001/2020001/article/00016-eng.htm [accessed 2021-09-13]
11. Mialki K, House LA, Mathews AE, Shelnutt KP. Covid-19 and College Students: Food Security Status before and after the Onset of a Pandemic. Nutrients 2021 Feb 15;13(2):628 [FREE Full text] [doi: 10.3390/nu13020628] [Medline: 33672058]
12. Son C, Hegde S, Smith A, Wang X, Sasangohar F. Effects of COVID-19 on College Students' Mental Health in the United States: Interview Survey Study. J Med Internet Res 2020 Sep 03;22(9):e21279 [FREE Full text] [doi: 10.2196/21279] [Medline: 32805704]
13. Tasso AF, Hisli Sahin N, San Roman GJ. COVID-19 disruption on college students: Academic and socioemotional implications. Psychol Trauma 2021 Jan;13(1):9-15. [doi: 10.1037/tra0000996] [Medline: 33382329]
14. Molock SD, Parchem B. The impact of COVID-19 on college students from communities of color. J Am Coll Health 2021 Jan 27:1-7. [doi: 10.1080/07448481.2020.1865380] [Medline: 33502970]
15. Fried E, Papanikolaou F, Epskamp S. Mental Health and Social Contact During the COVID-19 Pandemic: An Ecological Momentary Assessment Study. PsyArXiv. Preprint published online April 24, 2020 2020. [doi: 10.31234/osf.io/36xkp]
16. Kleiman EM, Yeager AL, Grove JL, Kellerman JK, Kim JS. Real-time Mental Health Impact of the COVID-19 Pandemic on College Students: Ecological Momentary Assessment Study. JMIR Ment Health 2020 Dec 15;7(12):e24815 [FREE Full text] [doi: 10.2196/24815] [Medline: 33207308]
17. Huckins JF, daSilva AW, Wang W, Hedlund E, Rogers C, Nepal SK, et al. Mental Health and Behavior of College Students During the Early Phases of the COVID-19 Pandemic: Longitudinal Smartphone and Ecological Momentary Assessment Study. J Med Internet Res 2020 Jun 17;22(6):e20185 [FREE Full text] [doi: 10.2196/20185] [Medline: 32519963]
18. Mack DL, DaSilva AW, Rogers C, Hedlund E, Murphy EI, Vojdanovski V, et al. Mental Health and Behavior of College Students During the COVID-19 Pandemic: Longitudinal Mobile Smartphone and Ecological Momentary Assessment Study, Part II. J Med Internet Res 2021 Jun 04;23(6):e28892 [FREE Full text] [doi: 10.2196/28892] [Medline: 33900935]
19. Qiu J, Shen B, Zhao M, Wang Z, Xie B, Xu Y. A nationwide survey of psychological distress among Chinese people in the COVID-19 epidemic: implications and policy recommendations. Gen Psychiatr 2020;33(2):e100213 [FREE Full text] [doi: 10.1136/gpsych-2020-100213] [Medline: 32215365]
20. Mei SL, Yu JX, He BW, Li JY. Psychological investigation of university students in a university in Jilin Province. Med Soc (Berkeley) 2011;24(5):84-86.
21. Wang R, Chen F, Chen Z, Li T, Harari G, Tignor S, et al. StudentLife: assessing mental health, academic performance and behavioral trends of college students using smartphones. 2014 Presented at: 2014 ACM International Joint Conference on Pervasive and Ubiquitous Computing; September 13-17, 2014; Seattle, WA. [doi: 10.1145/2632048.2632054]
22. Brogly C, Lizotte D, Bauer M. Ecological Momentary Assessment eXtensions 3 (EMAX3) Proposal: An App for EMA-Type Research. 2021 Presented at: ICTS4eHealth 2021 Conference; September 5-8, 2021; Athens.
23. Aharony N, Pan W, Ip C, Khayal I, Pentland A. Social fMRI: Investigating and shaping social mechanisms in the real world. Pervasive Mob Comput 2011 Dec;7(6):643-659. [doi: 10.1016/j.pmcj.2011.09.004]
24. Burns MN, Begale M, Duffecy J, Gergle D, Karr CJ, Giangrande E, et al. Harnessing context sensing to develop a mobile intervention for depression. J Med Internet Res 2011 Aug 12;13(3):e55 [FREE Full text] [doi: 10.2196/jmir.1838] [Medline: 21840837]
25. Torous J, Kiang MV, Lorme J, Onnela J. New Tools for New Research in Psychiatry: A Scalable and Customizable Platform to Empower Data Driven Smartphone Research. JMIR Ment Health 2016 May 05;3(2):e16 [FREE Full text] [doi: 10.2196/mental.5165] [Medline: 27150677]
26. Brogly C, Shoemaker JK, Lizotte DJ, Kueper JK, Bauer MA. Smart Healthy Campus: A mobile application to identify lifestyle indicators related to undergraduate mental health. JMIR Form Res 2021 [FREE Full text] [doi: 10.2196/29160]
27. Mohr DC, Zhang M, Schueller SM. Personal Sensing: Understanding Mental Health Using Ubiquitous Sensors and Machine Learning. Annu Rev Clin Psychol 2017 May 08;13:23-47 [FREE Full text] [doi: 10.1146/annurev-clinpsy-032816-044949] [Medline: 28375728]

28. Almeida DM. Resilience and Vulnerability to Daily Stressors Assessed via Diary Methods. Curr Dir Psychol Sci 2016 Jun 23;14(2):64-68. [doi: 10.1111/j.0963-7214.2005.00336.x]
29. Fox MD, Bailey DC, Seamon MD, Miranda ML. Response to a COVID-19 Outbreak on a University Campus - Indiana, August 2020. MMWR Morb Mortal Wkly Rep 2021 Jan 29;70(4):118-122 [FREE Full text] [doi: 10.15585/mmwr.mm7004a3] [Medline: 33507894]
30. The Healthy Minds Network, American College Health Association. The impact of COVID-19 on college student well-being. American College Health Association. URL: https://www.acha.org/documents/ncha/Healthy_Minds_NCHA_COVID_Survey_Report_FINAL.pdf [accessed 2021-09-13]
31. Godin G. The Godin-Shephard Leisure-Time Physical Activity Questionnaire. Heal Fit J Canada 2011;4(1):18-22. [doi: 10.14288/hfjc.v4i1.82]
32. Lee RM, Robbins SB. Measuring belongingness: The Social Connectedness and the Social Assurance scales. J Couns Psychol 1995 Apr;42(2):232-241. [doi: 10.1037/0022-0167.42.2.232]
33. Kroenke K, Spitzer RL, Williams JBW. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med 2001 Sep;16(9):606-613 [FREE Full text] [doi: 10.1046/j.1525-1497.2001.016009606.x] [Medline: 11556941]
34. Spitzer RL, Kroenke K, Williams JBW, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med 2006 May 22;166(10):1092-1097. [doi: 10.1001/archinte.166.10.1092] [Medline: 16717171]
35. Diener E, Wirtz D, Tov W, Kim-Prieto C, Choi D, Oishi S, et al. New Well-being Measures: Short Scales to Assess Flourishing and Positive and Negative Feelings. Soc Indic Res 2009 May 28;97(2):143-156. [doi: 10.1007/s11205-009-9493-y]
36. Smith BW, Dalen J, Wiggins K, Tooley E, Christopher P, Bernard J. The brief resilience scale: assessing the ability to bounce back. Int J Behav Med 2008;15(3):194-200. [doi: 10.1080/10705500802222972] [Medline: 18696313]
37. Raes F, Pommier E, Neff KD, Van Gucht D. Construction and factorial validation of a short form of the Self-Compassion Scale. Clin Psychol Psychother 2011;18(3):250-255. [doi: 10.1002/cpp.702] [Medline: 21584907]
38. Tylka TL, Wood-Barcalow NL. The Body Appreciation Scale-2: item refinement and psychometric evaluation. Body Image 2015 Jan;12:53-67. [doi: 10.1016/j.bodyim.2014.09.006] [Medline: 25462882]
39. Crocker J, Wolfe CT. Contingencies of self-worth. Psychol Rev 2001 Jul;108(3):593-623. [doi: 10.1037/0033-295x.108.3.593] [Medline: 11488379]
40. Pearl RL, Puhl RM. Measuring internalized weight attitudes across body weight categories: validation of the modified weight bias internalization scale. Body Image 2014 Jan;11(1):89-92. [doi: 10.1016/j.bodyim.2013.09.005] [Medline: 24100004]
41. Lindner D, Tantleff-Dunn S. The Development and Psychometric Evaluation of the Self-Objectification Beliefs and Behaviors Scale. Psychol Women Q 2017 Mar 20;41(2):254-272. [doi: 10.1177/0361684317692109]
42. COVID-19 self-assessment. Ontario. URL: https://covid-19.ontario.ca/self-assessment/ [accessed 2021-09-13]
43. Lovibond P, Lovibond SH. The structure of negative emotional states: comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. Behav Res Ther 1995 Mar;33(3):335-343. [doi: 10.1016/0005-7967(94)00075-u] [Medline: 7726811]
44. NEFF KD. The Development and Validation of a Scale to Measure Self-Compassion. Self Identity 2003 Jul;2(3):223-250. [doi: 10.1080/15298860309027]
45. Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect: the PANAS scales. J Pers Soc Psychol 1988 Jun;54(6):1063-1070. [doi: 10.1037//0022-3514.54.6.1063] [Medline: 3397865]
46. Tracy JL, Robins RW. TARGET ARTICLE: "Putting the Self Into Self-Conscious Emotions: A Theoretical Model". Psychol Inq 2004 Apr;15(2):103-125. [doi: 10.1207/s15327965pli1502_01]
47. Luce KH, Crowther JH. The reliability of the Eating Disorder Examination-Self-Report Questionnaire Version (EDE-Q). Int J Eat Disord 1999 Apr;25(3):349-351. [doi: 10.1002/(sici)1098-108x(199904)25:3<349::aid-eat15>3.0.co;2-m] [Medline: 10192002]

Abbreviations

EMA: Ecological Momentary Assessment
EMAX1: Ecological Momentary Assessment eXtensions, 1st edition
EMAX2: Ecological Momentary Assessment eXtensions, 2nd edition
SHC: Smart Healthy Campus
SPE: Student Pandemic Experience

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Protocol

Participatory Surveillance of COVID-19 in Lesotho via Weekly Calls: Protocol for Cell Phone Data Collection

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Abstract

Background: The increase in cell phone ownership in low- and middle-income countries (LMIC) has created an opportunity for low-cost, rapid data collection by calling participants on their cell phones. Cell phones can be mobilized for a myriad of data collection purposes, including surveillance. In LMIC, cell phone–based surveillance has been used to track Ebola, measles, acute flaccid paralysis, and diarrheal disease, as well as noncommunicable diseases. Phone-based surveillance in LMIC is a particularly pertinent, burgeoning approach in the context of the COVID-19 pandemic. Participatory surveillance via cell phone could allow governments to assess burden of disease and complements existing surveillance systems.

Objective: We describe the protocol for the LeCellPHIA (Lesotho Cell Phone PHIA) project, a cell phone surveillance system that collects weekly population-based data on influenza-like illness (ILI) in Lesotho by calling a representative sample of a recent face-to-face survey.

Methods: We established a phone-based surveillance system to collect ILI symptoms from approximately 1700 participants who had participated in a recent face-to-face survey in Lesotho, the Population-based HIV Impact Assessment (PHIA) Survey. Of the 15,267 PHIA participants who were over 18 years old, 11,975 (78.44%) consented to future research and provided a valid phone number. We followed the PHIA sample design and included 342 primary sampling units from 10 districts. We randomly selected 5 households from each primary sampling unit that had an eligible participant and sampled 1 person per household. We oversampled the elderly, as they are more likely to be affected by COVID-19. A 3-day Zoom training was conducted in June 2020 to train LeCellPHIA interviewers.

Results: The surveillance system launched July 1, 2020, beginning with a 2-week enrollment period followed by weekly calls that will continue until September 30, 2022. Of the 11,975 phone numbers that were in the sample frame, 3020 were sampled, and 1778 were enrolled.

Conclusions: The surveillance system will track COVID-19 in a resource-limited setting. The novel approach of a weekly cell phone–based surveillance system can be used to track other health outcomes, and this protocol provides information about how to implement such a system.

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KEYWORDS

COVID-19; cell phones; mHealth; Africa south of the Sahara; surveillance

Introduction

The proliferation of cell phone ownership in sub-Saharan Africa (SSA) [1-3] over the past 10 years has created the opportunity to collect health data via cell phones [4-6]. As of 2019, 45% of the population had mobile services, and 50% of the population will have a phone by 2025, translating to almost 1 billion people in SSA owning a cell phone [7]. Because cell phones have created an opportunity for low-cost, rapid-data collection, public health actors use cell phones for a myriad of public health purposes, creating a growing evidence base about the feasibility and validity of cell phone surveys [8-10].

In SSA, the main remote data collection modes are interactive voice response (IVR — "automated voice calls"), SMS, and computer-assisted telephone interviews (CATI — live interviewer administering the survey). Because literacy is not universal in many low- and middle-income countries (LMIC), CATI — although usually the most expensive approach — is the ideal mode for cell phone surveys aiming to contact the general population. When contacting a known population such as health professionals, who are literate and should have digital proficiency, IVR or SMS can be appropriate. Response rates are significantly higher using CATI than using IVR or SMS [4]. Although response rates vary by country, a recent study in Nigeria documented a 15% CATI random digit dial (RDD) response rate, 3% for IVR, and 0.2% for SMS [11]. RDD is a popular sampling approach [10,12], but even with quota sampling, RDD consistently creates a sample that is more male, educated, and urban than the target population [2,11-14]. Therefore, the optimal way to interview a representative sample by cell phone is to enroll participants during a face-to-face interview [13,15].

A critical application of remote data collection in global health is surveillance. Surveillance by phone is low-cost, is efficient, and allows data collection in remote locations. Surveillance via cell phone can be conducted using any of the aforementioned modes to collect data from either health facility staff, community health workers, or lay people. Studies in the Central African Republic [16] and Togo are examples of health care workers using apps to increase the completeness and timeliness of disease surveillance reports coming from health facilities [17]. In Côte D'Ivoire, a surveillance system relied on community health workers to text health facility staff if any of 5 infectious diseases (suspect measles, yellow fever, acute flaccid paralysis, cholera, and meningitis) were detected. This approach resulted in the first 3 of the aforementioned diseases having substantially higher reporting than before the system was implemented [18]. In a similar design to the study in Côte D'Ivoire, health care workers in Niger participated in a human (acute flaccid paralysis and measles) and animal (rabies and peste des petits ruminants) surveillance system via weekly calls [19].

In contrast, participatory surveillance engages a public (lay) population at risk to report on their health-using technology (often using a mobile phone via internet, SMS, or calls) to collect data independent of the health care system [20]. In Tanzania, women in an informal settlement were enrolled via convenience sampling and randomized to send either daily or every-other-day text messages about occurrence of their child's diarrhea [21]. Over the 4-month study, the overall response rate for the study was 47%, and diarrhea was reported more frequently during daily texting compared with less frequent texting. Although examples of participatory surveillance in SSA are limited, participatory surveillance has increased worldwide due to the COVID-19 pandemic [22-24].

The increased use of cell phone–based surveillance is pertinent in the context of the COVID-19 pandemic since in-person data collection was discouraged, particularly at the beginning of the pandemic. All countries have faced substantial challenges confronting the COVID-19 pandemic. LMIC, in particular, were able to address certain challenges such as improving lab capacity quickly, but other challenges posed by COVID-19 such as underdeveloped surveillance systems require long-term investment to improve [25]. Thus, participatory COVID-19 surveillance can be valuable in shaping the national response and allocation of resources. Participatory surveillance data, which would allow governments to assess COVID-19 burden, mortality, and location of outbreaks, would complement existing surveillance systems and be shared with country COVID-19 task forces who would respond to new cases following national response guidelines.

The cell phone–based participatory surveillance system presented in this manuscript was enacted in Lesotho, a landlocked country with a population just over 2 million people within Southern Africa. After a lockdown from April 30, 2020 to May 5, 2020, Lesotho reported its first case of COVID-19 on May 13, 2020 [26]. This is in contrast with neighboring South Africa, which by the end of April 2020 already had over 5000 cases [27]. The difference between countries can mostly be attributed to a lack of testing in Lesotho, as the country relied on testing suspect cases in South Africa, where the infrastructure was overwhelmed. COVID-19 infections in Lesotho spiked in December 2020 due to the influx of migrant workers returning from South Africa for the holiday season [28]. As of April 2021, Lesotho had conducted 71,129 COVID-19 tests, of which 10,707 (15.1%) were positive [29], and recorded 315 deaths [30].

The participatory surveillance system we present (called LeCellPHIA [Lesotho Cell Phone PHIA]) fulfills the first aim of the World Health Organization's global COVID-19 surveillance objectives as published on March 20, 2020: monitor trends in COVID-19 disease at national and global levels [31]. Specifically, we tracked influenza-like illness (ILI) by conducting surveillance via a cell phone survey targeting recent face-to-face survey participants to create a population-based, nationally representative estimate of COVID-19 disease burden

in Lesotho. The objective of this manuscript is to detail the methods used to implement the participatory surveillance system.

Methods

Study Design

Overview of Study Design

We are contacting participants via CATI weekly for 27 months (July 1, 2020 to September 30, 2022) to report ILI symptoms as a proxy for COVID-19 symptoms. We inquire about fever, dry cough, and shortness of breath for the participants as well as their household members. As this is syndromic surveillance, we do not ask about testing.

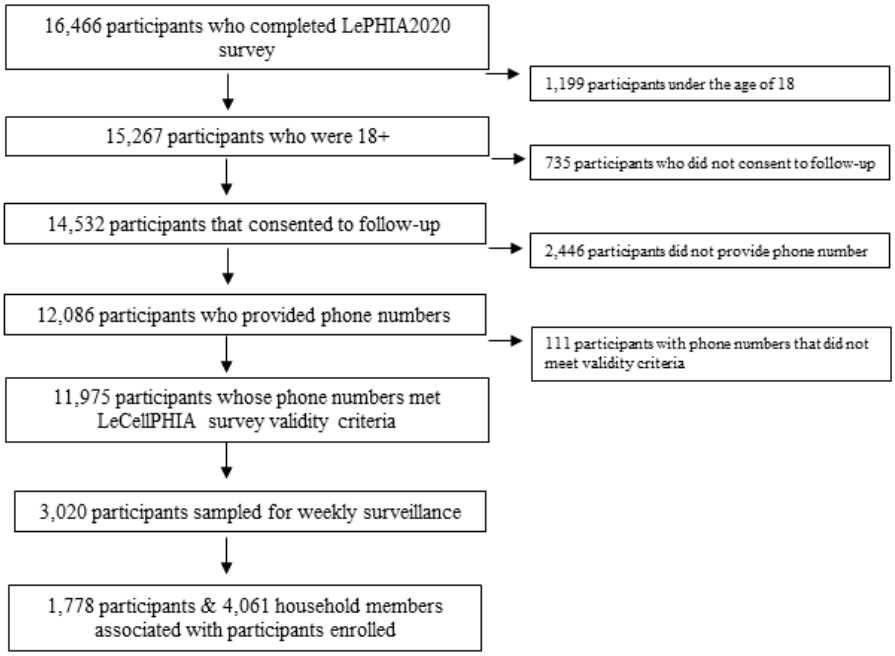
Parent Study

With an HIV prevalence rate of 25.6%, Lesotho has one of the highest rates in the world [32]. The 2020 Lesotho Population HIV Impact Assessment (LePHIA2020) was a cross-sectional, household-based, nationally representative survey that assessed the prevalence of key HIV-related health indicators such as HIV incidence, prevalence, viral load suppression, and risk behaviors and described uptake of key HIV prevention, care, and treatment services [33]. This 2-stage cluster survey took place between December 2019 and March 2020 and included 9665 households and 16,466 individuals, with a 93.1% household response rate. All adults aged 15 years and older in the household who slept in the house the night before were invited to participate. There was a 93.6% individual interview response rate and 93.2% HIV testing response rate.

Sample Frame

All LePHIA2020 participants who completed the survey were asked if they agreed to be contacted for future research in the next 3 years. The sample frame included all LePHIA2020 participants aged ≥18 years that completed the LePHIA2020 interview, consented to follow-up, and provided a valid phone number. This equates to approximately 11,975 participants of the 15,267 people aged 18 years and older (79%) who were interviewed for LePHIA2020 (see Figure 1).

Figure 1. Study enrollment flowchart. LeCellPHIA: Lesotho Cell Phone PHIA; LePHIA2020: 2020 Lesotho Population-Based HIV Impact Assessment; PHIA: Population-based HIV Impact Assessment.



Cleaning Phone Numbers

The LePHIA2020 data are collected via tablets which allows for data quality assurance. The sole data entry parameter for the question about the participant's phone number was that the data had to be numeric. Therefore, phone numbers of varying lengths were entered, of which some included country codes. With the goal of creating a sample frame that includes only valid phone numbers, a data analyst worked in close collaboration with the Lesotho team to identify phone numbers that were numerically feasible. For this study, phone numbers between the length of 8 and 12 digits — but excluding 10 digits — were considered valid. This range allowed for Lesotho and South African phone numbers with and without a country code. Phone numbers with a length of 10 digits are invalid because no definite rule can be given to determine whether it was a South African number with a missing digit or a Lesotho number with an extra digit. Depending on the number of the digits the phone number started with, it was classified as a Lesotho or South African phone number; then, all phone numbers were coded in a consistent manner so that the interviewer could copy and paste the phone number from the survey software into the phone.

Pulsing

Despite including only numerically feasible phone numbers in our sample frame, we still expected a notable amount of nonresponse. To improve the estimate of the percent of phone numbers that would be classified as noncontact, we conducted

"pulsing" [34]. Before creating the sample, 3 supervisors called 100 phone numbers that were randomly sampled and excluded from the LeCellPHIA sample frame. Pulsing is calling each phone number once, and if the call rings, allowing the call to ring only once before hanging up. The goal was not to speak to the person whose phone number we called but to record whether the phone number had the possibility of being answered. There were 3 possible outcomes for each call: the call rang; the subscriber was unavailable (due to network issues, the participant being out of service, or the phone being switched off); or the phone number did not exist, which meant the phone number was no longer in use and thus could not be answered.

Sampling

For LeCellPHIA, we followed the sample design for LePHIA2020 by including all 342 primary sampling units (PSUs) from the 10 districts. Within each PSU, we oversampled households (HHs) with elderly defined as age ≥60 years, with sampling ratio of 2:1 between HHs with and without elderly. We randomly selected 5 HHs in each PSU from those HHs that had eligible participants. From each sampled HH, 1 person 18 years of age or older was sampled. Based on prior cell phone studies in SSA, we assumed a 25% noncontact rate and 10% refusal rate. To obtain the target sample size of 5 persons per PSU (1710 persons across all PSUs), we called approximately 9 persons in each PSU in the first call (3020 persons across all PSUs) to end with approximately 1710 people in our sample. To increase our sample size, we asked all 1710 people about their household members' symptoms (average of 2.9 people per household). Given that the virus can spread among family members, we set an intraclass correlation (ICC) of 0.25. Assuming an ICC of 0.25 and average HH size of 3, the design effect within the household was 1+(3[average size of HH]–1)*0.25 [ICC]= 1.5. Thus, the effective sample size in each HH was 3/1.5 = 2, resulting in an effective overall sample size of 3420.

Training

All interviewers were recruited from the recently finished LePHIA2020 and thus had been previously trained by ICAP in ethics, building rapport, and using tablets for data collection, among other topics. Survey personnel were selected based on their LePHIA2020 performance, and all were proficient in English and Sesotho. Before training, each interviewer received a tablet, headphones, Wi-Fi router, and a lockbox to secure the aforementioned equipment. The 2 supervisors underwent a 1-day training followed by a 3-day LeCellPHIA interviewers' virtual training via Zoom. All interviewers connected from their homes. Staff in the Lesotho ICAP office joined the meeting in a socially distanced room. The curriculum of the training covered how to conduct phone interviews, how to use the software (SurveyCTO), objectives of the research, workflow, responsibilities, monitoring, and COVID-19 information. Specific to COVID-19, survey staff were trained on COVID-19 transmission risk factors, how to mitigate spread in the home and in the community, and other general knowledge about the virus. Slack, a channel-based message platform, is used as the main communication channel between interviewers, supervisors, and ICAP staff. There are Slack channels to communicate about process-related challenges and COVID-19 questions, and there is a private channel for interviewers to communicate and a private channel for supervisory-level staff.

Pilot

All 20 interviewers practiced the survey by calling both LeCellPHIA supervisors and 20 randomly selected LePHIA2020 participants who consented to follow-up but were not part of the selected LeCellPHIA sample. Each interviewer made at least 15 calls; these were recorded and reviewed by supervisors and the survey coordinator to evaluate how each interviewer performed. We used the pilot performance to select the 16 best-performing interviewers for the survey, while 4 remained on a hiring wait list.

Questionnaire

The participatory COVID-19 syndromic surveillance questions were developed using Centers for Disease Control and Prevention (CDC) guidance and through consultation with local staff. The enrollment questionnaire, administered only during the first 2 weeks of data collection, had 28 questions (Figure 2). The weekly surveillance questionnaire has between 8 and 11 questions, depending on whether the participant or household member is reported sick the previous week (Figure 3). Abbreviated verbal consent scripts, questionnaires, and other participant-facing documents were translated by ICAP into Sesotho from English.

Figure 2. Lesotho Cell Phone Population-based HIV Impact Assessment (LeCellPHIA) participant enrollment steps. ILI: influenza-like illness.

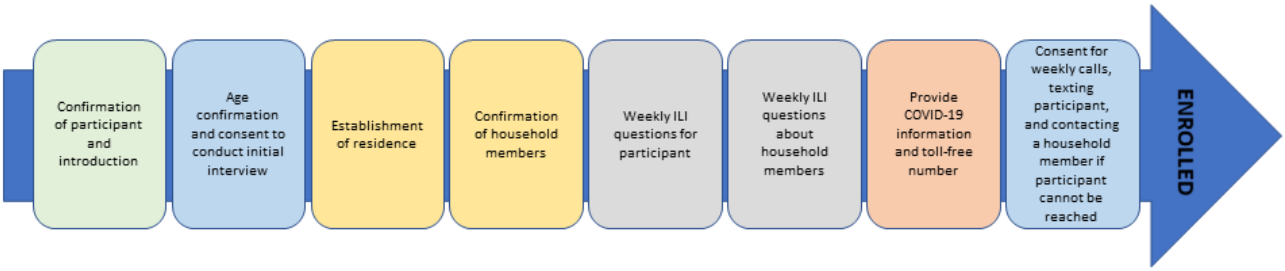
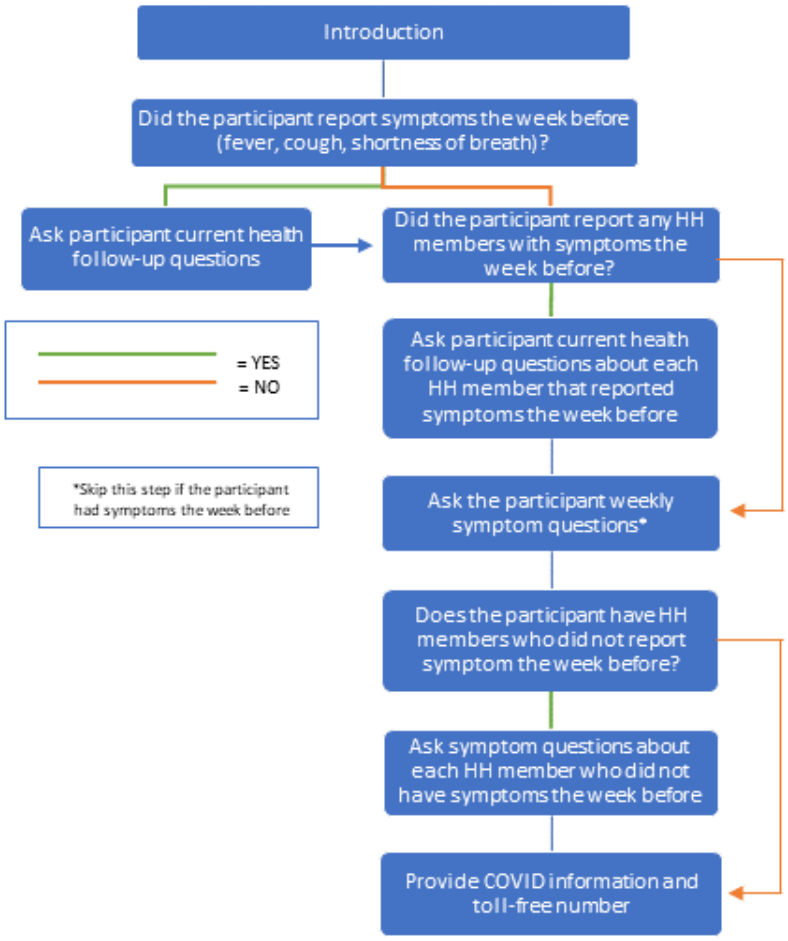


Figure 3. Weekly surveillance questions for Lesotho Cell Phone Population-based HIV Impact Assessment (LeCellPHIA) participants about influenza-like symptoms experienced by themselves and household (HH) members.



Software

Questionnaires were programmed into the SurveyCTO format using a Microsoft Excel template, then uploaded onto the project's SurveyCTO server. SurveyCTO's case management system allows the data management team to assign interviewers a weekly participant list to call. Each week, the data management team generates a new list based on the previous week's results.

Using the SurveyCTO Collect version 2.70.3 mobile application on an Android (operating system 7) tablet, interviewers access the participant list assigned to them to conduct their weekly interviews. The participant list automatically updates (ie, removes a participant) when a submitted form indicates any of the following: (1) a participant completed the interview for the week or (2) a participant withdrew from the study. If a participant is called 4 times in a week (and a form was submitted each time), then the participant is also removed from the list as 4 is the maximum number of contacts in a week. Once a form is saved and finalized on the SurveyCTO Collect app, it is encrypted, and the data are no longer accessible on the device. Once the data are sent to the SurveyCTO server, the data can only be downloaded using a private encryption key.

SurveyCTO's audio audit feature is used for supervision purposes. A random selection of 20% of calls is recorded for supervisors to listen to. Due to security features on the Android operating system of the devices used for data collection, only the interviewer side of the call could be heard.

Enrollment

To enroll a random sample of approximately 1710 participants, 16 interviewers were assigned 150 participants to call. Interviewers called participants from a private space in their own home or office, ensuring confidentiality. The interviewer wore headphones with a microphone to improve the acoustics and privacy of the calls. The interviewers enrolled participants between July 1, 2020 and July 13, 2020. If the phone number was busy or not picked up, interviewers called back later for a minimum of 7 call attempts over the 2 weeks, using alternate phone numbers if provided. During the enrollment period, there was a daily debrief call between the afternoon and evening shift for all staff that had worked that day. Interviewers called approximately 20 new participants per shift for 7 shifts, then used the remaining 3 shifts at the end of enrollment to solely call back noncontacts.

Participants who answered the phone call were eligible if they confirmed they participated in LePHIA2020, lived in the same home where LePHIA2020 was conducted or planned to go back to the home in the next year, confirmed they were over 18 years of age, provided abbreviated verbal consent, and could hear and understand questions in English or Sesotho. Participants who

were otherwise eligible but were not currently living in the house where they answered LePHIA2020 questions were put on a monthly callback list if the participant indicated they would return home sometime in the next 12 months.

During the enrollment phone calls, interviewers oriented the participant to the purpose of the call, confirmed eligibility, and if eligible, administered up to 3 consents. The initial consent included information about the purpose of the survey, described the requirement of the participants, clarified that participation is voluntary, outlined the anticipated burden (length of study), and provided information on the incentive. Once consented, the interviewer then used the household roster from LePHIA2020 to establish which household members were still living with that participant and asked about ILI symptoms for the participant and their household members. The second abbreviated verbal consent, which occurred at the end of the baseline phone call, consented the participant to weekly calls to ask about ILI symptoms for the participant and their household members. If the participant consented, a third abbreviated verbal consent asked if the participant agreed for the interviewer to contact a household member who provided their cell phone number during LePHIA2020 or to SMS the participant, in case we could not get ahold of the participant for 2 or more weeks.

Procedures and Weekly Surveillance

After 2 weeks of participant enrollment, weekly surveillance began. A data collection week begins on Thursday and ends on Tuesday. Every Sunday evening, the New York team produces a list of participants who have yet to be called during the past survey week to help ensure that all study participants are called at least once by the end of collection week. Calling does not occur on Wednesdays so as to give the data team time to create new call lists for interviewers based on the previous week's results (for example, removing a participant who refused or changing the questions for a participant who reported being ill).

If a participant or their household members report ILI symptoms the week before, the participant is first asked if those symptoms have improved. Then, interviewers inquire about participants and their household members who did not have ILI symptoms the week before. All participants are asked if they would like the Government of Lesotho's toll free COVID-19 hotline phone number. Interviewers offer to answer participants' questions about COVID-19 at the end of each call.

Interviewers conduct calls mornings, afternoons, evenings, and weekends to increase the likelihood of contacting participants. Interviews are scheduled at specific times that potential participants designated, according to their schedules. Interviewers call the same participant for the duration of the study. For the first month of data collection, interviews took place 7 days a week. After reviewing the data for patterns in responsiveness, the team decided that no day had a particularly high response rate, so the staff started working 6 days a week and eventually 5. As the survey continued, the staff adjusted the days and times that they work to 4 shifts a week.

If a participant cannot be contacted for 2 weeks and they consented during enrollment for the interviewer to call a household member, the household member is called. If a participant cannot be contacted for 2 weeks and they had not consented to contacting a household member but consented to receive a text message, the interviewer texts the participant. If a participant who had consented to contacting a household member is not reached via the household member for a week, the participant is texted the following week by the interviewer if the participant consented to being texted.

If a participant cannot be contacted for 2 months, they are removed from weekly calls and instead are called monthly. If during these monthly calls, the participant is reached, they are returned to the weekly call list.

Survey Delivery and Data Collection

The data collection team is comprised of 16 interviewers who report to 2 supervisors and 1 call center manager. Questionnaire data are collected on password-encrypted tablets using SurveyCTO software. The software presents a list, unique to each interviewer, of participant names and phone numbers. Independent of the survey software, the interviewer tracks which participants are called that day. A participant may need to be called multiple times during a shift due to not picking up the call or asking to be called back. The interviewer only uploads 1 form per contacted participant per shift to SurveyCTO. All survey data and voice recordings are stored in the device memory and then submitted to the SurveyCTO server whenever transmission is possible (internet connection needed), preferably every day but at minimum once a week to minimize risk of data loss. The same tablet is used to call participants and record data.

Incentives

Participants are compensated for their time with a small amount of phone credit. Studies have shown that in 2 countries (Uganda and Bangladesh), an airtime incentive improved response rates [35]. The World Bank ran a 6-country study in Africa, during which participants were called monthly. Participants received incentives during that study, and response rates were greater than 90% in all countries [6,15]. For this study, the incentive is sent as phone credit, and there is no handling of cash or in-person disbursement of compensation. All participants were given 35 maloti (US $2) by LeCellPHIA administrative staff within 2 weeks of enrolling. Thereafter, participants are given a monthly incentive dependent on how many calls they participated in that month. Between the months of July and December, the incentives were sent by mobile phone companies in Lesotho. However, the administrative process of transferring the money and phone numbers to the mobile phone companies and then the companies sending the incentive was not completed in a timely matter. Due to these delays in phone credit disbursement, which were noted by survey participants, a LeCellPHIA staff began distributing the incentive in-house.

Supervision and Monitoring

SurveyCTO audio records a preprogrammed percentage of randomly selected interviews and uploads them to the server. Recordings begin at the start of selected calls. Interviewer monitoring was more intensive at the beginning of data collection. Supervisors targeted interviewers who underperformed as compared to their peers. Indicators to measure interviewer performance include response rates and

efficiency. During the first month of data collection, supervisors met virtually with interviewers multiple times a week to share performance feedback. From month 2 of data collection onward, supervisors conduct one-on-one sessions biweekly with interviewers to check on their well-being, listen to their concerns, and boost their morale.

Institutional Review Board Approval, Ethics, Consent

The Lesotho National Research Ethics Committee approved LeCellPHIA with exemption from committee review. It was determined to be a continuation of LePHIA2020, which had already been approved, and the Columbia University Institutional Review Board (IRB) determined the same. The CDC International Task Force scientific committee and the CDC IRB reviewed the protocol and deemed the research nonhuman subjects. Due to the remote nature of data collection (ie, no in-person interaction) and the minimal risk to participants, we requested a modification to written signed informed consent. Participants were read an abbreviated standardized verbal disclosure (consent) of key study information that emphasized the voluntary nature of the survey.

Statistical Analysis

Power Calculation

We calculated the margin of error for a 95% CI to estimate the proportion of ILI through self-reported symptoms. An effective sample size of 3420 produces a 2-sided 95% CI with a margin of error of 1.4% when the proportion of ILI is 10% and the design effect is 1.3 given a loss-to-follow-up rate of 30%. The potential loss in efficiency due to cluster sampling is minimal in this study due to the large number of PSUs and a small number of persons in each PSU. We used a design effect of 1.3 to primarily reflect the impact of sample weights**.** We oversampled older individuals, as cell phone ownership rate is lower and ILI rate is higher in this population.

Data Management and Analysis

The data team developed a cleaning plan that included processes for screening data for duplication, transcription errors, measurement errors, internal consistency, out of range and invalid values, and outliers.

We create weekly point estimates of ILI by downloading the survey data from the SurveyCTO platform, which are then cleaned for analysis. Because participants are often called more than once, we retain the most complete survey for analysis. The data are weighted for unequal probability of selection, nonresponse, and potential undercoverage of the sampling frame. The point estimate of ILI prevalence rate with 95% CI is calculated accounting for the stratified, multistage, cluster sample design and is sent to CDC Lesotho and Lesotho Ministry of Health colleagues, usually 3 days after data collection finished.

A monitoring form is also updated weekly to track interviewer response rates and performance, as well as to provide a breakdown of symptoms and a summary of overall data, for both individual participants and their respective household members.

Results

Over 99% (11,975/12,086, 99.08%) of phone numbers of LePHIA2020 participants who provided consent for follow-up were valid and thus included in the sample frame. We sampled 3020 LePHIA2020 participants. Interviewers enrolled participants for 2 weeks, beginning July 1, 2020. Ultimately 1778 participants were enrolled. Weekly phone calls enquiring about the participant's symptoms as well as household members listed during the face-to-face survey began the third week of July 2020 and are scheduled to continue until the end of September 2022.

Discussion

The COVID-19 pandemic caused the already rapidly advancing field of remote data collection in SSA to evolve even faster [36], as collecting data via cell phones was the safest option during periods of high community transmission and national lockdowns. A similar influx of cell phone–based approaches was seen after the Ebola outbreak of 2014-2015 in West Africa, when surveillance via cell phone became more prominent, particularly employing health care staff, such as those working in a health facility or community health workers, to report data [37-41]. Compared with facility-based approaches, participatory surveillance in SSA is less frequent. This protocol manuscript presents the approach used in Lesotho to create weekly estimates of ILI.

There are limitations to cell phone–based data collection that should be considered before establishing a participatory surveillance system. If cell phone ownership is below 80%, undercoverage will occur and could cause coverage bias, impacting the outcome of interest [42]. Specifically, if those who own a cell phone (and thus are part of the sample frame) are different from those without a cell phone in ways that are correlated to the outcome of interest, the estimates will be biased [43]. If mobile phone network coverage is limited mainly to urban areas, then the systematic exclusion of those in rural areas could also create bias in the outcome of interest. Thus, we recommend carefully examining mobile phone ownership in the study setting before attempting participatory surveillance in LMIC. If participants may be hesitant to report the outcome of interest, due to social desirability bias or fear of reporting repercussions, the interviewers must work hard to establish rapport and avoid measurement error.

The usefulness of cell phone–based surveillance systems in resource-limited settings for epidemic response was established by previous studies [44]. Our study built on this work and created population-based, nationally representative estimates of ILI. Whereas previous studies mainly created counts of an outcome, LeCellPHIA creates incidence point estimates with 95% CIs. Because many COVID-19 cases are asymptomatic, the surveillance system may underreport total cases but nonetheless reflects ILI trends across the country.

A surveillance system that can track epidemic trends has the potential to create a more effective response to, in this case, COVID-19. By surveying lay people, we create data in contexts

where community health workers or health facility staff are occupied with other tasks. LeCellPHIA can be used as a blueprint to create other population-based cell phone surveillance systems for future outbreaks.

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Conflicts of Interest

None declared.

References

1. The Mobile Economy Sub-Saharan Africa 2018. GSMA. 2018. URL: https://data.gsmaintelligence.com/api-web/v2/research-file-download?id=33292323&file=The%20Mobile%20Economy%20Sub-Saharan%20Africa%202018%20Infographic.pdf [accessed 2021-08-14]
2. Poushter J, Oates R. Cell Phones in Africa: Communication Lifeline. Pew Research Center. 2015 Apr 15. URL: https://www.pewresearch.org/global/2015/04/15/cell-phones-in-africa-communication-lifeline/ [accessed 2021-08-14]
3. Hyder AA, Wosu AC, Gibson DG, Labrique AB, Ali J, Pariyo GW. Noncommunicable disease risk factors and mobile phones: A proposed research agenda. J Med Internet Res 2017 May 05;19(5):e133 [FREE Full text] [doi: 10.2196/jmir.7246] [Medline: 28476722]
4. Gibson DG, Pereira A, Farrenkopf BA, Labrique AB, Pariyo GW, Hyder AA. Mobile phone surveys for collecting population-level estimates in low- and middle-income countries: A literature review. J Med Internet Res 2017 May 05;19(5):e139 [FREE Full text] [doi: 10.2196/jmir.7428] [Medline: 28476725]
5. Greenleaf AR, Gibson DG, Khattar C, Labrique AB, Pariyo GW. Building the evidence base for remote data collection in low- and middle-income countries: Comparing reliability and accuracy across survey modalities. J Med Internet Res 2017 May 05;19(5):e140 [FREE Full text] [doi: 10.2196/jmir.7331] [Medline: 28476728]
6. Dabalen A, Etang A, Hoogeveen J, Mushi E, Schipper Y, von Engelhardt J. Mobile phone panel surveys in developing countries: A practical guide for microdata collection. World Bank Group. 2016 Jun 27. URL: https://elibrary.worldbank.org/doi/abs/10.1596/978-1-4648-0904-0 [accessed 2021-08-14]
7. The Mobile Economy Sub-Saharan Africa 2020. GSMA. 2020. URL: https://www.gsma.com/mobileeconomy/sub-saharan-africa/ [accessed 2021-08-14]
8. Labrique A, Blynn E, Ahmed S, Gibson D, Pariyo G, Hyder AA. Health surveys using mobile phones in developing countries: Automated active strata monitoring and other statistical considerations for improving precision and reducing biases. J Med Internet Res 2017 May 05;19(5):e121 [FREE Full text] [doi: 10.2196/jmir.7329] [Medline: 28476726]
9. Gibson DG, Pariyo GW, Wosu AC, Greenleaf AR, Ali J, Ahmed S, et al. Evaluation of mechanisms to improve performance of mobile phone surveys in low- and middle-income countries: Research protocol. JMIR Res Protoc 2017 May 05;6(5):e81 [FREE Full text] [doi: 10.2196/resprot.7534] [Medline: 28476729]
10. L'Engle K, Sefa E, Adimazoya EA, Yartey E, Lenzi R, Tarpo C, et al. Survey research with a random digit dial national mobile phone sample in Ghana: Methods and sample quality. PLoS One 2018 Jan 19;13(1):e0190902 [FREE Full text] [doi: 10.1371/journal.pone.0190902] [Medline: 29351349]
11. Lau CQ, Cronberg A, Marks L, Amaya A. In search of the optimal mode for mobile phone surveys in developing countries. A comparison of IVR, SMS, and CATI in Nigeria. Survey Research Methods 2019;13(3):305-318. [doi: 10.4324/9781351044677-35]
12. Leo B, Morello R, Mellon J, Peixoto T, Davenport ST. Do mobile phone surveys work in poor countries? SSRN Journal 2015:1. [doi: 10.2139/ssrn.2623097]
13. Greenleaf AR, Gadiaga A, Choi Y, Guiella G, Turke S, Battle N, et al. Automated and interviewer-administered mobile phone surveys in Burkina Faso: Sociodemographic differences among female mobile phone survey respondents and nonrespondents. JMIR Mhealth Uhealth 2020 Jul 14;8(7):e17891 [FREE Full text] [doi: 10.2196/17891] [Medline: 32673250]
14. Larmarange J, Kassoum O, Kakou E, Fradier Y, Sika L, Danel C, DOD-CI ANRS 12 287 group. Feasibility and representativeness of a random sample mobile phone survey in Côte d'Ivoire. Population 2016;71(1):117-129 [FREE Full text] [doi: 10.3917/pope.1601.0119]
15. Croke K, Dabalen A, Demombybes G, Giugale M, Hoogeveen J. Collecting high frequency panel data in Africa using mobile phone interviews. Policy Research Working Paper; No. 6097. World Bank Group. 2012. URL: https://openknowledge.worldbank.org/handle/10986/9313 [accessed 2021-08-14]
16. El-Khatib Z, Shah M, Zallappa SN, Nabeth P, Guerra J, Manengu CT, et al. SMS-based smartphone application for disease surveillance has doubled completeness and timeliness in a limited-resource setting - evaluation of a 15-week pilot program

in Central African Republic (CAR). Confl Health 2018;12:42 [FREE Full text] [doi: 10.1186/s13031-018-0177-6] [Medline: 30386418]
17. Guerra J, Davi KM, Rafael FC, Assane H, Imboua L, Diallo FBT, et al. Case study of Argus in Togo: An SMS and web-based application to support public health surveillance, results from 2016 to 2019. PLoS One 2020;15(12):e0243131 [FREE Full text] [doi: 10.1371/journal.pone.0243131] [Medline: 33259550]
18. Clara A, Ndiaye SM, Joseph B, Nzogu MA, Coulibaly D, Alroy KA, et al. Community-based surveillance in Côte d'Ivoire. Health Secur 2020 Jan;18(S1):S23-S33. [doi: 10.1089/hs.2019.0062] [Medline: 32004127]
19. Greenleaf A, Vogel L. Interactive voice response technology for data collection in Sub-Saharan Africa. Viamo. 2018 Apr. URL: https://www.viamo.io/wp-content/uploads/2018/07/Viamo-Brief-Data-Collection1595.pdf [accessed 2021-08-14]
20. Smolinski MS, Crawley AW, Olsen JM, Jayaraman T, Libel M. Participatory disease surveillance: Engaging communities directly in reporting, monitoring, and responding to health threats. JMIR Public Health Surveill 2017 Oct 11;3(4):e62 [FREE Full text] [doi: 10.2196/publichealth.7540] [Medline: 29021131]
21. Rego R, Watson S, Ishengoma P, Langat P, Otieno HP, Lilford R. Effectiveness of SMS messaging for diarrhoea measurement: a factorial cross-over randomised controlled trial. BMC Med Res Methodol 2020 Jun 30;20(1):174 [FREE Full text] [doi: 10.1186/s12874-020-01062-3] [Medline: 32605536]
22. Sudre CH, Keshet A, Graham MS, Joshi AD, Shilo S, Rossman H, et al. Anosmia, ageusia, and other COVID-19-like symptoms in association with a positive SARS-CoV-2 test, across six national digital surveillance platforms: an observational study. The Lancet Digital Health 2021 Jul:1. [doi: 10.1016/s2589-7500(21)00115-1]
23. Mehl A, Bergey F, Cawley C, Gilsdorf A. Syndromic surveillance insights from a symptom assessment app before and during COVID-19 measures in Germany and the United Kingdom: Results from repeated cross-sectional analyses. JMIR Mhealth Uhealth 2020 Oct 09;8(10):e21364 [FREE Full text] [doi: 10.2196/21364] [Medline: 32997640]
24. Mahmud AS, Chowdhury S, Sojib KH, Chowdhury A, Quader MT, Paul S, et al. Participatory syndromic surveillance as a tool for tracking COVID-19 in Bangladesh. Epidemics 2021 Jun;35:100462 [FREE Full text] [doi: 10.1016/j.epidem.2021.100462] [Medline: 33887643]
25. El-Sadr WM, Justman J. Africa in the path of Covid-19. N Engl J Med 2020 Jul 16;383(3):e11. [doi: 10.1056/nejmp2008193]
26. Charumira S. Lesotho records first coronavirus case a week after lifting lockdown. The Guardian. 2020 May 13. URL: https://www.theguardian.com/world/2020/may/13/lesotho-records-first-coronavirus-case-a-week-after-lifting-lockdown [accessed 2021-08-14]
27. Stiegler N, Bouchard J. South Africa: Challenges and successes of the COVID-19 lockdown. Ann Med Psychol (Paris) 2020 Sep;178(7):695-698 [FREE Full text] [doi: 10.1016/j.amp.2020.05.006] [Medline: 32836300]
28. Charumbira S. 'We can't cope': Lesotho faces Covid-19 disaster after quarantine failures. The Guardian. 2021 Jan 08. URL: https://www.theguardian.com/global-development/2021/jan/08/we-cant-cope-lesotho-faces-covid-19-disaster-after-quarantine-failures [accessed 2021-08-14]
29. Nacosec. Facebook. URL: https://www.facebook.com/nacosec [accessed 2021-02-03]
30. Coronavirus Resource Center. Johns Hopkins University & Medicine. URL: https://coronavirus.jhu.edu [accessed 2021-08-14]
31. Public health surveillance for COVID-19: interim guidance. World Health Organization. 2020 Dec 16. URL: https://www.who.int/publications/i/item/who-2019-nCoV-surveillanceguidance-2020.8 [accessed 2021-08-14]
32. Ministry of Health - Lesotho, Centers for Disease Control and Prevention (CDC), ICAP at Columbia University. Lesotho Population-based HIV Impact Assessment (LePHIA) 2016-2017: Final Report. PHIA Project. 2019 Sep. URL: https://phia.icap.columbia.edu/lephia-final-report/ [accessed 2021-08-14]
33. Porter L, Bello G, Nkambule R, Justman J. HIV general population surveys: Shedding light on the status of HIV epidemics and informing future actions. J Acquir Immune Defic Syndr 2021 Aug 01;87(Suppl 1):S2-S5. [doi: 10.1097/QAI.0000000000002701] [Medline: 34166307]
34. Lau C, di Tada N. Identifying non-working phone numbers in Africa for response rate calculations. Surv Pract 2017 Dec 28:1. [doi: 10.29115/sp-2018-0020]
35. Gibson DG, Wosu AC, Pariyo GW, Ahmed S, Ali J, Labrique AB, et al. Effect of airtime incentives on response and cooperation rates in non-communicable disease interactive voice response surveys: randomised controlled trials in Bangladesh and Uganda. BMJ Glob Health 2019;4(5):e001604 [FREE Full text] [doi: 10.1136/bmjgh-2019-001604] [Medline: 31565406]
36. Himelein K, Eckman S, Lau C, McKenzie D. Mobile phone surveys for understanding COVID-19 impacts: Part I sampling and mode. World Bank Blogs. 2020 Apr 07. URL: https://blogs.worldbank.org/impactevaluations/mobile-phone-surveys-understanding-covid-19-impacts-part-i-sampling-and-mode [accessed 2021-08-14]
37. Berman A, Figueroa ME, Storey JD. Use of SMS-based surveys in the rapid response to the Ebola outbreak in Liberia: Opening community dialogue. J Health Commun 2017;22(sup1):15-23. [doi: 10.1080/10810730.2016.1224279] [Medline: 28854132]
38. Cáceres VM, Cardoso P, Sidibe S, Lambert S, Lopez A, Pedalino B, et al. Daily zero-reporting for suspect Ebola using short message service (SMS) in Guinea-Bissau. Public Health 2016 Sep;138:69-73. [doi: 10.1016/j.puhe.2016.03.006] [Medline: 27106280]

39. Himelein K, Kastelic JG. The socio-economic impacts of Ebola in Liberia: Results from a high frequency cell phone survey. World Bank Group. 2015 Apr 13. URL: https://openknowledge.worldbank.org/handle/10986/21893?show=full [accessed 2021-08-14]
40. Kuehne A, Lynch E, Marshall E, Tiffany A, Alley I, Bawo L, et al. Mortality, morbidity and health-seeking behaviour during the Ebola epidemic 2014-2015 in Monrovia results from a mobile phone survey. PLoS Negl Trop Dis 2016 Aug;10(8):e0004899 [FREE Full text] [doi: 10.1371/journal.pntd.0004899] [Medline: 27551750]
41. Feng S, Grépin KA, Chunara R. Tracking health seeking behavior during an Ebola outbreak via mobile phones and SMS. NPJ Digit Med 2018;1:51 [FREE Full text] [doi: 10.1038/s41746-018-0055-z] [Medline: 31304330]
42. Lessler JT, Kalsbeek WD. Nonsampling Error in Surveys. Hoboken, NJ: John Wiley & Sons, Inc; 1992.
43. Mulry M. Coverage Error. In: Lavrakas PJ, editor. Encyclopedia of Survey Research Methods. Thousand Oaks, CA: Sage Publications, Inc; 2011:162-166.
44. Brinkel J, Krämer A, Krumkamp R, May J, Fobil J. Mobile phone-based mHealth approaches for public health surveillance in sub-Saharan Africa: a systematic review. Int J Environ Res Public Health 2014 Nov 12;11(11):11559-11582 [FREE Full text] [doi: 10.3390/ijerph111111559] [Medline: 25396767]

Abbreviations

CATI: computer-assisted telephone interview
CDC: Centers for Disease Control and Prevention
HH: household
ICC: intraclass correlation
ILI: influenza-like illness
IRB: Institutional Review Board
IVR: interactive voice response
LeCellPHIA: Lesotho Cell Phone PHIA
LePHIA2020: 2020 Lesotho Population-Based HIV Impact Assessment
LMIC: low- and middle-income country
PHIA: Population-based HIV Impact Assessment
PSU: primary sampling unit
RDD: random digit dial
SSA: sub-Saharan Africa

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Protocol

Exploring the Well-being of Health Care Workers During the COVID-19 Pandemic: Protocol for a Prospective Longitudinal Study

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Abstract

Background: Health care workers (HCWs) have experienced several stressors associated with the COVID-19 pandemic. Structural stressors, including extended work hours, redeployment, and changes in organizational mandates, often intersect with interpersonal and personal stressors, such as caring for those with COVID-19 infections; worrying about infection of self, family, and loved ones; working despite shortages of personal protective equipment; and encountering various difficult moral-ethical dilemmas.

Objective: The paper describes the protocol for a longitudinal study seeking to capture the unique experiences, challenges, and changes faced by HCWs during the COVID-19 pandemic. The study seeks to explore the impact of COVID-19 on the mental well-being of HCWs with a particular focus on moral distress, perceptions of and satisfaction with delivery of care, and how changes in work structure are tolerated among HCWs providing clinical services.

Methods: A prospective longitudinal design is employed to assess HCWs' experiences across domains of mental health (depression, anxiety, posttraumatic stress, and well-being), moral distress and moral reasoning, work-related changes and telehealth, organizational responses to COVID-19 concerns, and experiences with COVID-19 infections to self and to others. We recruited HCWs from across Canada through convenience snowball sampling to participate in either a short-form or long-form web-based survey at baseline. Respondents to the baseline survey are invited to complete a follow-up survey every 3 months, for a total of 18 months.

Results: A total of 1926 participants completed baseline surveys between June 26 and December 31, 2020, and 1859 participants provided their emails to contact them to participate in follow-up surveys. As of July 2021, data collection is ongoing, with participants nearing the 6- or 9-month follow-up periods depending on their initial time of self-enrollment.

Conclusions: This protocol describes a study that will provide unique insights into the immediate and longitudinal impact of the COVID-19 pandemic on the dimensions of mental health, moral distress, health care delivery, and workplace environment of HCWs. The feasibility and acceptability of implementing a short-form and long-form survey on participant engagement and data retention will also be discussed.

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KEYWORDS

COVID-19; health care worker; pandemic; mental health; wellbeing; survey; design; longitudinal; prospective; protocol; challenge; impact; distress; perception

Introduction

Background

Throughout the COVID-19 pandemic, health care workers (HCWs) have served on the frontlines of disease management and response. In their roles, HCWs have experienced increased workloads, risks of redeployment, and exposure to SARS-CoV-2 while caring for the surge of patients. At the same time, HCWs may be concerned about the safety and well-being of themselves, their families, and their loved ones. Within a larger context, HCWs are situated in working environments that may be experiencing rapid changes, such as implementation of new safety protocols, adapting to telehealth service delivery, or contending with redeployment. These changes in the workplace are further compounded by increasingly challenging work environments, where HCWs may encounter difficult moral-ethical dilemmas (eg, tending to patients without adequate personal protective equipment (PPE), providing services on platforms unfamiliar to the provider and patients), which may have severe and enduring consequences for their mental health and well-being.

Research following the 2003 severe acute respiratory syndrome (SARS) epidemic illustrates the significant and persevering distress that HCWs may experience in the aftermath of an infectious outbreak. Among SARS survivors, HCWs experienced elevated symptoms of anxiety one month following SARS recovery [1] and higher levels of stress, depression, and anxiety at one-year postoutbreak [2] compared to non-HCW survivors. Evidence from the SARS epidemic also highlighted the vulnerability of those working on the frontlines, including job stress related to managing changes to working environments, feelings of loneliness and social isolation, and anxiety and fear in response to increased exposures to the virus [3,4]. In comparison to hospital administrative staff, frontline HCWs reported significantly higher psychological impairment, insomnia, and exhaustion [5].

Studies conducted early during the COVID-19 pandemic similarly found that HCWs on the front line were more severely distressed compared to nonfrontline HCWs [6-8]. In other cross-sectional studies, evidence also points to the devastating toll of the pandemic on the mental health of HCWs. In a study of nurses and physicians in Wuhan, China, over 60% of respondents reported concerning mental health symptoms across standardized measures of anxiety, depression, and sleep [9]. Similar increases in psychological distress, burnout, and worsened mental health were reported in frontline HCWs in other countries [10-13].

Some of the distress experienced by HCWs could be ethical or moral in nature. HCWs' experiences during the pandemic involve making difficult decisions that may not always be aligned with their ethical or moral values. These may involve tending to patients without appropriate PPE, balancing increases in patient caseloads and potentially compromising the quality of care provided, having to make difficult decisions to turn away patients without care due to shortages of hospital beds or ventilators, and disagreements or conflicts arising from the allocation of lifesaving treatments or vaccines [14,15]. Expanding beyond organizational levels, rapidly changing public health policies, and perceived delays in responses from leaders, employers, and municipal, provincial, and federal governments may perpetuate feelings of distrust and betrayal, further triggering complex emotional reactions. Indeed, moral distress may arise when individuals find themselves in difficult emotional states when the perceived ethical actions deviate from what they may be tasked to do. The frequency and impact of morally distressing events may be amplified during the current pandemic [14,15]. If unaddressed, these instances of moral distress can lead to moral injury, defined as the psychological distress resulting from transgressing one's moral beliefs or standards through action or inaction [16,17]. Despite evidence of mental distress, little empirical attention has been paid to the examination of moral-ethical dilemmas and associated moral distress during current and past epidemics and pandemics.

Further, the myriad of challenges HCWs face at the individual and organizational levels greatly threaten their physical and mental health, as well as their professional development. Specifically, increased rates of absenteeism reported by HCWs not only contribute to added burden of care for colleagues but more importantly highlight the systemic need for additional support for HCWs [18]. Meanwhile, reviews suggest that increased workloads, occupational stress and burnout, and organizational changes are expected to pose critical challenges in future to the long-term retention of HCWs [19]. Taken together, research is urgently needed to understand HCWs' experiences during the COVID-19 pandemic, including

challenges and changes in the workplace, moral-ethical dilemmas, evolving occupational duties, standards of care, service delivery, and the effects of COVID-19 on dimensions of mental health and well-being.

Research Aims

This paper describes the protocol and initial response rates for a longitudinal study seeking to capture the unique experiences, challenges, and changes faced by HCWs during the COVID-19 pandemic. The study was launched in June 2020 and is ongoing. Future publications from this study will use the data collected to explore (1) the impact of COVID-19 on the mental well-being of HCWs, (2) perceptions of and satisfaction with delivery of care, and (3) how changes in work structure are tolerated among HCWs providing services.

Methods

Summary of Design

Our study employs an observational, prospective, longitudinal panel design using the web-based data collection platform Research Electronic Data Capture (REDCap). Participants completed questionnaires at baseline and will be completing follow-up questionnaires at 3-month intervals for a total of 18 months. Interested participants self-selected into an open survey and chose to complete a short version or long version of the survey at baseline. The protocols of this study were reviewed and approved by the research ethics board at Western University (WREM 115894) and Lawson Health Research Institute (REDA 9968). Details of the protocol are reported below following the general guidelines from the Checklist for Reporting of Results of Internet E-Surveys (CHERRIES) [20].

Participant Selection and Recruitment

A convenience snowball sampling approach is used to recruit HCWs. Recruitment methods include word of mouth, emails to professional networks, web-based advertisement through the Lawson Health Research Institute, social media, participant recruitment websites (eg, ParticipAid [21]), and targeted media releases. The representativeness of participants was monitored throughout the recruitment period. Recruitment efforts are adjusted to target specific regions or segments to improve the representation on dimensions of gender, region, and occupational distribution of health care workers within Canada. Participants include male and female English- and French-speaking HCWs with a minimum age of 18 years. HCWs are defined as individuals who provide health care treatment and advice based on formal training and experience or who work to directly support those providers in a clinical setting. Participating HCWs must be currently working in Canada or have worked in Canada as an HCW at some point in time between the start of the COVID-19 pandemic (March 2020) and the start of data collection (June 26, 2020). Participation in the study is voluntary, and participants are not compensated for survey completions.

Procedure

The study duration is catered to participant availability and varies depending on whether the participant selected the short-form or long-form survey (Table 1). Both English and French versions of the survey are available based on the language preference of participants. Validated scales in French are used where available, and in the absence of translated and validated versions, translation is completed by professional translators with certificates of translation provided. Informed consent is obtained through a Letter of Information (LOI), presented to participants at the beginning of the survey at baseline, and again during each of the follow-up surveys. The LOI is presented on REDCap, and participants are informed that their consent is implied should they proceed to the following pages of the survey.

A short-form version of the survey is available at baseline (approximately 10 minutes) and consists of 6 measures. A longer option, consisting of 12 measures, is available for participants who indicate they have the time (approximately 15-25 minutes). The long version can be completed immediately at baseline or returned within a 6-week window after beginning the baseline measures. Following baseline, participants are requested to complete a follow-up survey (approximately 15 minutes) every 3 months for a period of 18 months (see Table 1). To save time, participants can skip certain modules if there was no change from previous time points (eg, if their employment status did not change). Participants can also review and change answers before advancing to the following page.

Table 1. Data collection tools for the short-form, long-form, and follow-up surveys.

Collection of assessments/domains	Short form	Long form	Follow-up
Demographics	✓	✓	
Work-related changes/appraisals	✓	✓	✓
Telehealth experiences		✓	✓
Organizational response	✓	✓	✓
COVID-19 exposure/concerns	✓	✓	✓
Mental health			
Patient Health Questionnaire-9		✓	✓
Generalized Anxiety Disorder-7 scale		✓	✓
Posttraumatic Stress Disorder Checklist for DSM-5[a]	✓	✓	✓
Well-Being Index		✓	✓
Moral injury, ethical climate, and moral reasoning			
Measure of Moral Distress for Healthcare Professionals	✓	✓	✓
Moral Injury Outcome Scale		✓	
Ethical Environment Questionnaire		✓	✓
Oxford Utilitarianism Scale		✓	

[a]DSM-5: *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition.

Measures

The web-based survey was constructed in consultation with international research teams and collaborators to evaluate the crosscultural effects of the COVID-19 pandemic. Measures were selected to ensure comparability across countries. In addition, a literature search was conducted to identify potential novel measures related to the assessment of effects of the COVID-19 pandemic. The usability and functionality of the survey were tested by the research team, including adaptive questioning, branching functions, and longitudinal response collections. Questions were presented in the same order, as shown in Table 2.

Table 2. Categories and types of questions included in the survey.

Category	Question types
Basic demographics	All participating HCWs[a] are asked to report their province or territory of residence, age, and ethnicity.[b,c] Participants choosing to complete the long form questionnaire are also asked to report their gender, marital status, characteristics of area of residence (eg, rural or city), and education level.
Work-related/telehealth	Participants are asked about work demographics, the proportion of their time spent working on-site versus remotely, the proportion of their time working directly with patients, and whether they provided care to patients with suspected or confirmed COVID-19. HCWs providing services remotely are asked closed- and open-ended questions about the changes to their delivery of care and their experiences with telehealth. The telehealth questions were derived from a University of Missouri quality improvement survey and other research exploring the application of telehealth and telemedicine in various populations [22-25].
Organizational response to COVID-19	Participants are asked to self-report on the effectiveness and satisfaction with the support and communication of their organization in response to the COVID-19 pandemic. Items were drawn from the Pandemic Experiences and Perceptions Survey [26], a measure created in response to the COVID-19 pandemic. This survey measures organizational response to the pandemic in the domains of disruption, resource adequacy, COVID-19 risk perception, positive work life impact, and leadership [26]. For the purpose of our study, we are collecting data on the resource adequacy, risk perception, positive work life impact, and leadership domains.
COVID-19 exposure/concerns	Participants are asked to report their history of suspected or confirmed exposure to and infection with COVID-19 individually and for family members, as well as any associated direct impact the infections had on them. The items were adapted from the Coronavirus Health Impact Survey, which was developed based on ongoing research and collaborations between the National Institute of Mental Health Intramural Research Program Mood Spectrum Collaboration, the Child Mind Institute, the New York State Nathan S Kline Institute for Psychiatric Research, and researchers from Johns Hopkins University [27].
Mental health questionnaires	Symptoms of mental distress are evaluated using self-report measures, including a measure of depression (the Patient Health Questionnaire-9 [28]),[b] posttraumatic stress disorder (the PTSD Checklist for DSM-5 [29]), generalized anxiety (the Generalized Anxiety Disorder-7 scale [30]),[b] and workplace well-being and burnout (Well-Being Index [31]).[b] Additional questions were included to determine the extent to which mental health symptoms may have been influenced or exacerbated by the pandemic.
Moral distress, ethical climate, and moral reasoning	Moral distress, moral injury, ethical workplace climate, and moral reasoning are assessed using self-report measures. Perceptions of the general ethical climate in the HCWs' workplaces will be evaluated using the Ethics Environment Questionnaire [32]. Individual experiences with specific morally distressing situations (eg, "Watch patient care suffer because of a lack of provider continuity") are evaluated using the Measure of Moral Distress for Healthcare Professionals [33]. Multidimensional moral injury is evaluated using the Moral Injury Outcome Scale[b] [34]. Moral-ethical decision-making tendencies are assessed using the Oxford Utilitarianism Scale[b] [35].

[a]HCW: health care worker.

[b]Represents a measure that is available only on the long-form version of the web-based survey.

[c]Ethnicity was added at a later time via an ethics amendment to the original protocol, and a portion of participants who are completing the 12-month follow-up survey will have the option to answer questions on their racial and ethnic background.

Data Analytic Plan

Descriptive and Exploratory Analyses

Mixed methods descriptive and exploratory analyses will be conducted to understand the state of mental well-being and moral distress of sampled HCWs. Quantitative descriptive statistics will examine age, gender, education, occupation, illness-related variables (eg, whether currently or formerly positive for COVID-19), psychological and moral variables, and satisfaction with telehealth. These will include general descriptive statistics, measures of internal consistency, correlational analyses, and group-based analyses on similarities and differences. Exploratory analyses will include hierarchical multivariate analyses, structural equation modelling, and cluster analyses to determine manifestations of mental and/or moral distress. Qualitative, open-ended data, including participant descriptions of changes to their care delivery, impact of moral distress, and general feedback on organizational support and pandemic responses will be analyzed using content and thematic analysis.

Longitudinal Analyses

Data at baseline and each of the follow-up periods will be analyzed using exploratory and confirmatory mixed effects modeling and latent growth modeling. Longitudinal analyses will explore changes in dimensions of mental health, moral injury, and distress in relation to care delivery and/or work settings, organizational responses, and COVID-19-related changes and exposures over time.

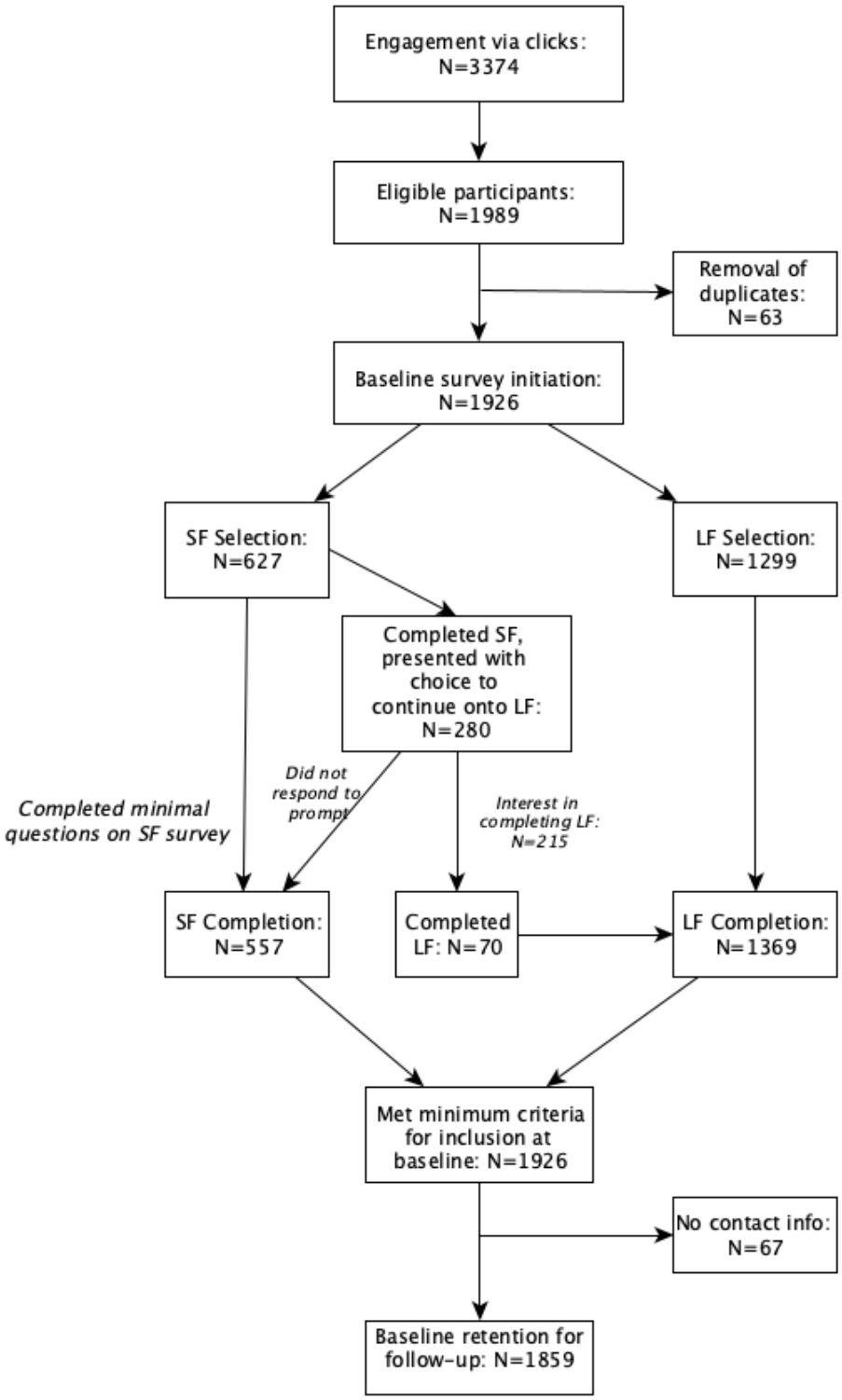
Results

Survey Completion and Representativeness

A total of 1926 participants completed baseline surveys between June 26 and December 31, 2020. Of these, 1859 participants provided their emails for follow-up survey invitations. The majority (71%, n=1299) of baseline participants initially selected the long-form survey. Subsequent prompts encouraged

participants completing the short-form surveys to complete the long version, which resulted in 25% conversion of those prompted and an overall increase in long-form survey data. Figure 1 details the flow of survey completion from initial interest and engagement via survey links.

Figure 1. Participant flow for baseline completion rates. Info: information; LF: long-form survey; SF: short-form survey.



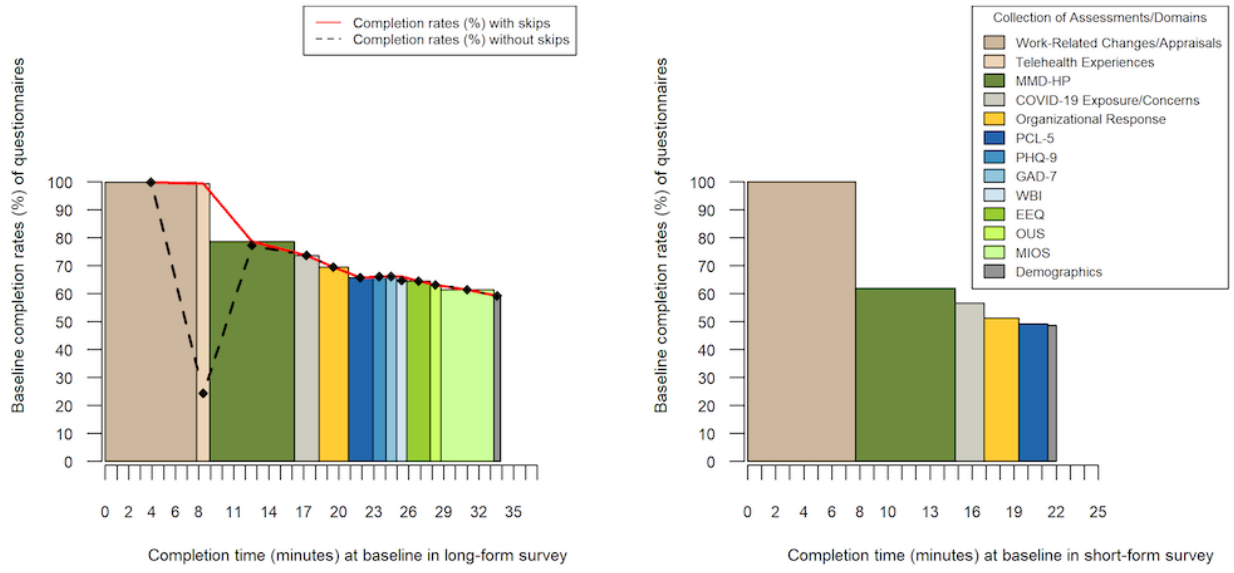
We further examined the preliminary representativeness of our baseline sample against a Canadian national database of health care workforce metadata with over 37 million health care workers on the distribution of top professions and genders [36]. Relative to the national sample, which comprises roughly 68% nurses and 14% physicians, our baseline sample from self-reported professions included 40.27% (n=557) nurses and 3.90% (n=54) physicians, representing differences of 28% and 10%, respectively. For other top health care disciplines, such as personal support workers, paramedics, physical therapists, and social workers, our sample was relatively representative, with differences in percentage distributions of 1.2% to 5.6%.

Finally, female nurses were underrepresented in our sample by a percentage difference of 32%, whereas female HCWs in other disciplines and male HCWs were relatively representative in relation to the national sample (percentage differences of <1% to 7%).

Participant Data Retention

Depending on whether participants completed the short-form or long-form survey at baseline, completion time varied by approximately 12 minutes, with the long-form survey taking a median of 34 minutes and the short-form survey taking a median of 22 minutes to complete. Survey completion also varied by questionnaire. For the long-form survey, baseline completion for initial eligibility, work-related, and telehealth items were completed by nearly all participants (100%), with participation declining to <80% for COVID-19–related questions and to <70% for mental health– and moral distress–related self-report questionnaires (n/N values are not reported for the percentages here, as they represent changes in rates of completion as opposed to changes in sample size). This trend was similar for short-form questionnaire completion, but with a steeper decline, and with completion of the full set of questionnaires between 50% and 60% (see Figure 2). Although the dropout rate was comparable to those found in previous research evaluating completion rates of web-based surveys in relation to the length of the surveys, this study was able to maintain 100% initial completion for the first section of questions about work-related changes and responses to COVID-19, whereas others have reported 10% instantaneous dropout [37]. Furthermore, although previous studies examined participation under regular circumstances using university student samples, this study sampled HCWs who are likely time-restricted because of their busy schedules. Taken together, the choice between short- and long-form surveys and the option to convert to the long form is a promising approach to maximize participation and retention.

Figure 2. Completion rates of individual questionnaires at baseline.



Finally, based on the date of self-selection and enrollment in the study, participants receive system-generated links to complete follow-up surveys every three months. The baseline retention with email addresses (N=1859) is being used as a reference point to evaluate subsequent participant retention, attrition, and sensitivity analyses during each of the follow-up periods. As of July 2021, a total of 848/1859 participants (45.6%) had completed the 3-month follow-up, whereas 1011/1859 (54.4%) missed the response window. Data collection is ongoing into the 6-month and 9-month follow-up periods. Full data collection for the longitudinal study is expected to be completed by August 8, 2022.

Discussion

This paper details the protocol for a longitudinal study that will examine the impact of the COVID-19 pandemic on the mental well-being of HCWs, with a focus on moral distress, perceptions of and satisfaction with delivery of care, and perceptions of changes in work structure among HCWs providing services. Using convenience snowball sampling and diverse recruitment platforms, this study is reaching a large national sample of HCWs from a range of disciplines and backgrounds. Participants recruited are relatively diverse and comparable to national samples of HCW distributions. Following baseline completion, we retained 1859 HCWs for subsequent longitudinal follow-ups. The longitudinal data will provide important profiles of HCWs during key milestones of the pandemic in Canada and offer insights in understanding and predicting the development or worsening of mental health and moral injury over time as the pandemic persists. In particular, the collected data will shed light on the organizational and environmental stressors and their associations with changes in the experiences of HCWs with moral dilemmas, moral distress, and mental well-being.

A strength of this study that may contribute to the large sample size for both recruitment and retention is the option to complete either the short or long form of the survey. With the choice to select either form, we sought to reduce barriers of participation as a result of survey fatigue and self-perceived time restrictions to accommodate the busy schedules of HCWs. To further encourage completion of the long-form survey, we also implemented prompts to encourage those who completed the short-form survey to complete the long-form survey in subsequent follow-ups. This option yielded a 25% success rate in conversion to the long-form survey. This represents a relatively novel approach, which was designed to maximize survey retention while minimizing barriers [38]. A challenge in this process was the time difference in completion between short- and long-form surveys. Based on data completion rates and times at baseline, the difference between the two surveys is estimated to range between 5 and 15 minutes, with the short-form survey taking a median of 22 minutes to complete. Given the initial time commitment required for the short-form survey, this may have discouraged some of the participants from converting to the long-form survey based on their perceived time restraints.

As of July 2021, data collection is ongoing, with participants nearing the 6- or 9-month follow-up periods depending on their initial time of self-enrollment. This study demonstrates the utility and feasibility of offering both a short-form and long-form survey for the collection of prospective, longitudinal data from HCWs. This format of recruitment and data collection may be useful when implemented with other populations experiencing time restrictions or busy schedules. Finally, this study will offer key insights into the mental well-being and moral challenges of HCWs as they cope with the ongoing pandemic. The findings will lend a voice to the HCWs and their unique experiences of challenges and change during the protracted pandemic and associated restrictions. Knowledge gained will better equip us to anticipate and prepare for future challenges, such as long-term support and retention of HCWs. Armed with this knowledge, policy makers and clinicians can make evidence-based decisions to prevent and mitigate the risks to the psychological well-being of HCWs both generally and specifically as they recover from the pandemic.

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Conflicts of Interest

None declared.

References

1. Cheng S, Wong CW, Tsang J, Wong KC. Psychological distress and negative appraisals in survivors of severe acute respiratory syndrome (SARS). Psychol Med 2004 Oct;34(7):1187-1195 [FREE Full text] [doi: 10.1017/s0033291704002272] [Medline: 15697045]
2. Lee AM, Wong JG, McAlonan GM, Cheung V, Cheung C, Sham PC, et al. Stress and psychological distress among SARS survivors 1 year after the outbreak. Can J Psychiatry 2007 Apr 01;52(4):233-240. [doi: 10.1177/070674370705200405] [Medline: 17500304]
3. Maunder R, Hunter J, Vincent L, Bennett J, Peladeau N, Leszcz M, et al. The immediate psychological and occupational impact of the 2003 SARS outbreak in a teaching hospital. CMAJ 2003 May 13;168(10):1245-1251 [FREE Full text] [Medline: 12743065]
4. Maunder R, Lancee WJ, Rourke S, Hunter JJ, Goldbloom D, Balderson K, et al. Factors associated with the psychological impact of severe acute respiratory syndrome on nurses and other hospital workers in Toronto. Psychosom Med 2004;66(6):938-942 [FREE Full text] [doi: 10.1097/01.psy.0000145673.84698.18] [Medline: 15564361]
5. Bai Y, Lin CC, Lin CY, Chen JY, Chue CM, Chou P. Survey of stress reactions among health care workers involved with the SARS outbreak. Psychiatr Serv 2004 Sep;55(9):1055-1057. [doi: 10.1176/appi.ps.55.9.1055] [Medline: 15345768]
6. Dai Y, Hu G, Xiong H, Qiu H, Yuan X. Psychological impact of the coronavirus disease 2019 (COVID-19) outbreak on healthcare workers in China. medRxiv Preprint posted online on March 6, 2020. [doi: 10.1101/2020.03.03.20030874]
7. Lai J, Ma S, Wang Y, Cai Z, Hu J, Wei N, et al. Factors associated with mental health outcomes among health care workers exposed to coronavirus disease 2019. JAMA Netw Open 2020 Mar 02;3(3):e203976 [FREE Full text] [doi: 10.1001/jamanetworkopen.2020.3976] [Medline: 32202646]
8. De Kock JH, Latham HA, Leslie SJ, Grindle M, Munoz S, Ellis L, et al. A rapid review of the impact of COVID-19 on the mental health of healthcare workers: implications for supporting psychological well-being. BMC Public Health 2021 Jan 09;21(1):104 [FREE Full text] [doi: 10.1186/s12889-020-10070-3] [Medline: 33422039]

9. Huang Y, Zhao N. Generalized anxiety disorder, depressive symptoms and sleep quality during COVID-19 outbreak in China: a web-based cross-sectional survey. Psychiatry Res 2020 Jun;288:112954 [FREE Full text] [doi: 10.1016/j.psychres.2020.112954] [Medline: 32325383]
10. Kachadourian LK, Feder A, Murrough JW, Feingold JH, Kaye-Kauderer H, Charney D, et al. Transdiagnostic psychiatric symptoms, burnout, and functioning in frontline health care workers responding to the COVID-19 pandemic. J Clin Psychiatry 2021 Apr 27;82(3). [doi: 10.4088/jcp.20m13766]
11. Orrù G, Marzetti F, Conversano C, Vagheggini G, Miccoli M, Ciacchini R, et al. Secondary traumatic stress and burnout in healthcare workers during COVID-19 outbreak. Int J Environ Res Public Health 2021 Jan 05;18(1):337 [FREE Full text] [doi: 10.3390/ijerph18010337] [Medline: 33466346]
12. Shreffler J, Petrey J, Huecker M. The impact of COVID-19 on healthcare worker wellness: a scoping review. West J Emerg Med 2020 Aug 17;21(5):1059-1066 [FREE Full text] [doi: 10.5811/westjem.2020.7.48684] [Medline: 32970555]
13. Spoorthy M, Pratapa SK, Mahant S. Mental health problems faced by healthcare workers due to the COVID-19 pandemic-A review. Asian J Psychiatr 2020 Jun;51:102119 [FREE Full text] [doi: 10.1016/j.ajp.2020.102119] [Medline: 32339895]
14. COVID-19 and moral distress: setting the stage. Canadian Medical Association. URL: https://www.cma.ca/sites/default/files/pdf/Moral-Distress-E.pdf [accessed 2021-07-20]
15. Roycroft M, Wilkes D, Pattani S, Fleming S, Olsson-Brown A. Limiting moral injury in healthcare professionals during the COVID-19 pandemic. Occup Med (Lond) 2020 Jul 17;70(5):312-314 [FREE Full text] [doi: 10.1093/occmed/kqaa087] [Medline: 32428213]
16. Shay J. Odysseus in America: Combat Trauma and the Trials of Homecoming. New York, NY: Simon & Schuster; Nov 25, 2003.
17. Litz BT, Stein N, Delaney E, Lebowitz L, Nash WP, Silva C, et al. Moral injury and moral repair in war veterans: a preliminary model and intervention strategy. Clin Psychol Rev 2009 Dec;29(8):695-706. [doi: 10.1016/j.cpr.2009.07.003] [Medline: 19683376]
18. Tujjar O, Simonelli M. Absenteeism of frontline healthcare workers during Covid-19: the need for a framework of support. SN Compr Clin Med 2020 Oct 28;19:1-3 [FREE Full text] [doi: 10.1007/s42399-020-00609-1] [Medline: 33134848]
19. Jamebozorgi AH, Agoush L, NooriHekmat S, Shokri A, Sadatmoosavi A, Shirvani M, et al. Coronavirus and its impacts on health workers retention: a systematic review and meta-synthesis. Research Square Preprint posted online on February 23, 2021. [FREE Full text] [doi: 10.21203/rs.3.rs-220298/v1]
20. Eysenbach G. Improving the quality of Web surveys: the Checklist for Reporting Results of Internet E-Surveys (CHERRIES). J Med Internet Res 2004 Sep 29;6(3):e34 [FREE Full text] [doi: 10.2196/jmir.6.3.e34] [Medline: 15471760]
21. ParticipAid. URL: https://participaid.co/ [accessed 2021-09-09]
22. Becevic M, Boren S, Mutrux R, Shah Z, Banerjee S. User satisfaction with telehealth: study of patients, providers, and coordinators. Health Care Manag 2015;34(4):337-349 [FREE Full text] [doi: 10.1097/hcm.0000000000000081]
23. Brown S. Primary care provider's perceptions of telehealth adoption (Order No AAI10163004). APA PsycInfo. 2017.
24. Hicks L, Fleming DA, Desaulnier A. The application of remote monitoring to improve health outcomes to a rural area. Telemed J E Health 2009 Sep;15(7):664-671 [FREE Full text] [doi: 10.1089/tmj.2009.0009] [Medline: 19694598]
25. Sandberg J, Trief PM, Izquierdo R, Goland R, Morin PC, Palmas W, et al. A qualitative study of the experiences and satisfaction of direct telemedicine providers in diabetes case management. Telemed J E Health 2009 Oct;15(8):742-750 [FREE Full text] [doi: 10.1089/tmj.2009.0027] [Medline: 19780691]
26. Leiter MP. Mind Garden. URL: https://www.mindgarden.com/346-pandemic-experiences-perceptions-survey [accessed 2021-06-16]
27. Merikangas K, Milham M. The CoRonavIruS Health Impact Survey (CRISIS) V0.1. GitHub. URL: https://github.com/nimh-mbdu/CRISIS/tree/d94bae3eba7b225f89fb310eae881d1d73ee9126 [accessed 2021-09-09]
28. Spitzer RL, Kroenke K, Linzer M, Hahn SR, Williams JBW, deGruy FV, et al. Health-related quality of life in primary care patients with mental disorders: results from the PRIME-MD 1000 study. JAMA 1995 Nov 15;274(19):1511. [doi: 10.1001/jama.1995.03530190025030]
29. Weathers FW, Litz BY, Keane TM, Palmieri PA, Marx BP, Schnurr PP. PTSD Checklist for DSM-5 (PCL-5). US Department of Veterans Affairs. 2013. URL: https://www.ptsd.va.gov/professional/assessment/adult-sr/ptsd-checklist.asp [accessed 2021-09-09]
30. Spitzer RL, Kroenke K, Williams JBW, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med 2006 May 22;166(10):1092-1097. [doi: 10.1001/archinte.166.10.1092] [Medline: 16717171]
31. Dyrbye L, Satele D, Shanafelt T. Ability of a 9-item well-being index to identify distress and stratify quality of life in US workers. J Occup Environ Med 2016;58(8):810. [doi: 10.1097/jom.0000000000000798]
32. McDaniel C. Development and psychometric properties of the Ethics Environment Questionnaire. Med Care 1997 Sep;35(9):901-914. [doi: 10.1097/00005650-199709000-00003] [Medline: 9298079]
33. Epstein EG, Whitehead PB, Prompahakul C, Thacker LR, Hamric AB. Enhancing understanding of moral distress: the measure of moral distress for health care professionals. AJOB Empir Bioeth 2019 Apr 19;10(2):113-124. [doi: 10.1080/23294515.2019.1586008] [Medline: 31002584]

34. Yeterian J, Berke DS, Carney JR, McIntyre-Smith A, St Cyr K, King L, Members of the Moral Injury Outcomes Project Consortium. Defining and measuring moral injury: rationale, design, and preliminary findings from the Moral Injury Outcome Scale Consortium. J Trauma Stress 2019 Jun;32(3):363-372 [FREE Full text] [doi: 10.1002/jts.22380] [Medline: 30947372]
35. Kahane G, Everett JAC, Earp BD, Caviola L, Faber NS, Crockett MJ, et al. Beyond sacrificial harm: a two-dimensional model of utilitarian psychology. Psychol Rev 2018 Mar;125(2):131-164 [FREE Full text] [doi: 10.1037/rev0000093] [Medline: 29265854]
36. Health Workforce Database metadata. Canadian Institute for Health Information. URL: https://www.cihi.ca/en/health-workforce-database-metadata [accessed 2021-06-16]
37. Hoerger M. Participant dropout as a function of survey length in internet-mediated university studies: implications for study design and voluntary participation in psychological research. Cyberpsychol Behav Soc Netw 2010 Dec;13(6):697-700 [FREE Full text] [doi: 10.1089/cyber.2009.0445] [Medline: 21142995]
38. Teague S, Youssef GJ, Macdonald JA, Sciberras E, Shatte A, Fuller-Tyszkiewicz M, SEED Lifecourse Sciences Theme. Retention strategies in longitudinal cohort studies: a systematic review and meta-analysis. BMC Med Res Methodol 2018 Nov 26;18(1):151 [FREE Full text] [doi: 10.1186/s12874-018-0586-7] [Medline: 30477443]

Abbreviations

CoE: Centre of Excellence on Post-Traumatic Stress Disorder and Related Mental Health Conditions
HCW: health care worker
LOI: Letter of Information
PPE: personal protective equipment
REDCap: Research Electronic Data Capture
SARS: severe acute respiratory syndrome

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Protocol

The Impact of COVID-19–Related Restrictions on Social and Daily Activities of Parents, People With Disabilities, and Older Adults: Protocol for a Longitudinal, Mixed Methods Study

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Abstract

Background: The COVID-19 pandemic has led to wide-scale changes in societal organization. This has dramatically altered people's daily activities, especially among families with young children, those living with disabilities such as spinal cord injury (SCI), those who have experienced a stroke, and older adults.

Objective: We aim to (1) investigate how COVID-19 restrictions influence daily activities, (2) track the psychosocial effects of these restrictions over time, and (3) identify strategies to mitigate the potential negative effects of these restrictions.

Methods: This is a longitudinal, concurrent, mixed methods study being conducted in British Columbia (BC), Canada. Data collection occurred at four time points, between April 2020 and February 2021. The first three data collection time points occurred within phases 1 to 3 of the Province of BC's Restart Plan. The final data collection coincided with the initial distribution of the COVID-19 vaccines. At each time point, data regarding participants' sociodemographics, depressive and anxiety symptoms, resilience, boredom, social support, instrumental activities of daily living, and social media and technology use were collected in an online survey. These data supplemented qualitative videoconference interviews exploring participants' COVID-19–related experiences. Participants were also asked to upload photos representing their experience during the restriction period, which facilitated discussion during the final interview. Five groups of participants were recruited: (1) families with children under the age of 18 years, (2) adults with an SCI, (3) adults who experienced a stroke, (4) adults with other types of disabilities, and (5) older adults (>64 years of age) with no self-reported disability. The number of participants we could recruit from each group was limited, which may impact the validity of some subgroup analyses.

Results: This study was approved by the University of British Columbia Behavioural Research Ethics Board (Approval No. H20-01109) on April 17, 2020. A total of 81 participants were enrolled in this study and data are being analyzed. Data analyses are expected to be completed in fall 2021; submission of multiple papers for publication is expected by winter 2021.

Conclusions: Findings from our study will inform the development and recommendations of a new resource guide for the post–COVID-19 period and for future public health emergencies.

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KEYWORDS

COVID-19; longitudinal study; spinal cord injury; disability; adult; occupational disruption; stroke; older adults

Introduction

COVID-19 is the third zoonotic virus to infect humans in as many decades and was first identified in Wuhan, China, near the end of 2019 [1]. The origin of the virus, course of transmission, and treatment of infection are still under investigation, but initial understandings of the epidemiology suggest a genome that is 75% to 80% identical to SARS-CoV [1]. Once the severity of the virus was realized, the World Health Organization characterized COVID-19 as a pandemic on March 11, 2020 [2], and recommended the implementation of an evolving series of public health and social measures. These included "measures or actions by individuals, institutions, communities, local and national governments and international bodies to slow or stop the spread of COVID-19" [3]. At a community level these measures involve employees working from home where possible, distance learning, avoiding crowding, wearing a mask, closure of nonessential services, reorganization of health care services, and government-directed calls to stay at home. For the purpose of this paper, the term "restrictions" will be used to refer to the abovementioned measures, including physical distancing and limited in-person interactions with others. The first COVID-19 case in Canada was reported on January 25, 2020 [4]. The initial response by the Canadian government included calls for social distancing, which was later clarified to mean keeping physical distance from others [4], although these terms continue to be used interchangeably in many contexts. As health is a provincial responsibility in Canada, the restrictions vary by province and are subject to change depending on the number of COVID-19 cases in the given location.

Concerns have been raised about the unintended negative consequences of the pandemic restrictions among a variety of groups, including families with young children, those living with disabilities such as spinal cord injury (SCI) or stroke, and older adults. British Columbia's (BC's) Restart Plan [5] consists of four phases calling for varying restrictions primarily related to physical distancing (Table 1), resulting in decreased in-person interactions and disruption of social and daily activities.

Table 1. British Columbia's Restart Plan for COVID-19 restrictions.

Phase start date	Restriction period	Restrictions
March 2020	Phase 1	• Essential services reopen or remain open in compliance with provincial health orders • Declaration of public health emergency • Banned mass gatherings of >50 people • Restricted visitation in health care facilities
May 18, 2020	Phase 2	• Many businesses to reopen with extra precautions and physical distancing measures in place • Childcare, hairdressers, gyms, salons, and other services reopen • Medical services, such as psychology, dentistry, massage, chiropractic, and occupational and physical therapies, resume
June 24, 2020	Phase 3	• Faith-based organizations resume in-person gatherings up to 50 people • Designated visitors limited to one person for those living in long-term or assisted-living care facilities • Limited hours of operation for restaurants, bars, cafés, and breweries with distancing measures in place
Conditional	Phase 4	• Entering this phase is dependent on community immunity, wide vaccination, and broad successful treatments • Once one of the three above factors is met, larger gatherings at concerts, conventions, tourism events, and other events can resume

Easing of restrictions to allow transition between phases is dependent on new developing knowledge about COVID-19, tracking of confirmed and recovered cases, new outbreaks, and observing how other regions are responding to the pandemic [5]. The restrictions, in place to reduce transmission and ultimately stop the spread of the virus [3], have many unintended consequences, such as financial strain along with psychosocial implications. In an attempt to mitigate the financial stressors that many people are experiencing, the BC Recovery Benefit was offered as "a one-time direct deposit payment for eligible families, single parents or individuals" [6]. The Canadian Emergency Response Benefit was an additional income support measure that eligible Canadians could claim [7]. These programs offer support for lost income resulting from job loss and ongoing unemployment due to the COVID-19 pandemic; however, they do not address the psychosocial issues that arise with the loss of employment, changes in routine, and overall disruption to social and daily activities, which are vital determinants of health [8]. The loss in daily routine combined with physical distancing can lead to increased isolation and loneliness, ultimately reducing mental health and overall well-being [8]. It is important to consider how these psychosocial changes may occur for

families with young children, those living with disabilities such as SCI and stroke, and older adults.

For parents with school-aged children, COVID-19 responses have led to school closures and home-based online learning, which has resulted in an increased need for parental supervision [9]. This has placed additional stressors on parents, who may be dealing with employment changes (eg, unemployment, reduced hours, and working from home) and financial pressures; they also must respond to changing needs for their children's schooling and daycare. Further challenges may arise for single-parent families, those who have restricted access to out-of-household familial supports, and those experiencing domestic violence [10]. Early COVID-19 studies indicated that negative mood increased for parents and children and "work disruptions" also increased [11]. These findings suggest that parents and their children are facing unique challenges during the COVID-19 pandemic that are impacting their mood and productivity and are likely contributing to declining mental health for the family as a whole [11].

The risks associated with COVID-19 may be further exacerbated in vulnerable populations, such as individuals with disabilities who may have compromised immune systems or face mobility challenges. According to the Canadian Survey on Disability, 81.3% of people with disabilities report using an aid or assistive device, such as a wheelchair or hand and arm supports, to facilitate movement [12]. Using mobility aids or equipment presents additional risks specific to COVID-19, as some prevention strategies may be more difficult for people with disabilities [3]. For instance, they may not be able to stay 1 to 2 meters away from others if they rely on a caregiver for personal care, or they may not be able to don a mask independently [13].

Additionally, it is important to consider the concerns regarding the reduced well-being among older adults due to physical distancing and isolation resulting from these COVID-19 restrictions [14]. Due to the increased risk of infection and fatality among older adults, aged 65 years and over, health officials advise this group "to stay home, and self-isolate" [15]. This has resulted in considerable changes in the daily and social activities for the 8 million older Canadians [5]. Furthermore, there are already indications that the well-being of older adults has declined due to physical distancing and isolation resulting from COVID-19 restrictions [14,16].

At this time, there is limited understanding of how prolonged restrictions influence social and daily activities as well as health and well-being, particularly among families with children, people with disabilities such as SCI or stroke, and older adults. It is crucial to consider the unique challenges that COVID-19 restrictions create for those who may not have been considered when these policies were developed [2,5]. Having more inclusive guidance requires a deeper level of understanding of the lived experience of various populations during the shifting and wide-reaching pandemic restriction period. Therefore, the aims of this study are (1) to understand how COVID-19 restrictions change what people do and how they carry out their daily activities, (2) to track the psychosocial effects of these restrictions over time, and (3) to identify strategies to mitigate the negative potential effects of these restrictions.

Methods

Overview

This study used a longitudinal, concurrent, mixed methods design with four data collection time points: time point 1 (T1), time point 2 (T2), time point 3 (T3), and time point 4 (T4). Qualitative description was used as the qualitative methodology for this study [17-19]. The Good Reporting of A Mixed Methods Study (GRAMMS) guideline [20] has been followed for the study protocol and for reporting the results. Quantitative data were collected using an online survey with self-reported questionnaires that participants completed 7 days prior to each interview.

Eligibility Criteria

Community-dwelling adults over the age of 19 years living in BC, who self-identified as being comfortable writing and speaking in English, were recruited. Participants were excluded if they reported having moderate to severe cognitive impairment or aphasia.

A heterogeneous sample of 81 adults in BC were recruited. This included (1) parents with school-aged children (10/81, 12%), (2) people with SCI (22/81, 27%), (3) people who have experienced a stroke (26/81, 32%), (4) individuals with other disabilities (13/81, 16%), and (5) older adults without self-identified disabilities (10/81, 12%).

Recruitment and Consent

Participants were recruited using the following methods: (1) online postings at the International Collaboration on Repair Discovery and Reach BC websites, (2) reaching out to people who have consented to being contacted again from previous studies, and (3) advertisements on the researchers' social media pages (eg, Twitter and Facebook). Recruitment took place during the initial phase of restrictions in BC, from April to May 2020, and the number of participants was ultimately limited by funding. Those interested in participating contacted the research team by phone or email to learn more about the study and determine eligibility. Informed consent was obtained at each study time point.

Patient and Public Involvement

To date, patients or the public were not involved in the design, conduct, reporting, or dissemination plans of our research. However, this is a protocol paper, and the research is not complete. Patients or the public will likely still be included in the dissemination plans of our research, as the potential toolkit to be developed from this research will involve input from participants.

Data Collection and Outcome Measures

Overview

We used Qualtrics XM (Qualtrics) to obtain consent, collect demographic information, and administer patient-reported outcome measures (PROMs). PROMs allow us to collect

quantitative data on subjective psychosocial constructs [21]. Participants were given the link to the Qualtrics survey and asked to complete the survey within 7 days; an interview was then scheduled. We conducted semistructured interviews via teleconference using Zoom (Zoom Video Communications) to collect qualitative data on participants' experiences with COVID-19 restrictions. Prior to being used with study participants, the survey was pilot-tested with research team members and one participant who had experienced a stroke. In order to increase accessibility to the survey, if the person was unable to complete the survey online, it was administered over the telephone.

Demographic Information

Prior to the first interview, we collected data on participants' age, city of residence, country of birth, sex, gender, first language, living situation, educational level, income at baseline, employment status, chronic illnesses, and status regarding COVID-19 (ie, whether they have tested positive or been exposed to someone who had tested positive).

Outcome Measures

Overview

The measures listed below were captured in the survey, which was to be completed 1 week prior to the interview at each time point. The measures are described in detail in Table 2, which documents the constructs measured, number of items, number of subscales, response ranges and anchors, and scoring.

Table 2. Outcome measures used to collect data at each of the four time points.

Measure	Construct	Items, n	Subscales, n	Names of subscales	Response range and anchors	Scoring and score range
Connor-Davidson Resilience Scale 25	Resilience	25	1	N/A[a]	0 (not true at all) to 4 (true nearly all the time)	0 (minimum) to 100 (maximum)
Hospital Anxiety and Depression Scale	Generalized anxiety and depression	14	2	• Anxiety • Depression	0 (none) to 4 (extreme)	0 (none/low) to 40 (extreme)
Keele Assessment of Participation	Activity participation	11	1	N/A	1 (all the time) to 5 (none of the time)	Restricted (some, little, none) and not restricted (all, most)
Life Space Assessment	Space mobility	9	1	N/A	Life-space level (1-5), the degree of independence (2=no assistance, 1.5=equipment only, and 1=personal assistance), and the frequency of movement (1=less than once a week, 2=1-3 times each week, 3=4-6 times each week, and 4=daily)	0 (totally bedbound) to 120 (moved out of town every day without assistance)
Multidimensional Scale of Perceived Social Support	Social support	12	3	• Family • Friends • Significant other	1 (very strongly disagree) to 7 (very strongly agree)	12 to 84
Multidimensional State Boredom Scale	State boredom	29	5	• Targeting disengagement • High arousal • Inattention • Low arousal • Time perception	1 (strongly disagree) to 7 (strongly agree)	29 to 203
Social Networking Usage Questionnaire	Social networking usage	19	1	N/A	1 (never) to 5 (always)	19 to 95
Technology Readiness Index 2.0	Individual's technology readiness	16	4	• Optimism • Innovativeness • Discomfort • Insecurity	1 (strongly disagree) to 5 (strongly agree)	16 to 80

[a]N/A: not applicable; this subscale did not have a unique name.

Anxiety and Depression

The Hospital Anxiety and Depression Scale [22] measures anxiety and depression. Evaluation of this scale among primary care patients and the general public has demonstrated good concordance with clinical diagnoses of anxiety and depression, good sensitivity to change, and a mean Cronbach α of .83 [23].

Resilience

The Connor-Davidson Resilience Scale 25 [24] is a self-administered scale that measures resilience and how well people can cope with, and bounce back after, stressful events and tragedies. The reported Cronbach α for this measure is .93 [24] when used in a sample of adults from the general population.

Boredom

Boredom was assessed with the Multidimensional State Boredom Scale [25]. The Cronbach α for the total measure was .96 [26] upon development of the questionnaire.

Social Support

The Multidimensional Scale of Perceived Social Support [27] was used to assess perceived social support in three factor groups: family, friends, or significant other. The Cronbach α for the total score of this scale was .88 [27] in a sample including adolescents and adults.

Activity Participation

The Keele Assessment of Participation [28] measures participation in activities such as work, education, and socialization as well as in activities of daily living. The Cronbach α of this measure has been reported as .93 with a sample of adults aged 50 years and older [28].

Space Mobility

The Life Space Assessment reports on how frequently and far people have traveled out of the room in which they sleep during the previous 4 weeks. This assessment is moderately correlated with the Reintegration to Normal Living Index with Spearman ρ correlations ranging from 0.509 to 0.538. The 9-day test-retest reliability (intraclass correlation coefficient) has been reported to be 0.876 [29] among people with SCI.

Social Networking

The Social Networking Usage Questionnaire measures social media usage—academic, entertainment, and socialization—in online spaces. Questions regarding academic usage were removed from the questionnaire as these did not apply to our participants. A Cronbach α of .83 has been reported with university students [30].

Technology Use

The Technology Readiness Index 2.0 [31] is used to assess participants' readiness to embrace new technologies. The Cronbach coefficients for all the dimensions were higher than .60 [32] in a heterogenous sample of adults aged 18 years and older.

Substance Use

The demographic questionnaire included five questions related to substance use; for example, "Do you use tobacco products?" and a clarification question asking, "Are you using more or less than you did before COVID-19?" These questions were repeated for marijuana use, alcohol, other drugs, and prescription drugs.

Semistructured Interviews

Following the completion of the surveys, participants took part in semistructured interviews on the University of British Columbia's (UBC's) secure Zoom platform to maintain physical distance. Three interview guides were created (Multimedia Appendix 1): a guide for the first interview at T1, a guide for the interviews at T2 and T3, and a guide for the final interview at T4. Participants were asked about their experiences with daily activities, changes in activity, their feelings about these changes, and strategies they used to cope with the impact of COVID-19 restrictions. Each interview guide was tested in three pilot interviews prior to being used with participants. Each participant was assigned the same interviewer for each of their interviews to facilitate rapport and relevance of follow-up questions based on previous interviews. At the start of the first interview, the interviewer confirmed any changes to the demographic information collected by the survey at each subsequent interview (eg, living arrangements and employment status).

Participants were also invited to take pictures during the course of the study that represent their daily and social experiences during the period of COVID-19 restrictions. The photos acted as a catalyst to enrich the sharing of information, as interviewers prompted participants to share the meaning behind the photos. Participants were invited to send photos to the research coordinator at each time point, which were then combined into a collage by the research team. The interviewer shared the collage with participants in the final interview and asked them to choose two to three photos from the collage and describe what the photos meant to them in the context of the COVID-19 restrictions.

The interviews were recorded on a password-protected Zoom account as well as on a voice recorder as a backup, to ensure accuracy of the transcription, and were then transcribed verbatim. Participants were anonymized with a unique participant ID; the key matching the ID with the name and contact information for each participant is kept in a password-protected and encrypted Microsoft Excel file on a secure UBC server. When transcribing the interviews, each participant's ID was used to refer to them and other proper nouns were replaced with pseudonyms. Participants received a Can $30 (US $23.78) honorarium after each interview.

Training

The data collection team consists of eight interviewers and 17 transcribers. Interviewers were trained three times over the course of the project: twice before data collection and once before the fourth and final interview. The latter session served as a refresher and provided training on new content added to the interview guide. Transcribers used transcription templates for all interviews and they time-stamped passages to be clarified or verified by the interviewer. Most members of the transcription team were experienced and did not require additional training. Novice transcribers received a tutorial from a study team member.

Research Team Characteristics

The research team for this study is a large group of coinvestigators who are professors, educators, researchers, and other university employees. Interviewers and transcribers included volunteers who are university educated. Information on the positioning of the research team will be reported in further detail as relevant to each publication on the study findings.

Data Analysis

Quantitative Data Analyses

Before conducting the quantitative analyses, data will be imported from Qualtrics to SPSS (IBM Corp). First, univariate statistics will be used to account for the number and percent of missing data in each measure. The patterns of missing values for each measure will then be visualized. Missing value patterns will be evaluated carefully to determine missing data mechanisms (ie, missing completely at random, at random, or not at random) [33]. In addition, to determine whether the observed missing value patterns are related to other variables in the study, for each measure that contains missing values, an indicator variable will be developed. The indicator variable will separate the participants who provided complete responses to that measure from the participants who did not complete that measure. Logistic regression will be used to determine whether other variables in the study, including demographic variables, can statistically predict the indicator variable. If none of the variables in the logistic regression analyses predicts the indicator variable, it can be concluded that the missing pattern mechanisms are missing completely at random or missing at random. If the values are missing completely at random or missing at random, and the percentage of the missing values is less than 30%, we will impute the missing values using a multiple imputation technique. Multiple imputation will result in multiple sets of plausible values for each missing value. In these analyses, the multiple imputation will be used to compute five plausible values for each missing value. The missing values will then be replaced by the mean of the five plausible values. Multiple imputation analyses will be run for each measure that contains missing values in each group separately. After imputing the missing values, to test our hypotheses and research questions, the following statistical analyses will be used. First, univariate analyses (eg, mean, sum, standard deviation, variance, range, and frequency) will describe the sample. In cross-sectional analyses, multivariate analyses of variance will be used to test whether there is a statistically significant difference between groups on the outcome variables. Correlational analyses, including the Pearson correlation coefficient (r), will be used to test the strength of the associations between different variables. Regression analyses (eg, linear regression and logistic regression) will be used to estimate the relationship between dependent variables and the outcome variables.

To analyze the longitudinal data, hierarchical linear modeling (HLM) growth curve analysis will be used to investigate the changes in the participants over time [34]. HLM growth curve analysis has several benefits over repeated-measures analysis of variance. First, HLM can be used when the interval between the time points is not equal and when data contain missing values. In addition, in contrast to the repeated-measures analysis of variance, HLM focuses on individual differences over time by considering each participant's initial intercept and slope score, while repeated-measures analysis of variance focuses on the group differences [35].

Qualitative Data Analyses

Transcripts will be analyzed using content analysis to develop a qualitative description [18] of events and experiences of participants within and across the four time points. Analyses will be conducted separately for each of the participant groups—families, people with SCI, people with stroke, people with disabilities, and older adults—and each time point; they will then be combined, if appropriate, to examine trends over time or themes across groups [36]. A subteam of researchers will analyze each group. Because of the large research team, the blend of novice and experienced researchers, and the five participant groups, a consistent approach to coding will be facilitated by developing coding manuals with notations to explain coding decisions [37]. We anticipate creating multiple codebooks based on participant status, data collection time point, and omnibus analyses. These coding guides remain flexible to the possibility of adding new codes and recoding previous interviews. For each coding team, two primary coders will read and reread transcripts, code the first two to three interviews, compare codes, and discuss any discrepancies with the coding team. This coding guide will then be applied to subsequent interviews and revised in consultation with the qualitative research team for each participant group. During initial coding, the primary analysts will assign tentative codes to each idea reflective in the text, which are recorded in a codebook. The codebook and sample quotes supporting the codes will be shared with senior researchers. After integrating the comments from the senior researchers, the coders will code the next three to four interviews separately and once again compare their codes to ensure consistency in applying the codebook, updating as needed to reflect new or revised codes. The codebook developed at T1 will be used to code T2 interviews, updated with new codes developed at T2, which will be applied and updated at T3 and then again at T4; that is, codebooks will be updated as interviews are conducted throughout the longitudinal study. The coding procedure will be applied to each participant group separately, requiring four iterations of five participant group codebooks. Codes will then be organized into categories representing and interpreting the main topics shared by participants. The final qualitative description is expected to be presented as a set of themes and their interrelationships, supported by illustrative quotes from participants to explain their experiences of pandemic restrictions during the study period.

To integrate quantitative and qualitative data, there are three potential models of integration that may be used. Our primary approach will be to analyze both data sources separately. We will also explore the possibility of sequential analysis in which quantitative or qualitative analysis is used to inform a subsequent analysis using the alternative type of data [37] (eg, we may identify different types of experiences based on the qualitative data and compare scores on quantitative measures among participants who have similar experiences, or vice versa).

With regard to trustworthiness [38], an audit trail includes reflexive memos to document research discussions, possible biases, and analytical decisions (ie, dependability and confirmability). Comparing qualitative themes with numerical results from the PROMs will be used as a form of data triangulation and will generate questions to consider in refining qualitative themes. Researcher triangulation will occur within each subteam, in their analysis of a specific participant group, and in the larger team, where all researchers will be involved across all participant groups. Where available, member checking will further enhance analytical rigor.

Results

Approval for the study was obtained from the UBC Behavioural Research Ethics Board (Approval No. H20-01109) on April 17, 2020. This research was unfunded. A total of 81 participants were enrolled in this study and data are being analyzed. Data analyses are expected to be completed in fall 2021; submission of multiple papers for publication is expected by winter 2021.

Discussion

Overview

Interviewing and surveying a heterogenous sample of participants during the COVID-19 restrictions present an opportunity for insight into perceived constraints, barriers, and strategies to cope with this unusual period. Therefore, our longitudinal investigation into changes in activity, participation, and well-being informs recommendations for the post–COVID-19 period and for future public health emergencies. We anticipate that this study will provide information to practitioners working in public health, with patient groups highlighted in this research, by identifying gaps in services. Further, the findings are relevant across disciplines, as mental health is increasingly a priority for health, education, and social service sectors, as well as government portfolios. With a better understanding of changes in physical and social activities and self-management strategies, there is potential for development of a guide that will provide information, resources, and strategies for managing periods of isolation. Future research in this area is needed to inform the development and evaluation of such a resource guide.

Our knowledge translation plan will target families with school-aged children, people with disabilities such as SCI and stroke, and older adults. We will leverage existing communication tools, such as websites (eg, health authorities in BC), presentations at provincial practice forums, and social media (eg, Twitter). Building on existing partnerships with the Canadian Association of Occupational Therapists in BC and our research centers (eg, GF Strong and ICORD [International Collaboration on Repair Discoveries]), a summary will be prepared for their websites and electronic newsletters to assist us with the implementation of our findings.

Limitations

This study has two main limitations. First, this study relied on online or phone use for data collection; therefore, all participants needed access to and familiarity with the required technology. Findings are, therefore, generalizable to others with similar characteristics and advantages. Second, funding limitations restricted the number of participants we could recruit for each group, which may make some quantitative subgroup analyses challenging and limit our ability to achieve theoretical sufficiency with our qualitative analysis.

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Conflicts of Interest

None declared.

Multimedia Appendix 1
Interview guides for the interviewers.
[DOCX File , 19 KB - resprot_v10i9e28337_app1.docx]

References

1. Perlman S. Another Decade, Another Coronavirus. N Engl J Med 2020 Feb 20;382(8):760-762 [FREE Full text] [doi: 10.1056/NEJMe2001126] [Medline: 31978944]
2. Listings of WHO's response to COVID-19. World Health Organization. 2020 Jun 29. URL: https://www.who.int/news/item/29-06-2020-covidtimeline [accessed 2021-08-18]
3. Coronavirus Disease 2019 (COVID-19): Situation Report – 72. Geneva, Switzerland: World Health Organization; 2020 Apr 01. URL: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200401-sitrep-72-covid-19.pdf?sfvrsn=3dd8971b_2 [accessed 2021-08-24]
4. COVID-19 intervention timeline in Canada. Canadian Institute for Health Information. 2020. URL: https://www.cihi.ca/en/covid-19-intervention-timeline-in-canada [accessed 2021-08-18]

5. BC's economic recovery plan. Government of British Columbia. 2021. URL: https://www2.gov.bc.ca/gov/content/safety/emergency-preparedness-response-recovery/covid-19-provincial-support/bc-restart-plan [accessed 2021-08-18]
6. BC Recovery Benefit. Government of British Columbia. 2021. URL: https://www2.gov.bc.ca/gov/content/economic-recovery/recovery-benefit [accessed 2021-08-18]
7. Canada Emergency Response Benefit (CERB). Government of Canada. 2020. URL: https://www.canada.ca/en/services/benefits/ei/cerb-application.html [accessed 2021-08-18]
8. Hou W, Lai F, Ben-Ezra M, Goodwin R. Regularizing daily routines for mental health during and after the COVID-19 pandemic. J Glob Health 2020 Dec;10(2):1-3 [FREE Full text] [doi: 10.7189/jogh.10.020315] [Medline: 33110518]
9. Prime H, Wade M, Browne DT. Risk and resilience in family well-being during the COVID-19 pandemic. Am Psychol 2020;75(5):631-643. [doi: 10.1037/amp0000660] [Medline: 32437181]
10. Kofman YB, Garfin DR. Home is not always a haven: The domestic violence crisis amid the COVID-19 pandemic. Psychol Trauma 2020 Aug;12(S1):S199-S201 [FREE Full text] [doi: 10.1037/tra0000866] [Medline: 32478558]
11. Gassman-Pines A, Ananat EO, Fitz-Henley J. COVID-19 and parent-child psychological well-being. Pediatrics 2020 Oct;146(4):1-9 [FREE Full text] [doi: 10.1542/peds.2020-007294] [Medline: 32764151]
12. Disability in Canada: Initial findings from the Canadian Survey on Disability. Statistics Canada. 2015. URL: https://www150.statcan.gc.ca/n1/pub/89-654-x/89-654-x2013002-eng.htm [accessed 2021-08-18]
13. Mörchen M, Kapoor H, Varughese S. Disability and COVID-19. Community Eye Health 2020;33(109):10-11 [FREE Full text] [Medline: 33304037]
14. Banerjee D, D'Cruz M, Sathyanarayana Rao T. Coronavirus disease 2019 and the elderly: Focus on psychosocial well-being, agism, and abuse prevention – An advocacy review. J Geriatr Ment Health 2020;7(1):4. [doi: 10.4103/jgmh.jgmh_16_20]
15. Older adults and COVID-19. Ottawa Public Health. 2021. URL: https://www.ottawapublichealth.ca/en/public-health-topics/Older_Adults_and_COVID-19.aspx [accessed 2021-08-24]
16. Yang Y, Li W, Zhang Q, Zhang L, Cheung T, Xiang Y. Mental health services for older adults in China during the COVID-19 outbreak. Lancet Psychiatry 2020 Apr;7(4):e19 [FREE Full text] [doi: 10.1016/S2215-0366(20)30079-1] [Medline: 32085843]
17. Sandelowski M. What's in a name? Qualitative description revisited. Res Nurs Health 2010 Feb;33(1):77-84. [doi: 10.1002/nur.20362] [Medline: 20014004]
18. Sandelowski M. Whatever happened to qualitative description? Res Nurs Health 2000 Aug;23(4):334-340. [doi: 10.1002/1098-240x(200008)23:4<334::aid-nur9>3.0.co;2-g] [Medline: 10940958]
19. Chafe R. The value of qualitative description in health services and policy research. Healthc Policy 2017 Feb 06;12(3):12-18 [FREE Full text] [doi: 10.12927/hcpol.2017.25030]
20. O'Cathain A, Murphy E, Nicholl J. The quality of mixed methods studies in health services research. J Health Serv Res Policy 2008 Apr;13(2):92-98. [doi: 10.1258/jhsrp.2007.007074] [Medline: 18416914]
21. Deshpande P, Rajan S, Sudeepthi BL, Abdul Nazir C. Patient-reported outcomes: A new era in clinical research. Perspect Clin Res 2011 Oct;2(4):137-144 [FREE Full text] [doi: 10.4103/2229-3485.86879] [Medline: 22145124]
22. Woolrich RA, Kennedy P, Tasiemski T. A preliminary psychometric evaluation of the Hospital Anxiety and Depression Scale (HADS) in 963 people living with a spinal cord injury. Psychol Health Med 2006 Feb;11(1):80-90. [doi: 10.1080/13548500500294211] [Medline: 17129897]
23. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. J Psychosom Res 2002 Feb;52(2):69-77. [doi: 10.1016/s0022-3999(01)00296-3] [Medline: 11832252]
24. Connor KM, Davidson JR. Development of a new resilience scale: The Connor-Davidson Resilience Scale (CD-RISC). Depress Anxiety 2003;18(2):76-82. [doi: 10.1002/da.10113] [Medline: 12964174]
25. Fahlman SA, Mercer-Lynn KB, Flora DB, Eastwood JD. Development and validation of the multidimensional state boredom scale. Assessment 2013 Feb;20(1):68-85. [doi: 10.1177/1073191111421303] [Medline: 21903683]
26. Oxtoby J, King R, Sheridan J, Obst P. Psychometric analysis of the Multidimensional State Boredom Scale and its condensed versions. Assessment 2018 Oct;25(7):826-840. [doi: 10.1177/1073191116662910] [Medline: 27507788]
27. Zimet GD, Dahlem NW, Zimet SG, Farley GK. The Multidimensional Scale of Perceived Social Support. J Pers Assess 1988 Mar;52(1):30-41. [doi: 10.1207/s15327752jpa5201_2]
28. Wilkie R, Peat G, Thomas E, Hooper H, Croft PR. The Keele Assessment of Participation: A new instrument to measure participation restriction in population studies. Combined qualitative and quantitative examination of its psychometric properties. Qual Life Res 2005 Oct;14(8):1889-1899. [doi: 10.1007/s11136-005-4325-2] [Medline: 16155776]
29. Lanzino D, Sander E, Mansch B, Jones A, Gill M, Hollman J. Life Space Assessment in spinal cord injury. Top Spinal Cord Inj Rehabil 2016;22(3):173-182 [FREE Full text] [doi: 10.1310/sci2203-173] [Medline: 29339859]
30. Gupta S, Bashir L. Social Networking Usage Questionnaire: Development and validation in an Indian higher education context. Turk Online J Distance Educ 2018;19(4):214-227. [doi: 10.17718/tojde.471918]
31. Parasuraman A, Colby CL. An updated and streamlined Technology Readiness Index. J Serv Res 2014 Jun 22;18(1):59-74. [doi: 10.1177/1094670514539730]
32. Blut M, Wang C. Technology readiness: A meta-analysis of conceptualizations of the construct and its impact on technology usage. J Acad Mark Sc 2019 Aug 5;48(4):649-669. [doi: 10.1007/s11747-019-00680-8]

33. Rubin DB. Inference and missing data. Biometrika 1976;63(3):581-592. [doi: 10.1093/biomet/63.3.581]
34. Heo M, Faith MS, Mott JW, Gorman BS, Redden DT, Allison DB. Hierarchical linear models for the development of growth curves: An example with body mass index in overweight/obese adults. Stat Med 2003 Jun 15;22(11):1911-1942. [doi: 10.1002/sim.1218] [Medline: 12754724]
35. Shin JH. Application of repeated-measures analysis of variance and hierarchical linear model in nursing research. Nurs Res 2009 May;58(3):211-217. [doi: 10.1097/nnr.0b013e318199b5ae]
36. Braun V, Clarke V. Reflecting on reflexive thematic analysis. Qual Res Sport Exerc Health 2019 Jun 13;11(4):589-597. [doi: 10.1080/2159676x.2019.1628806]
37. Zhang W, Creswell J. The use of "mixing" procedure of mixed methods in health services research. Med Care 2013 Aug;51(8):e51-e57. [doi: 10.1097/mlr.0b013e31824642fd]
38. Nowell LS, Norris JM, White DE, Moules NJ. Thematic analysis: Striving to meet the trustworthiness criteria. Int J Qual Methods 2017 Oct 02;16(1):1-13 [FREE Full text] [doi: 10.1177/1609406917733847]

Abbreviations

BC: British Columbia
GRAMMS: Good Reporting of A Mixed Methods Study
HLM: hierarchical linear modeling
ICORD: International Collaboration on Repair Discoveries
PROM: patient-reported outcome measure
SCI: spinal cord injury
T1: time point 1
T2: time point 2
T3: time point 3
T4: time point 4
UBC: University of British Columbia

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Protocol

Informing the Development of a Standardized Clinical Definition of Neonatal Abstinence Syndrome: Protocol for a Modified-Delphi Expert Panel

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Abstract

Background: Neonatal abstinence syndrome (NAS) is a postnatal withdrawal syndrome that most commonly results from prenatal opioid exposure. Every 15 minutes, an infant is born in the United States with signs of NAS. The field lacks a standardized clinical definition of NAS, complicating discussions on programmatic and policy development to support opioid-exposed mothers and infants.

Objective: The goal of this paper is to describe a protocol for a systematic expert panel process to inform the development of a clinical definition of NAS.

Methods: We will conduct two three-round online modified-Delphi panels using the ExpertLens system and will follow the recommendations for Conducting and REporting of DElphi Studies (CREDES). One panel will focus on developing key components of a clinical definition of NAS, and the second panel will focus on neonatal opioid withdrawal syndrome (NOWS), which is a term that has come into use to differentiate opioid-exposed infants from infants exposed to other substances in utero. However, there is lack of agreement on the precise clinical definition of NOWS and how it is distinct from or overlaps with NAS. Each panel will complete two rating rounds and a discussion round using a similar protocol. We will analyze all rating data descriptively and determine the presence of agreement within and between the two panels. We will also perform thematic analysis of the qualitative comments to contextualize the panel findings.

Results: The panels were convened between October 29 and December 17, 2020. Their results were disseminated and discussed at a national conference on NAS that took place on March 17-18, 2021.

Conclusions: A standardized clinical definition of NAS will help to better characterize NAS incidence and to design effective clinical, public health, and policy interventions to support opioid-exposed mother-infant dyads.

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KEYWORDS

Delphi; ExpertLens; expert panel; neonatal abstinence syndrome; neonatal opioid withdrawal syndrome; neonatal withdrawal; neonatal; neonates; opioid; opioids; withdrawal; infants; clinical; newborn; newborns; perinatal; postnatal

Introduction

From 2000 to 2016, the United States experienced a seven-fold increase in neonatal abstinence syndrome (NAS) [1,2], also known as neonatal opioid withdrawal syndrome (NOWS) [3,4]. NAS is a postnatal withdrawal syndrome most commonly caused by prenatal opioid exposure [5]. An infant is born every 15 minutes with signs of NAS, and total hospital costs for NAS-related births exceeded US $500 million in 2014 in the United States [2]. The incidence of NAS varies substantially across the states, ranging from 0.7 cases per 1000 live births (Hawaii) to 33.4 per 1000 births (West Virginia) [6,7]. However, these statistics have an important limitation: the field lacks a standardized clinical definition of NAS.

NAS is a heterogenous condition that may result from both maternal nonprescribed opioid use *and* prescribed opioids such as the use of medication for opioid use disorder (eg, methadone and buprenorphine) [5]. NAS may also be associated with other prenatal exposures such as benzodiazepines and nicotine [8]. Moreover, the clinical presentation of NAS is highly variable [9], leading to a lack of consensus around the definition, which has downstream consequences for surveillance [10] and policy efforts. Some infants have mild signs of withdrawal that can be managed with targeted nonpharmacologic interventions, whereas others require multiple medications to control their symptoms during weeks-long hospitalizations [11]. The relationship between maternal opioid dose and NAS severity is also unclear [12-16]. Given its unpredictability and variable presentation, there is a need to develop a standardized definition of NAS to accurately characterize the burden of this public health challenge, and consequently design effective clinical, public health, and policy interventions to support opioid-exposed mother-infant dyads.

To address this need, the U.S. Department of Health and Human Services (HHS) contracted with the RAND Corporation, a nonprofit research institution, to engage national experts in a rigorous process to develop a standardized clinical definition of NAS. This work contributes to a multipronged HHS initiative on NAS [17]. Engaging experts with a range of expertise is both critical and appropriate to defining this complex condition because there is no consensus around its clinical definition. Here, we describe our protocol for the systematic online engagement of national experts to provide input to inform the development of a standardized clinical definition of NAS.

Methods

Design

Our approach to expert engagement will consist of two modified-Delphi expert panels to explore the presence of agreement around key components of a clinical definition of NAS. The study design was developed in consultation with a six-person advisory board of leading national experts on this topic who have been engaged with the HHS's initiative on NAS (see Multimedia Appendix 1). We will follow the guidance for Conducting and REporting of DElphi Studies (CREDES) [18].

To facilitate the process of expert engagement, especially during the COVID-19 pandemic, the modified-Delphi panel will be conducted completely online using ExpertLens, a previously evaluated platform for conducting iterative expert elicitation and stakeholder engagement panels [19-21]. Instead of traveling to a centralized location for an in-person meeting, ExpertLens participants provide answers to close-ended and open-ended questions, review automatically generated reports comparing their responses to close-ended questions with those of other participants, discuss group responses using a moderated discussion board, and revise their answers all from the comfort of their own homes or offices.

Participant Recruitment

On October 6, 2020, we reached out to 22 national experts on NAS, including neonatologists and general pediatricians, as well as those with expertise in clinical pharmacology and psychiatry, with an invitation to participate in these panels. In our recruitment efforts, we prioritized experts with significant clinical expertise in the care of infants with NAS. Identified experts were contacted via their publicly available email addresses and invited to express their interest in participating in this panel. The invitation email explained the purpose of the study, its funder, and the expected time commitment.

Panels and Panel Composition

After reviewing the list of all invitees who express interest in participating in this study, the research team will select experts to assemble two panels. One panel will focus on identifying key components of a clinical definition of NAS, and the other panel will define NOWS using a similar protocol.

The panels will be limited to approximately 9 experts as recommended by the RAND/UCLA Appropriateness Method (RAM) manual for conducting clinical expert panels [22]. We will aim for balance between the panels in terms of participants' professional backgrounds and geographic regions because there may be variation in how NAS is defined across disciplines and around the country. We will also aim to balance panels based on participants' stated preference for using NAS or NOWS (if known).

Data Collection

The data collection protocols will be developed based on a literature review performed by HHS and national experts, input from RAND subject matter experts, the HHS NAS initiative's advisory board, and a pilot test.

The data collection began in October-November 2020 and followed a typical modified-Delphi protocol, which includes two rounds of rating with a round of discussion between the two rating rounds (Figure 1) [22-24]. No additional rating rounds will be conducted if agreement is not reached after the final round of ratings.

Figure 1. Three-round ExpertLens design.

In Round 1, an assessment round, experts will be instructed to think about a full-term infant in the first week of life with no known medical conditions, and to rate and comment on different pieces of information about the infant and the mother: (1) prenatal exposure to opioids and/or other substances, (2) infant signs of withdrawal from opioids and/or other substances, and (3) toxicology test results (see Textbox 1 for additional details).

Textbox 1. Types of information about mother-infant dyads for panelists to consider in the ExpertLens process.

Information about whether or not the infant had prenatal exposure to…

- opioids alone
- opioids plus other substances (eg, benzodiazepines, selective serotonin reuptake inhibitors [SSRIs], tobacco)
- substances (eg, benzodiazepines, SSRIs, tobacco) but did not have prenatal exposure to opioids

Information about whether or not the infant…

- shows signs of opioid withdrawal
- signs of withdrawal from substances other than opioids
- shows dysregulation in at least one domain of infant development such as motor control (eg, hypertonia, tremors) or responses to stimuli (eg, exaggerated Moro reflex)
- requires nonpharmacologic measures to manage withdrawal
- requires medication to treat signs of withdrawal

Information about whether or not…

- the infant's toxicology test is positive for opioids alone
- the infant's toxicology test is positive for opioids plus other substances
- the infant's toxicology test is positive for substances other than opioids and is negative for opioids
- the mother's toxicology test is positive for opioids alone
- the mother's toxicology test is positive for opioids plus other substances
- the mother's toxicology test is positive for substances other than opioids and is negative for opioids

To provide their input on each piece of information, participants will use 9-point Likert-type scales to answer the following two questions and explain their ratings: (1) How necessary is this information for distinguishing between infants *with and without NAS [NOWS]*? (2) How helpful is this information for distinguishing between infants *with and without NAS [NOWS]?*

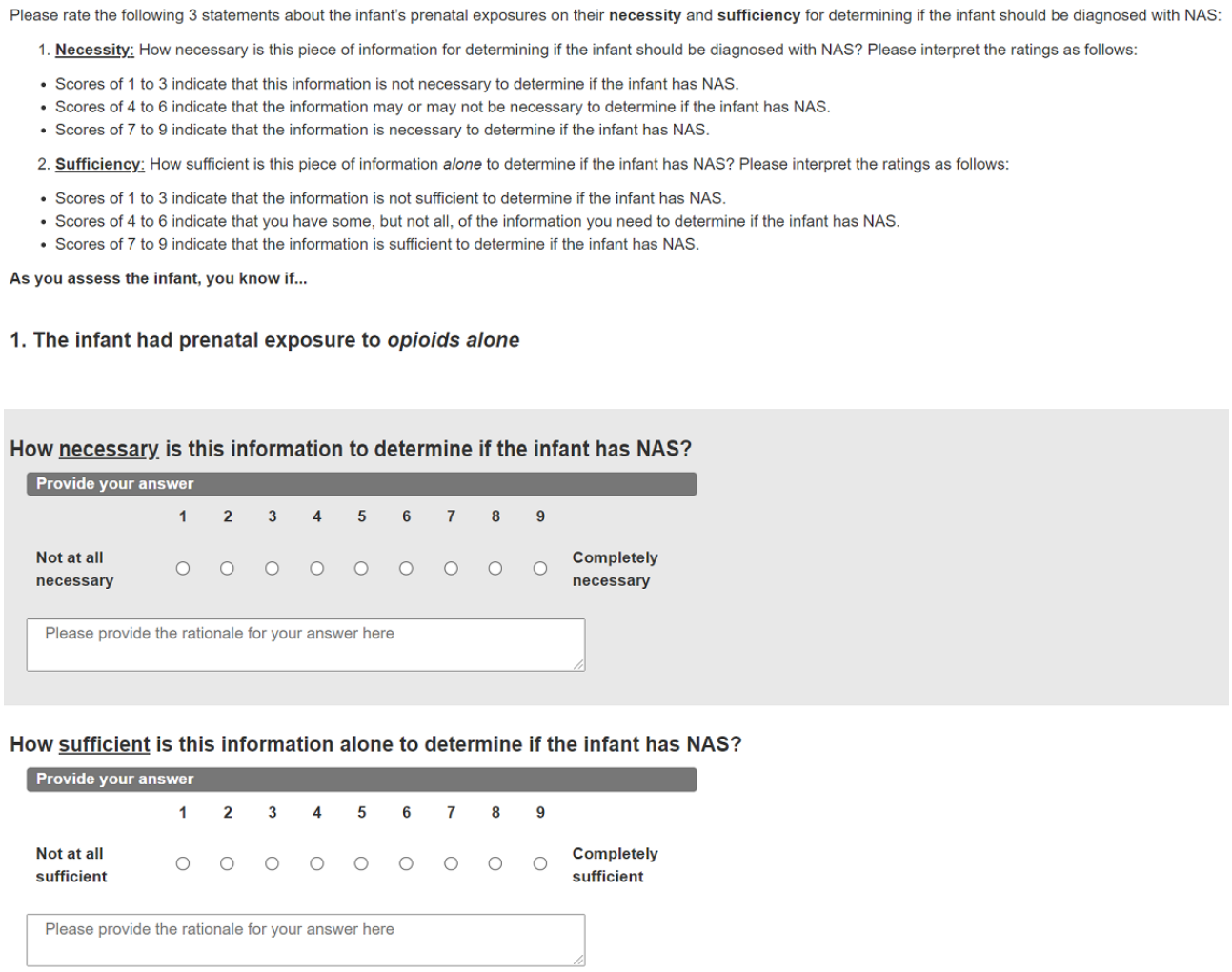
Because of the wide variation in the clinical manifestations of withdrawal in infants, experts will also be asked to use a 9-point Likert-type scale to respond to the following question that will

provide input on 10 common clinical signs of withdrawal as described by Gomez-Pomar et al [25]: How characteristic is this sign of NAS (NOWS)?

Moreover, participants will provide feedback on an alternative approach to assessing infant withdrawal that looks for dysregulation in four domains of infant functioning, rather than assessing signs and symptoms individually or in combination [26-28]. This approach is intended to give clinicians a holistic understanding of infants with opioid exposure to distinguish between infants with and without NAS or NOWS. Participants will review a brief description of this approach and then use 9-point Likert-type scales to answer the following questions: (1) How different is this approach from the way withdrawal signs are currently assessed in clinical practice? (2) How useful is this approach for assessing opioid withdrawal in an infant? (3) How feasible would it be to use this approach to distinguish between infants with and without NAS (NOWS)?

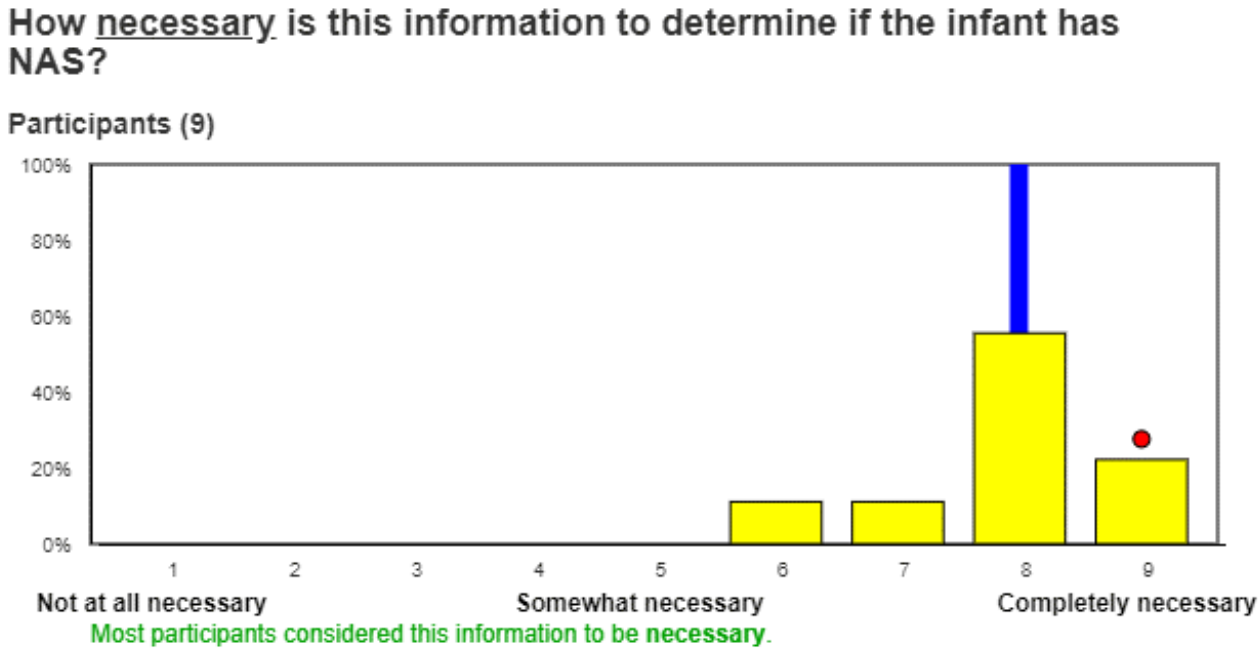
Finally, at the end of Round 1, we will ask participants to provide their suggested clinical definitions of both NAS and NOWS. These final open-ended questions will help to validate the results of our rating process and assess how experts' definitions may evolve over the course of the study. Figure 2 shows a screenshot for the questionnaire in Round 1.

Figure 2. Round 1 mock-up screenshot.



In Round 2, a feedback and discussion round, experts will receive an automatically generated personalized report showing how their individual responses to the rating questions compare to responses of other participants (Figure 3). The report will include a distribution of all responses, a group median response and its IQR, and a statement that explains if the group reached agreement, calculated as described in the RAM manual [22]. The report will also include a summary of comments participants made in Round 1.

Figure 3. Round 2 mock-up screenshot.



Participants will discuss the results of Round 1 using an anonymous, asynchronous, threaded discussion board. To protect confidentiality of participants' responses, we will use a randomly generated username such as Expert01. We anticipate that this discussion will focus on areas where there may be disagreement or potential confusion among experts. The discussions will be moderated by a clinical expert and a modified-Delphi expert using a previously published protocol for moderating ExpertLens discussions [29]. The same moderators will facilitate online discussions in both panels to ensure consistency.

In Round 3, a reassessment round, experts may choose to revise their Round 1 answers based on Round 2 feedback and discussion or leave them unchanged. Any modifications made to Round 1 questions will be clearly identified within ExpertLens. At the end of Round 3, we will ask experts a series of questions about their experience participating in this ExpertLens process.

We anticipate that each round will be open for 7-10 days, depending on participation rates. At the start of each round, participants will receive invitation emails that will include a description of what they are expected to do in each round, how to access and use the ExpertLens platform, and how long each round will be open. We will send up to three reminders during each round to encourage all participants to provide their input. No honoraria will be offered to study participants.

Data Analysis

We will use descriptive statistics to present the results of Round 1 and 3 ratings for each panel separately, focusing on the frequency distributions of responses to each question, as well as measures of central tendency (median) and dispersion (interpercentile range). Round 3 rating data will be used for the final identification of suggested definitional components of NAS and NOWS. We will determine the presence of agreement among experts for each rating question using the approach outlined in the RAM manual [22]. Briefly, this approach involves looking at the distribution of responses across the tertiles of scores on the 9-point scale (eg, scores 1-3, 4-6, and 7-9) as a way to explore agreement/disagreement. Disagreement exists when more than a third of responses are in the upper and the lower tertile at the same time. If there is no disagreement, a median of 6.5 and above will indicate a positive group decision.

We will also compare the rating results across the two panels to determine which pieces of information about the infant-mother dyad are necessary and helpful to distinguish between infants with and without NAS or NOWS. These analyses will be important for obtaining expert opinion on the extent to which these two terms differ or overlap, and what pieces of information may be important for developing clinical definitions for each.

To better explain why experts may disagree on which signs are most characteristic of NAS and NOWS, and to explain why some definitional components were selected for inclusion in the definitions of NAS and NOWS while others were not, we will thematically analyze qualitative data, including Round 1 and Round 3 explanations of ratings and Round 2 discussion comments. As in previous ExpertLens panels [30], we will group all Round 1 and 3 comments for a given question according to the score tertile. We will also group all discussion comments by the definitional component. Finally, we will collate and thematically organize the responses to the open-ended questions asking participants to provide their own suggested definitions of NAS and NOWS.

As in previous ExpertLens panels [31,32], a team of experienced qualitative researchers trained by the study's principal investigators will review and code all comments inductively to

identify recurrent themes. All coding results will be reviewed to ensure coding consistency and clinical accuracy of the interpretation of comments. Disagreements among coders will be discussed until consensus is achieved.

Interpretation, Validation, and Dissemination of Panel Findings

We will provide the advisory board with a synthesis of the quantitative and qualitative data described above. With these data, they will construct a proposed clinical definition of NAS and, depending on the findings from the ExpertLens process, of NOWS as well, using the key pieces of information prioritized by the panelists and drawing on expert input on how to best characterize the variable clinical manifestations of drug withdrawal, which is a major point of debate in the field [33-35].

Results of the online modified-Delphi process and the proposed clinical definitions will be shared with key stakeholders during a national conference on NAS convened by HHS. Participants will be given an opportunity to provide their input. The research team will collaborate with HHS and the advisory board to incorporate input from this national convening in order to refine the proposed clinical definition of NAS, which will be disseminated to key stakeholders, including clinicians, researchers, health system leadership, public health officials, and policymakers.

Results

The study was reviewed and approved by the RAND Human Subjects Protection Committee (Study ID: 2020-0293). Round 1 invitations were sent out on October 29, 2020. We completed the data collection on December 17, 2020 and disseminated panel results at a national conference on NAS that took place on March 17-18, 2021.

Discussion

Partnering with experts specializing in maternal-child health, HHS is leading an initiative to understand key issues impacting the longitudinal care of mothers and infants exposed to opioids and other substances. This protocol describes an innovative online approach to soliciting expert opinion, which allows for a nonburdensome engagement of leading national experts on the topic. Study strengths include a focus on a pressing policy issue, a creative approach to data collection during the COVID-19 pandemic, and automatic generation of personalized reports provided to each participant showing how the responses compare with those of other participants and whether or not the panel reached consensus. Study limitations include the engagement of a relatively small number of clinical experts, the possibility that participants may not complete all study rounds or not answer all questions, and a reliance on an online approach to data collection, which may not be a preferred mode of engagement for some experts that are more accustomed to meeting other panelists in person during the discussion round. Because we were able to conduct only one online panel on NAS and one on NOWS, future research should explore the replicability of our findings by conducting additional panels either online or in person.

In summary, a standard clinical definition for NAS is critically needed not only to improve care of the mother-infant dyad in both the short- and long-term but also to enhance the accuracy of surveillance efforts and data available for research. By leveraging input from national experts caring for opioid-exposed dyads, this work will contribute to addressing a longstanding gap in the field: the lack of a standardized clinical definition of NAS. This systematic approach offers a viable pathway for reducing variability in the clinical diagnosis of NAS, starting at the bedside. As an upstream building block for public health surveillance data and health services and health policy research, the bedside definition impacts downstream considerations in the care of mother-infant dyads. Developing a standard to clinically define NAS will advance key discussions on disease burden, immediate and longitudinal needs assessment, and resource planning for mother-infant dyads. In the next phase of this NAS initiative, HHS aims to continue this engagement with clinicians, researchers, and policymakers, while focusing on challenges and opportunities to improve program and policy planning at the local, state, and national levels.

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Conflicts of Interest

DK is a leader of the ExpertLens team. ExpertLens is a RAND-developed platform for conducting online modified-Delphi panels that will be used in this study to collect data. All other coauthors report no conflicts of interest.

Multimedia Appendix 1
Members of the Advisory Board for the Department of Health and Human Services initiative on neonatal abstinence syndrome.
[DOCX File , 14 KB - resprot_v10i9e25387_app1.docx]

References

1. Patrick SW, Schumacher RE, Benneyworth BD, Krans EE, McAllister JM, Davis MM. Neonatal abstinence syndrome and associated health care expenditures: United States, 2000-2009. JAMA 2012 May 09;307(18):1934-1940. [doi: 10.1001/jama.2012.3951] [Medline: 22546608]
2. Winkelman TNA, Villapiano N, Kozhimannil KB, Davis MM, Patrick SW. Incidence and costs of neonatal abstinence syndrome among infants with Medicaid: 2004-2014. Pediatrics 2018 Apr;141(4):e20173520 [FREE Full text] [doi: 10.1542/peds.2017-3520] [Medline: 29572288]
3. Neonatal opioid withdrawal syndrome and medication-assisted treatment with methadone and buprenorphine. US Food & Drug Administration. 2016. URL: https://www.fda.gov/drugs/drug-safety-and-availability/neonatal-opioid-withdrawal-syndrome-and-medication-assisted-treatment-methadone-and-buprenorphine [accessed 2020-10-27]
4. Patrick SW, Barfield WD, Poindexter BB, Committee on Fetus and Newborn, Committee on Substance Use and Prevention. Neonatal opioid withdrawal syndrome. Pediatrics 2020 Nov 26;146(5):e2020029074. [doi: 10.1542/peds.2020-029074] [Medline: 33106341]
5. Kocherlakota P. Neonatal abstinence syndrome. Pediatrics 2014 Aug;134(2):e547-e561. [doi: 10.1542/peds.2013-3524] [Medline: 25070299]
6. Ko JY, Patrick SW, Tong VT, Patel R, Lind JN, Barfield WD. Incidence of neonatal abstinence syndrome - 28 States, 1999-2013. MMWR Morb Mortal Wkly Rep 2016 Aug 12;65(31):799-802. [doi: 10.15585/mmwr.mm6531a2] [Medline: 27513154]
7. Villapiano NLG, Winkelman TNA, Kozhimannil KB, Davis MM, Patrick SW. Rural and urban differences in neonatal abstinence syndrome and maternal opioid use, 2004 to 2013. JAMA Pediatr 2017 Feb 01;171(2):194-196. [doi: 10.1001/jamapediatrics.2016.3750] [Medline: 27942711]
8. Chang PT, Aynilian GH, Cordell GA, Tin-Wa M, Fong HH, Perdue RE, et al. Isolation of flindersiamine, isoflindersiamine, and a new alkaloid, heliparvifoline, from Helietta parvifolia (Rutaceae). J Pharm Sci 1976 Apr;65(4):561-563. [doi: 10.1002/jps.2600650420] [Medline: 1271255]
9. Hudak ML, Tan RC, Committee on Drugs, Committee on Fetus and Newborn, American Academy of Pediatrics. Neonatal drug withdrawal. Pediatrics 2012 Feb;129(2):e540-e560. [doi: 10.1542/peds.2011-3212] [Medline: 22291123]
10. Chiang KV, Okoroh EM, Kasehagen LJ, Garcia-Saavedra LF, Ko JY. Standardization of state definitions for neonatal abstinence syndrome surveillance and the opioid crisis. Am J Public Health 2019 Sep;109(9):1193-1197. [doi: 10.2105/AJPH.2019.305170] [Medline: 31318590]
11. Jansson LM, Velez M, Harrow C. The opioid-exposed newborn: assessment and pharmacologic management. J Opioid Manag 2009;5(1):47-55 [FREE Full text] [Medline: 19344048]
12. Shirel T, Hubler CP, Shah R, Mager AB, Koch KL, Sheth D, et al. Maternal opioid dose is associated with neonatal abstinence syndrome in children born to women with sickle cell disease. Am J Hematol 2016 Jun;91(4):416-419. [doi: 10.1002/ajh.24307] [Medline: 26799428]
13. Desai RJ, Huybrechts KF, Hernandez-Diaz S, Mogun H, Patorno E, Kaltenbach K, et al. Exposure to prescription opioid analgesics in utero and risk of neonatal abstinence syndrome: population based cohort study. BMJ 2015 May 14;350(1):h2102 [FREE Full text] [doi: 10.1136/bmj.h2102] [Medline: 25975601]
14. Jones HE, Jansson LM, O'Grady KE, Kaltenbach K. The relationship between maternal methadone dose at delivery and neonatal outcome: methodological and design considerations. Neurotoxicol Teratol 2013;39:110-115 [FREE Full text] [doi: 10.1016/j.ntt.2013.05.003] [Medline: 24099621]
15. Jones HE, Dengler E, Garrison A, O'Grady KE, Seashore C, Horton E, et al. Neonatal outcomes and their relationship to maternal buprenorphine dose during pregnancy. Drug Alcohol Depend 2014 Jan 01;134:414-417 [FREE Full text] [doi: 10.1016/j.drugalcdep.2013.11.006] [Medline: 24290979]
16. Cleary BJ, Donnelly J, Strawbridge J, Gallagher PJ, Fahey T, Clarke M, et al. Methadone dose and neonatal abstinence syndrome-systematic review and meta-analysis. Addiction 2010 Dec;105(12):2071-2084. [doi: 10.1111/j.1360-0443.2010.03120.x] [Medline: 20840198]
17. Jilani SM, Giroir BP. Neonatal abstinence syndrome: leveraging health information technology to develop a data-driven national policy approach. Public Health Rep 2020;135(2):173-176 [FREE Full text] [doi: 10.1177/0033354920902476] [Medline: 32027558]
18. Jünger S, Payne SA, Brine J, Radbruch L, Brearley SG. Guidance on Conducting and REporting DElphi Studies (CREDES) in palliative care: Recommendations based on a methodological systematic review. Palliat Med 2017 Sep 13;31(8):684-706. [doi: 10.1177/0269216317690685] [Medline: 28190381]
19. Dalal S, Khodyakov D, Srinivasan R, Straus S, Adams J. ExpertLens: A system for eliciting opinions from a large pool of non-collocated experts with diverse knowledge. Technol Forecast Soc Change 2011 Oct;78(8):1426-1444. [doi: 10.1016/j.techfore.2011.03.021]
20. Khodyakov D, Grant S, Meeker D, Booth M, Pacheco-Santivanez N, Kim KK. Comparative analysis of stakeholder experiences with an online approach to prioritizing patient-centered research topics. J Am Med Inform Assoc 2017 May 01;24(3):537-543 [FREE Full text] [doi: 10.1093/jamia/ocw157] [Medline: 28011596]

21. Khodyakov D, Hempel S, Rubenstein L, Shekelle P, Foy R, Salem-Schatz S, et al. Conducting online expert panels: a feasibility and experimental replicability study. BMC Med Res Methodol 2011 Dec 23;11:174 [FREE Full text] [doi: 10.1186/1471-2288-11-174] [Medline: 22196011]
22. Fitch K, Bernstein S, Aguilar M, Burnand B, LaCalle J, Lazaro P. The RAND/UCLA Appropriateness Method User's Manual. RAND Corporation. 2001. URL: https://www.rand.org/pubs/monograph_reports/MR1269.html [accessed 2021-08-15]
23. Barber CE, Marshall DA, Alvarez N, Mancini GJ, Lacaille D, Keeling S, Quality Indicator International Panel. Development of cardiovascular quality indicators for rheumatoid arthritis: results from an international expert panel using a novel online process. J Rheumatol 2015 Sep 15;42(9):1548-1555 [FREE Full text] [doi: 10.3899/jrheum.141603] [Medline: 26178275]
24. Barber CE, Marshall DA, Mosher DP, Akhavan P, Tucker L, Houghton K, Arthritis Alliance of Canada Performance Measurement Development Panel. Development of system-level performance measures for evaluation of models of care for inflammatory arthritis in Canada. J Rheumatol 2016 Mar 15;43(3):530-540 [FREE Full text] [doi: 10.3899/jrheum.150839] [Medline: 26773106]
25. Gomez Pomar E, Finnegan LP, Devlin L, Bada H, Concina VA, Ibonia KT, et al. Simplification of the Finnegan Neonatal Abstinence Scoring System: retrospective study of two institutions in the USA. BMJ Open 2017 Sep 27;7(9):e016176 [FREE Full text] [doi: 10.1136/bmjopen-2017-016176] [Medline: 28963285]
26. Velez ML, McConnell K, Spencer N, Montoya L, Tuten M, Jansson LM. Prenatal buprenorphine exposure and neonatal neurobehavioral functioning. Early Hum Dev 2018 Feb;117:7-14. [doi: 10.1016/j.earlhumdev.2017.11.009] [Medline: 29223912]
27. Coyle MG, Salisbury AL, Lester BM, Jones HE, Lin H, Graf-Rohrmeister K, et al. Neonatal neurobehavior effects following buprenorphine versus methadone exposure. Addiction 2012 Nov 29;107(Suppl 1):63-73 [FREE Full text] [doi: 10.1111/j.1360-0443.2012.04040.x] [Medline: 23106928]
28. Velez M, Jansson LM. The opioid dependent mother and newborn dyad: non-pharmacologic care. J Addict Med 2008 Sep;2(3):113-120 [FREE Full text] [doi: 10.1097/ADM.0b013e31817e6105] [Medline: 19727440]
29. Khodyakov D, Grant S, Denger B, Kinnett K, Martin A, Peay H, et al. Practical considerations in using online modified-Delphi approaches to engage patients and other stakeholders in clinical practice guideline development. Patient 2020 Feb;13(1):11-21 [FREE Full text] [doi: 10.1007/s40271-019-00389-4] [Medline: 31544219]
30. Khodyakov D, Stockdale SE, Smith N, Booth M, Altman L, Rubenstein LV. Patient engagement in the process of planning and designing outpatient care improvements at the Veterans Administration Health-care System: findings from an online expert panel. Health Expect 2017 Feb 23;20(1):130-145 [FREE Full text] [doi: 10.1111/hex.12444] [Medline: 26914249]
31. Denger B, Kinnett K, Martin A, Grant S, Armstrong C, Khodyakov D. Patient and caregiver perspectives on guideline adherence: the case of endocrine and bone health recommendations for Duchenne muscular dystrophy. Orphanet J Rare Dis 2019 Aug 20;14(1):205 [FREE Full text] [doi: 10.1186/s13023-019-1173-7] [Medline: 31429780]
32. Khodyakov D, Grant S, Denger B, Kinnett K, Martin A, Booth M, et al. Using an online, modified Delphi approach to engage patients and caregivers in determining the patient-centeredness of Duchenne muscular dystrophy care considerations. Med Decis Making 2019 Nov;39(8):1019-1031 [FREE Full text] [doi: 10.1177/0272989X19883631] [Medline: 31722623]
33. Wachman EM, Schiff DM, Silverstein M. Neonatal abstinence syndrome: advances in diagnosis and treatment. JAMA 2018 Apr 03;319(13):1362-1374. [doi: 10.1001/jama.2018.2640] [Medline: 29614184]
34. Bagley SM, Wachman EM, Holland E, Brogly SB. Review of the assessment and management of neonatal abstinence syndrome. Addict Sci Clin Pract 2014 Sep 09;9(1):19 [FREE Full text] [doi: 10.1186/1940-0640-9-19] [Medline: 25199822]
35. Raffaeli G, Cavallaro G, Allegaert K, Wildschut ED, Fumagalli M, Agosti M, et al. Neonatal abstinence syndrome: update on diagnostic and therapeutic strategies. Pharmacotherapy 2017 Jul 02;37(7):814-823. [doi: 10.1002/phar.1954] [Medline: 28519244]

Abbreviations

CREDES: Conducting and REporting of DElphi Studies
HHS: U.S. Department of Health and Human Services
NAS: neonatal abstinence syndrome
NOWS: neonatal opioid withdrawal syndrome
RAM: RAND/UCLA Appropriateness Method

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Protocol

COVID-19 Health Crisis and Chronic Illness: Protocol for a Qualitative Study

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Abstract

Background: The acute nature of the COVID-19 pandemic has put a strain on health resources that are usually dedicated to chronic illnesses. Resulting changes in care practices and networks have had major repercussions on the experience of people with chronic disorders.

Objective: This paper presents the protocol of the Parcours, Associations, Réseau, Chronicité, Organisation, Usagers, Retour d'expérience, Soins (PARCOURS)-COVID study. The aim of this study is to evaluate the effects of reorganization of the health system on the usual care network of patients with chronic illness, which fosters and qualifies the quality and continuum of care provided. The first objective of this study is to document these patients' experiences through transformations and adaptations of their network, both in the practical dimension (ie, daily life and care) and subjective dimension (ie, psychosocial experience of illness and relationship to the health system). The second objective of the study is to understand and acknowledge these reorganizations during the COVID-19 lockdown and postlockdown periods. The third objective is to produce better adapted recommendations for patients with chronic illness and value their experience for the management of future health crisis.

Methods: The PARCOURS-COVID study is a qualitative and participatory research involving patient organizations as research partners and members of these organizations as part of the research team. Three group of chronic diseases have been selected regarding the specificities of the care network they mobilize: (1) cystic fibrosis and kidney disease, (2) hemophilia, and (3) mental health disorders. Four consecutive phases will be conducted, including (1) preparatory interviews with medical or associative actors of each pathology field; (2) in-depth individual interviews with patients of each pathology, analyzed using the qualitative method of thematic analysis; (3) results of both these phases will then be triangulated through interviews with members of each

patient's care ecosystem; and finally, (4) focus groups will be organized to discuss the results with research participants (ie, representatives of chronic disease associations; patients; and actors of the medical, psychosocial, and family care network) in a research-action framework.

Results: The protocol study has undergone a peer review by the French National Research Agency's scientific committee and has been approved by the research ethical committee of the University of Paris (registration number: IRB 00012020-59, June 28, 2020). The project received funding from August 2020 through April 2021. Expected results will be disseminated in 2021 and 2022.

Conclusions: Our findings will better inform the stakes of the current health crisis on the management of patients with chronic illness and, more broadly, any future crisis for a population deemed to be at risk. They will also improve health democracy by supporting better transferability of knowledge between the scientific and citizen communities.

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KEYWORDS

chronic illness; care; prevention; vulnerability; health democracy; COVID; qualitative study; COVID-19; pandemic; risk

Introduction

Since the 1970s and 1980s, the rise of chronic diseases has contributed to the creation and promotion of a paradigm, leading to a broader definition of "medicine" around the notion of "care," developed in medicine as well as in the fields of social sciences and moral philosophy. In order to potentiate its effects in terms of patients' quality of life, care needs to be deployed in a continuum of multiple relationships and practices combining medical, psychological, ethical, and social approaches [1-4].

The measures that resulted from the COVID-19 pandemic have led to prioritization of acute care, placing particular strain on the resources usually dedicated to the management of chronic pathologies. The COVID-19 outbreak in France has been characterized by a highly centralized reorganization of the health system as a response to the epidemic. This reorganization focused on taking care almost only of patients with COVID-19. In the media and across social networks, health professionals denounced these challenges, adding to the issue of infected patients' triage [5].

The management of a chronic disease requires the daily intervention and cooperation of many different actors, which define an ecosystem of care. Such an ecosystem is based on a network of actors and institutions—medical or nonmedical, which combines diverse approaches and practices and requires constant collaborations and negotiations [6,7]. This ecosystem of care is determined by the pathology and the specificities of medical follow-ups required, but it is also highly dependent on the patient's background and social environment, resources, and living conditions. It entails patients' empowerment and active participation in their care support [8-11]. COVID-19 lockdown measures seem to have disrupted the ecosystem of care for patients with chronic illness on two levels. First, medical appointments were postponed or suspended, leading to self-medication practices without medical follow-up or storage of medicines essential to the management of the chronic condition [12]. The quality of life of patients with chronic illnesses was directly affected, as concerns rose about their health status and their risks to COVID-19 infection and as usual interactions with caregivers and health professionals were limited or modified, through the use of teleconsultation. In the case of mental health disorders, closure of psychiatric care facilities led to the termination of therapeutic activities, although these were regarded as essential for some patients who are very sensitive to the environment and social interactions. Second, care was reduced to chemical treatments, sometimes even intensified to compensate for the lack of psychosocial care, even though they cause side effects that increase the risk of COVID-19 infection [13]. It seems that prescribed care was doubly restricted—reduced to only vital surgical operations and deprived of several of its broader dimensions (ie, psychosocial care, pain control, and support).

Moreover, living with a chronic illness requires individuals to build their personal capacity to mobilize their existing knowledge based on experiences to collectively address medical, psychological, and social vulnerabilities. Individuals rely on the support of network of care to limit the effects of these vulnerabilities, yet the resulting quality of life rests on a delicate balance, which is constantly co-constructed and renewed. The experience of being autonomous or dependent does not come solely from the fact of having or not having support; it is rather a singular combination of material and human, family, and professional support [14]. The occurrence of a health crisis can deeply compromise this balance, which is already tangled in ordinary times, and thus increase the vulnerability of people living with a chronic disease. Conversely, research has shown that living with a chronic disorder also leads individuals to develop specific strategies and skills. Experiencing chronic diseases requires the mobilization and acquisition of important knowledge and resources, especially regarding the management of uncertainty and risk in the health field [15]. Participation of associative or targeted information networks of users and patients is required in structuring and disseminating this expertise related to the experience of chronic disease management [16-18]. This experience makes patients with chronic illness particularly sensitive to public health and solidarity issues. It is, therefore, likely that the individual or collective experience of chronic disease has not only been a factor of vulnerability but also a factor of resources, inventions, and adaptation in the current crisis.

For all these reasons, we hypothesized that the COVID-19 health crisis created an *unbalance* in the ecosystem of care and that the experiences of patients with chronic illness need to be better understood. We designed a research protocol to document the experiences of these patients and their caregivers. For this purpose, we organized a focus group with a panel of patients' organization stakeholders, so as to identify their concerns and research needs. Several issues emerged from the focus groups. First, they acknowledged the inadequacy of COVID-19 public health measures with the experience of patients, as well as actors, professionals, or carers involved in the management of a chronic disease. Second, they asked for a better recognition of their experiential knowledge. Based on these elements, this paper presents the research protocol Parcours, Associations, Réseau, Chronicité, Organisation, Usagers, Retour d'expérience, Soins (PARCOURS)-COVID that uses a qualitative and participative methodology.

Methods

Objectives

The objective of the PARCOURS-COVID study is to document and highlight the experience of people with chronic diseases confronted to the health crisis by focusing on the changes that occur in their daily practices and ecosystem of care. It is led by the Institut de la Personne en Médecine, where social science researchers (history, philosophy and ethics, psychology, psychoanalysis, sociology, and anthropology), physicians, caregivers, and patient representatives collaborate to produce scientific knowledge in the medical humanities using a multidisciplinary approach developed over several years. The choice of adopting a qualitative approach by participatory research carried out with and among users, professionals, and caregivers, and supported by a strong involvement of chronic disease associations with respect to the project's design and conduct, has three distinct goals, as outlined below:

Objective 1

The first objective is to value the lived experience, that is both psychological and social, as well as existential and practical, and their representations—the ways in which chronic illness, COVID-19, and the health crisis, in general, are thought about and made explicit in the discourse of individuals with chronic disorders. Semidirective individual interviews with patients will be conducted to that effect.

Objective 2

The second objective is to document changes in the practices and organization of the chronic care ecosystem in order to identify factors that are adaptive or, on the contrary, deleterious to maintaining its balance. Interviews with players in the medical, family, or caregiver network designated by patients will be conducted regarding to meet this objective.

Objective 3

The third objective is to generate and disseminate recommendations for a better adaptation of the health system for patients with chronic illness in the case of another health crisis, to ensure that the preparation and management this crisis will respect patients' rights by promoting participation and involvement of patients and their associated organizations. Workshops with stakeholders in the health system will help transform and disseminate results to organizations and communities.

Study Design and Participant Recruitment

The PARCOURS-COVID study received funding from the French National Agency of Research (Agence Nationale de la Recherche) for 9 months, from August 2020 to April 2021. The work schedule was developed in order to conciliate the project's feasibility requirements with the achievement of its scientific and operational objectives in a short time frame. Thus, we opted for a rapid qualitative approach and a participatory study design involving patients and associations' members as research partners, an approached that has been previously validated [18]. This methodology is based on listening to the interviews, then synthetizing them according to themes predefined by the research team, while allowing new themes to emerge if necessary. Rapid qualitative methods are therefore partly deductive, while retaining their inductive component.

Chronic Pathology Groups

Three groups of chronic pathologies were identified regarding the care networks' specificities mobilized by them:

Group 1

Cystic fibrosis, a disease with a respiratory component and therefore a high risk of complication in the case of COVID-19, and kidney disease, both of which require a combination of hospital and nonhospital care (regular interventions by physiotherapists or home care nurses). Two main patients' organizations (Renaloo and Overcoming Cystic Fibrosis—*Vaincre la mucoviscidose*) agreed to participate in the patient recruitment, as well as other stages of the research.

Group 2

Hemophilia, a condition that is most often self-managed by regular intravenous injections that are self-administered (2 or 3 days per week). The day-to-day management of patients with hemophilia essentially relies on a close relationship with health care professionals, mainly hospital doctors and nurses from rare disease expertise centers and, less frequently, general practitioners. The French Haemophilia Association agreed to assist in patient recruitment and to participate in the research process.

Group 3

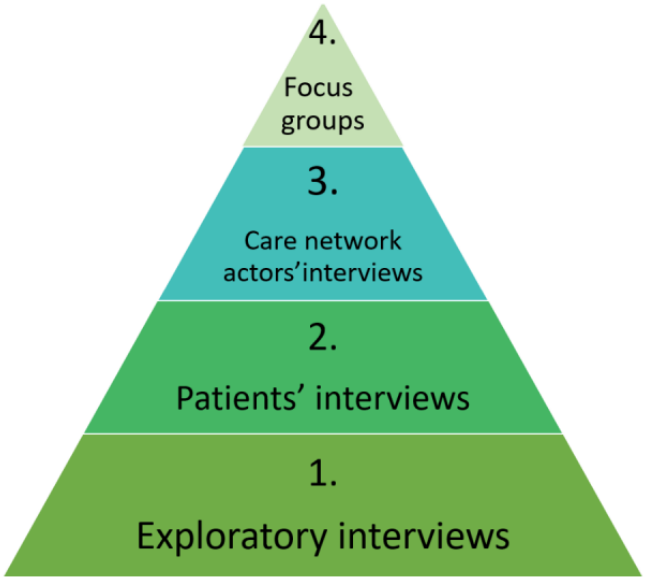
Mental health disorders, a group of conditions that will help understand the specific impact of the health crisis for people with mental health disorders that are very sensitive to the environment and to social interactions, both of which were particularly disrupted during lockdown. Patients with mental health disorders require forms of care that are essentially based on relations, through consultations but also through day hospitals, peer groups, among other alternatives. A variety of professional partners agreed to assist in patient recruitment and participation in research. Previous collaborations have also been initiated with health care professionals in the psychiatric sector.

Research Process

Overview

Four consecutive phases are scheduled, as follows: (1) preparatory interviews with medical or associative actors of each pathology's field; (2) semidirective interviews with patients from the three abovementioned groups; (3) results from both phases will be triangulated through semidirective interviews with members of the patient's care ecosystem, in order to review perspectives and gain a deeper understanding of the situation, through an analysis that will be carried out in close collaboration among social science researchers from several disciplines, patient associations, and caregivers; and finally, (4) focus-groups to discuss the results with research participants (Figure 1).

Figure 1. Four consecutive phases of the research study.



Phase 1: Exploratory Interviews

We will diversify entries in the field through our partnership with patient organizations. A series of preparatory interviews with key informants for each pathology will help identify specific situations and difficulties encountered during the crisis, including those concerning medical care, as well as the organization's involvement. This phase will therefore include 16 interviews in all: with each organization leader and their health professionals, a doctor, and a front-line professional per pathology. One or two researchers from the team will carry out the interviews via phone or videoconferencing, or in person, if the situation allows it. We will also discuss with the partner organization and health professionals the pertinence of adding some pathology-specific criteria, such as type of treatments or access to care.

Phase 2: In-depth Patient Interviews

The second phase of the research will be based on interviews with individuals with chronic disorders, to collect data on their experiences during the health crisis. We will combine the recruitment through the partner organizations along with the recruitment of patients through the health professionals we met during phase 1. This will allow us to interview patients that are at located varying distances from patient organizations. A total of 7 to 10 adult patients per disease group, as identified above, will be interviewed. Patient recruitment in the first group will be equally divided between the two diseases. The participants' situations will be diversified with regard to their socioeconomic characteristics and to ensure a balanced ratio of gender and various age groups and geographical locations (ie, between Paris and other regions or between the so-called COVID-19 "red and green zones"). This phase will thus include approximately 30 interviews with individuals with chronic disorders, conducted via phone by members of the research team (comprising only researchers or organization leaders that are part of the team).

Phase 3: In-depth Caregivers or Health Care Network Member Interviews

The third phase of the research will be based on interviews with members of the health care network of individuals with chronic disorders, in order to highlight their role as caregivers. They will be recruited with the cooperation and consent of patients from phase 2, who will be asked to name the two most important persons involved in the day-to-day management of their chronic disease. For instance, the care ecosystem could include health professionals, but also spouses, family, friends, or neighbors. At the rate of 1 to 2 actors identified per patient, the number of interviews can therefore be estimated to range between 30 and 60. The interviews will be conducted by members of the research team (only researchers or association leaders of the team).

Phase 4: Focus Groups for Feedback and Dissemination

In the fourth phase, focus groups will be organized to provide feedback to the participants and to discuss the results with them. Results from phases 2 and 3 will provide the basis for public policy recommendations. Participants of the focus group will include phase-2 and phase-3 interviewees on a voluntary basis. The focus groups will be led by the promoters of the present project, including the postdoctoral student (LV) who will be responsible for the organization and follow-up. Each focus group will discuss the main hypotheses and categories elaborated in by the research team and help deepen and validate them. The

discussions will be recorded and transcribed and then linked to the empirical data gathered in phases 1 to 3. We will present the thematically analyzed interviews and the resulting hypotheses to focus group participants in order to discuss and validate them with the principal stakeholders. Data collected from these focus group will be analyzed to produce recommendations and outcomes. This participatory research process aims to improve their transferability to medical populations, citizens, and health authorities [19]. It will thus help raise awareness, as well as produce recommendations concerning the monitoring and care of patients with chronic disorders in the event of a health crisis, for different audiences: health authorities, scientific and professional networks, as well as service users and citizens. A specific website and a social network outreach strategy will be deployed for this phase.

Data Analysis

Data analysis will take place continuously throughout the project and will begin in phase 1, with the production of summary sheets at the end of each interview. This process will help organize the data according to the various themes and perspectives that relate to the disciplines represented in the project. Emerging new themes will be included to feed conceptual categories. Return to the transcribed document will be possible, in order to find the exact verbatim of a statement identified in a sheet, to quote but also to identify the context. We will use the iterative process, which is characteristic of qualitative methodologies [20]. Our approach aims to build hypotheses through linking categories to empirical data.

During the descriptive phase of each case (ie, phases 2 and 3), a summary sheet will be produced for each interview, including a one-page summary of the interview from the interviewee's point of view, as well as a brief paragraph on the interview's relevance to the research issue. An account of the interviews and contacts made (ie, synthetic field diary) will also be produced by the researcher investigating the situation of each person within their health care network. The structure of these sheets will be discussed by all researchers involved in the study so that all the questions of interest to the various disciplines and user representatives can be considered. The results will be discussed and produced collectively through a series of working sessions in two formats, alternating between general meetings involving all research team members and smaller analysis workshops involving, each time, researchers of two disciplines and a member or an association or a professional.

By associating phases 2 and 3, we aim to cross-reference the points of view of different actors around the same situation and, thus, point to the role of some of them, which may remain hidden after a single interview [21]. This method will help reveal important but generally invisible players (pharmacist, medical secretary, etc), as well as adaptations of the forms of support between relatives that have been reconfigured by the containment measures. Comparing points of view also makes it possible to understand the plurality of definitions of the situation, an important dimension to be considered in the context of the health crisis, which is modifying everyone's expectations and requires continuous adaptation and negotiation. Finally, triangulating these two sources of data aims to capture the concrete and organizational reconfigurations of the health care ecosystems that are affected by the reorganization of health care resources, as well as their effects on the quality of medical and psychosocial care. Phases 2 and 3 will document more precisely objectives 1 and 2 defined above.

Ethics Approval and Consent to Participate

Two separate interview guides have been co-constructed with the research team, based on the exploratory focus group: one is dedicated to "patient" interviews for phase 2, the other to "professionals, helpers, professionals" for phase 3. They are the result of a multidisciplinary approach, since researchers and representatives of patient associations suggested themes using their respective epistemological or experiential references.

The interviews will be conducted in compliance with health regulations via phone or videoconferencing. They will all be recorded based on oral consent of the individuals, fully transcribed and anonymized, and made available to all the members of the research team. The protection of the data collected will be specified in an information letter given to each person asked to participate in the research.

Having a consent form signed multiplies the documents with the identity of the persons. This is why we have not opted for this procedure, in favor of an oral recording of the consent before starting the interview which, in our opinion, better guarantees anonymity. This consent is subsequently recorded in writing in the transcript of the interview. Furthermore, having someone sign a consent form when working in Sciences Humaines et Sociales (SHS) can significantly alter the relationship between the respondent and the interviewer before starting the discussion. Moreover, in the context of the health crisis and protective measures that we are all currently subject to, we will not find ourselves physically come in face-to-face contact with the respondent. Getting the respondent to sign will be even more difficult and will therefore be done electronically.

Ethical approval was received from Comité d'Éthique de la Recherche (Research Ethics Committee) of the University of Paris. The protocol has been registered (institutional review board [IRB] no. 00012020-59; June 28, 2020).

Availability of Data and Materials

Data will be stored in an encrypted form on a secure server of the University of Paris, in the cloud environment, accessible only to authorized researchers. The data processing implemented for the needs of this research will be done in compliance with the standard reference procedure (MR-004) and declared to the data protection officer's registry at the University of Paris.

Results

The protocol study has undergone a peer review by the French National Research Agency's scientific committee and has been approved by the Research Ethical Committee of the University of Paris (registration number: IRB 00012020-59 June 28th, 2020). The project received funding for the period August 2020 through April 2021. Expected results will be disseminated in 2021 and 2022.

Discussion

As the exploratory phase of the research is being finalized, several operational issues emerged that foster discussion. The health crisis made it more complex to access the field, requiring adaptation from the research team. We encountered difficulties to access patients with mental illness. This situation was largely caused by a heightened variety of patients' relationships with health care services, along with the fact that mental health organizations are loosely structured and scattered [22].

Realizing that the heterogeneity of chronic disease management requires a differentiated approach for each disease, we decided to adapt our recruitment to the specificities of each field. We changed our strategy to find other sources of entry into the field of mental health. We varied our entry points in the field, by diversifying the interlocutors: psychiatrists, psychologists, associations (the French National Union of Families and Friends of Mentally Ill People, UNAFAM), mutual self-help groups, patients' homes (via the social media platform Clubhouse). We integrated a new specialized researcher into the research team, Ana Marques, who helped us enter into a psychiatric hospital in the department of Seine-Saint-Denis, where COVID-19 has had significant repercussions in terms of overloading structures, forcing hospitals to undergo a drastic reorganization [23]. These adjustments allowed us to diversify the profile of recruited patients, as we gained accessed to them through various care structures (eg, psychiatric hospitals, medical-psychological centers).

To conclude, the preparatory interviews were essential to inform the specificities of each field of chronic disease and allowed us to adapt our patient recruitment strategy to begin phase 2 of the research. At the end of our research, our findings will better inform the stakes of the current health crisis on the management of patients with chronic disorders and, more broadly, any future crisis for a population deemed to be at risk. They will improve health democracy by supporting a better transferability of knowledge between the scientific and citizen communities.

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Authors' Contributions

All coauthors except LV designed the research protocol; ER and LV wrote the manuscript; and all coauthors have reviewed and approve the final text.

Conflicts of Interest

None declared.

References

1. Molinier P. Cross-vulnerabilities and discrete know-how. The care-proof working. In: Paperman P, Laugier S, editors. Caring for Others - Ethics and politics of care. Book in French. Paris: Éditions de l'École des Hautes Etudes en Sciences Sociales; 2006:339-357.
2. Lefève C. Should the care relationship be a relationship of friendship? In: Benaroyo L, editor. The Philosophy of Care. Ethics, medicine and society. Book in French. Paris: University Press of France; 2019:105-126.
3. Ricadat, Schwering K, Fradkin S, Boissel N, Aujoulat I. Adolescents and young adults with cancer: how multidisciplinary health care teams adapt their practices to better meet their specific needs. Psychooncology 2019 Jul;28(7):1576-1582. [doi: 10.1002/pon.5135] [Medline: 31145822]
4. Worms F. The moment of treatment. What do we hold on to? Book in French. Paris: University Press of France; 2010.
5. Lefève C. Extension of the sorting field. Article in French. AOC (Analyse Opinion Critique). 2020 Apr 20. URL: https://aoc.media/analyse/2020/04/19/extension-du-domaine-du-tri/ [accessed 2021-08-30]
6. Baszanger I. Chronic diseases and their negotiated order. Article in French. Revue Française de Sociologie 1986 Jan;27(1):3. [doi: 10.2307/3321642]
7. Karazivan P, Dumez V, Flora L, Pomey M, Del Grande C, Ghadiri DP, et al. The patient-as-partner approach in health care. Academic Medicine 2015;90(4):437-441. [doi: 10.1097/acm.0000000000000603]
8. Mol A. What care means. Rethinking the patient's free choice. Book in French. Paris: Presses des Mines; 2009:199.
9. Baszanger I. An uncertain autonomy: the patients and the healthcare system. In: Hirsch E, editor. Treaty of bioethics: II - Caring for the person, evolutions, therapeutic innovations. Book in French. France: Toulouse; 2010:189-198.
10. Fainzang S. From solidarity to autonomy: towards a redefinition of the parameters of the notion of autonomy. Theor Med Bioeth 2016 Dec;37(6):463-472. [doi: 10.1007/s11017-016-9385-5] [Medline: 27896525]
11. Velpry L. The patient's view: issues of theory and practice. Cult Med Psychiatry 2008 Jul;32(2):238-258. [doi: 10.1007/s11013-008-9086-2] [Medline: 18299968]

12. Drugs: change in purchasing habits during confinement. Article in French. Medscape News. 2020 May 05. URL: https://francais.medscape.com/voirarticle/3605935 [accessed 2021-08-31]
13. Chevance A, Gourion D, Hoertel N, Llorca P, Thomas P, Bocher R, et al. Ensuring mental health care during the SARS-CoV-2 epidemic in France: A narrative review. Article in French. Encephale 2020 Jul;46(3S):S3-S13 [FREE Full text] [doi: 10.1016/j.encep.2020.03.001] [Medline: 32312567]
14. Winance M. Dependency versus autonomy... On the meaning and impregnation of these notions in medico-social practices (commentary). Article in French. Sciences Sociales et Santé 2007 Dec;24(4):83 [FREE Full text] [doi: 10.3406/sosan.2007.1875]
15. Lovell AM, Pandolfo S, Das V, Laugier S. Facing disasters. A four-voice conversation on madness, care and the great collective distresses. Book in French. Paris: Ithaque; Oct 2013.
16. Barbot J. The Sick in Movements. AIDS-proof medicine and science. Book in French. Paris: Balland; 2002:307.
17. Gross O. Patient engagement in the service of the healthcare system. Book in French. Paris: Doin; 2017:168.
18. Taylor B, Henshall C, Kenyon S, Litchfield I, Greenfield S. Can rapid approaches to qualitative analysis deliver timely, valid findings to clinical leaders? A mixed methods study comparing rapid and thematic analysis. BMJ Open 2018 Oct 08;8(10):e019993 [FREE Full text] [doi: 10.1136/bmjopen-2017-019993] [Medline: 30297341]
19. Ricadat E, Schwering K, Aujoulat I, Boissel N. Between caregivers and researchers, what kind of communication? Example of action research carried out in a hematology department for adolescents and young adults. Article in French. Psycho-Oncol 2018 Aug 12;12(1):34-37. [doi: 10.3166/pson-2018-0022]
20. Olivier de Sardan JP. The Rigor of Quality. The empirical constraints of the socio-anthropological interpretation. Book in French. Louvain la Neuve, Belgium: Academia Editions; 2008:365.
21. Gojard S, Gramain A, Weber F. Family Responsibilities: Dependence and kinship in contemporary France. Book in French. Paris: La Découverte (The Discovery); 2003:420.
22. Coldefy M. Psychiatric care: organization and recent legislative developments. Article in French. Revue française des affaires sociales 2016(2):21-30 [FREE Full text] [doi: 10.3917/rfas.162.0021]
23. Mariette A, Pitti L. Covid-19 in Seine-Saint-Denis (2/2): how the health system increases inequalities. Article in French. Metropolitiques. 2020 Jul 10. URL: https://metropolitiques.eu/Covid-19-en-Seine-Saint-Denis-2-2-comment-le-systeme-de-sante-accroit-les.html [accessed 2021-08-31]

Abbreviations

IRB: institutional review board
PARCOURS: Parcours, Associations, Réseau, Chronicité, Organisation, Usagers, Retour d'expérience, Soins
SHS: Sciences Humaines et Sociales

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Protocol

Assessment of the Feasibility, Acceptability, and Impact of Implementing Seasonal Malaria Chemoprevention in Nampula Province, Mozambique: Protocol for a Hybrid Effectiveness-Implementation Study

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Abstract

Background: Malaria is a significant cause of morbidity and mortality in children aged under 5 years in Mozambique. The World Health Organization recommends seasonal malaria chemoprevention (SMC), the administration of four monthly courses of sulfadoxine-pyrimethamine (SP) and amodiaquine (AQ), to children aged 3-59 months during rainy season. However, as resistance to SP is widespread in East and Southern Africa, SMC has so far only been implemented across the Sahel in West Africa.

Objective: This protocol describes the first phase of a pilot project that aims to assess the protective effect of SP and AQ when used for SMC and investigate the levels of molecular markers of resistance of *Plasmodium falciparum* to antimalarial medicines in the study districts. In addition, it is important to understand whether SMC is a feasible and acceptable intervention in the context of Nampula Province, Mozambique.

Methods: This study will adopt a hybrid effectiveness-implementation design to conduct a mixed methods evaluation with six objectives: a molecular marker study, a nonrandomized controlled trial, an analysis of reported malaria morbidity indicators, a documentation exercise of the contextual SMC adaptation, an acceptability and feasibility assessment, and a coverage and quality assessment.

Results: Ethical approval for this study was granted by the Mozambican Ministry of Health National Bioethics Committee on September 15, 2020. Data collection began in October 2020, and data analysis is expected to be completed by August 2021.

Conclusions: This research will make a unique contribution to our understanding of whether the combination of SP and AQ, when used for SMC, can confer a protective effect against malaria in children aged 3-59 months in a region where malaria transmission is seasonal and SP resistance is expected to be high. If the project is successful, subsequent phases are expected to provide a more comprehensive assessment of the effectiveness and sustainability of SMCs.

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KEYWORDS

malaria; seasonal malaria chemoprevention; sulfadoxine-pyrimethamine amodiaquine; resistance; children under five; implementation research; Mozambique; Africa; mobile phone

Introduction

Background

An estimated 409,000 people die from malaria each year worldwide, and children aged under 5 years are particularly vulnerable, comprising 67% of all malaria deaths in 2019 [1]. The *high burden to high impact* approach, supported by the World Health Organization (WHO), the Roll Back Malaria Partnership to End Malaria and other partners, aims to prevent disease and save lives through strategies targeted to the contextual needs of 11 countries that together account for more than 70% of the world's malaria burden [2]. Mozambique has one of the highest incidence rates and absolute annual number of malaria cases globally [3]. Malaria causes 29% of all deaths and 42% of deaths among children aged under 5 years in Mozambique, rendering it the most significant national public health threat [4]. Mozambique has adopted the *high burden to high impact approach*, and the National Malaria Control Programme is working with partners toward the global vision of a malaria-free world. The National Malaria Control Program's strategic plan for 2017-2022 focuses on burden reduction in highly endemic areas and on sustaining gains in low transmission areas toward elimination [5].

Implementation of Seasonal Malaria Chemoprevention in Africa

Seasonal malaria chemoprevention (SMC) is "the intermittent administration of full treatment courses of an antimalarial medicine during the malaria season to prevent malarial illness, with the objective of maintaining therapeutic antimalarial drug concentrations in the blood throughout the period of greatest malarial risk" [6]. The currently recommended antimalarials for SMC are sulfadoxine-pyrimethamine (SP) and amodiaquine (AQ), which is administered monthly to children aged 3-59 months during the peak malaria transmission season, which typically coincides with the rainy season. A full course of SP and AQ (SPAQ) consists of 1 dose of SP and 3 doses of AQ, which are administered over a 3-day period. SMC typically involves four monthly cycles of SPAQ administration over the course of the malaria transmission season, which is referred to as a full *round*. The intervention can reduce the incidence of clinical episodes and severe malaria by approximately 75% [7]. It has also been shown that the intervention can be delivered safely at scale, achieving high coverage. The Achieving Catalytic Expansion of SMC in the Sahel (ACCESS-SMC) project scaled up SMC in 7 countries between 2015 and 2017, with few adverse drug reactions reported. SMC was associated with a protective effectiveness of 88% over 28 days in case-control studies conducted as part of ACCESS-SMC [8]. In Burkina Faso and The Gambia, the implementation of SMC was associated with reductions in the number of malaria deaths in hospitals during the high-transmission period, of 42% and 57%, respectively [8]. SMC could also avert millions of cases and thousands of deaths among children living in areas with highly seasonal malaria transmission [3]. In terms of cost, a multicountry cost-effectiveness analysis found that the weighted average economic cost of administering four monthly SMC cycles was US $3.63 per child, and ultimately, that SMC is a highly cost-effective intervention that substantially reduces malaria diagnostic and treatment costs [9].

SMC has been recommended by the WHO since 2012, for use in areas where more than 60% of annual malaria incidence occurs within 4 consecutive months, where there is a high burden of malaria in children, and where SPAQ retain their antimalarial efficacy [6,10]. To date, SMC has mainly been implemented in the Sahel region of sub-Saharan Africa, where *Plasmodium* falciparum is sensitive to both antimalarial medicines used in SMC. In 2019, 21.7 million children were targeted in 13 countries [1].

However, there is a potential risk of enhancing drug resistance and the potential for impaired development of naturally acquired immunity in children [11]. The impact of SMC on the immune response to malaria, possibly increasing the burden of malaria in later life, has not yet been proven. Studies have found that administering SMC in early life does not negatively affect the development of naturally acquired antibody responses to malaria [12,13]. In addition, there may be broader benefits of SMC, with lower parasitemia reported in health districts receiving SMC [14,15].

Challenges include the logistical burden of SMC distribution, particularly during the rainy season when access to remote areas may be compromised; however, adopting a decentralized, integrated approach through community-based distributors may support the sustainability of SMC [14]. The potential risk of development of drug resistance should be investigated further, which may pose a risk of suboptimal adherence [14]; however, the multicountry observational ACCESS-SMC study found that molecular markers of resistance occurred at very low levels [8]. Nonetheless, a few studies have found adherence to be an issue; for example, Ding et al [16] reported complete adherence in less than 20% of children receiving SMC in Niger for a full 3-day course in each cycle for four cycles.

Drug Resistance and SMC Efficacy

The WHO recommends that SMC is suitable in areas where the efficacy of SPAQ combination remains over 90% [6]. Resistance to SP or AQ may reduce the efficacy of SMC in protecting children against clinical malaria, although the relationship between the degree of resistance and the effectiveness of SMC has not yet been clearly defined. SP efficacy is threatened by drug resistance due to mutations in the dihydrofolate reductase (*dhfr*) and dihydropteroate synthetase (*dhps*) genes [17]. According to a study conducted in Mozambique, the prevalence of *dhfr* and *dhps* mutations was 5%-6% [18], with more recent research suggesting this may be as high as >80% [19]. However,

there is a paucity of data on the prevalence of SP resistance across Mozambique.

Clinical responses to SP are seriously compromised in many regions of the world, and SP is no longer recommended for the treatment of malaria episodes. However, it has been difficult to determine whether the efficacy of SP for chemoprevention is also compromised [20]. Extant evidence from intermittent preventive treatment in pregnancy suggests that the presence of resistance to SP may undermine therapeutic effectiveness [21-23]. However, SPAQ will likely still provide benefit, even when there is a high prevalence of resistance [24], and a systematic review reported that intermittent preventive treatment in pregnancy with SP protection against low–birth-weight outcomes is sustained even in areas with high levels of the quintuple mutant [25].

The Ministry of Health, National Malaria Control Programme Midterm Review of the Malaria Strategic Plan 2017-2022 has recommended SMC as a malaria control strategy to decrease transmission and accelerate impact in the highest burden locations [26]. This is in line with the WHO recommendation for individual approaches to implementing SMC based on local contexts and integrating delivery to existing programs and networks as much as possible, maximizing the potential use of community health workers and community volunteers [27]. Using community-based distributors for SMC also increased community members' trust in the intervention [28]. Strong health communication is required to ensure that community members understand and accept that SMC is a preventive intervention, especially as qualitative research in Ghana found that people could interpret the mass distribution of medicines for the purpose of curing symptoms rather than for prevention [28].

Study Rationale

Given the potential impact of SMC to avert many malaria infections and deaths, it is essential to investigate the role of drug resistance on the protective effect of SMC in Mozambique and to assess the feasibility and acceptability of implementing SMC in this context. In collaboration with the National Malaria Control Programme in Mozambique, Malaria Consortium will pilot SMC from November 2020 to February 2021, to a target population of approximately 72,000 children aged under 5 years in 2 districts of Nampula Province.

Study Aims

We will evaluate the SMC pilot with two primary aims: to determine the protective effect of SPAQ when used for SMC in this context and to assess the feasibility and acceptability of implementing SMC in terms of coverage, quality, and stakeholder perceptions. The study objectives are as follows: (1) to determine the baseline prevalence of SPAQ resistance and any increase in resistance prevalence after one annual round of SMC, (2) to determine whether receipt of SPAQ is associated with a reduction in the odds of clinically significant malaria outcomes, (3) to assess the change in reported malaria morbidity indicators through routine data, (4) to document the adaptation of SMC implementation to the Mozambican context, (5) to explore the feasibility and acceptability of SMC among stakeholders, and (6) to evaluate the process of SMC implementation in terms of distribution quality and coverage.

Methods

Study Setting

The study will be conducted in Malema, Mecuburi, and Lalaua districts in Nampula Province, northeastern Mozambique (Figures 1 and 2). Several key informant interviews may be conducted with stakeholders based in Maputo.

To identify suitable districts for SMC, an SMC suitability ranking was conducted by the WHO for all provinces. These criteria included a variety of factors such as (1) seasonality eligible for SMC (60% of rainfall concentrated in 4 months), (2) mortality (areas of highest under-five mortality using health management information system) data, (3) access to care (highest ranking given to areas where access to care was poor), and (4) treatment-seeking behavior (highest ranking given to areas where treatment-seeking behavior was poor). Using these four main categories, the average will be calculated to estimate the final ranking and identify the top 20 suitable districts to maximize the impact of SMC. From the list of suitable districts, an additional consideration was taken given the importance of implementing the intervention in an area where no other new interventions were taking place so that an evaluation could be implemented aiming at attributing change to the intervention under investigation. Hence, Malema and Mecuburi districts in Nampula Province were selected, with Lalaua as a comparator, as no indoor residual spraying or new long-lasting insecticidal nets were targeted in these areas, ensuring a robust evaluation component for this pilot study.

Figure 1. Nampula Province, Mozambique, where the study will be conducted. SMC: seasonal malaria chemoprevention.

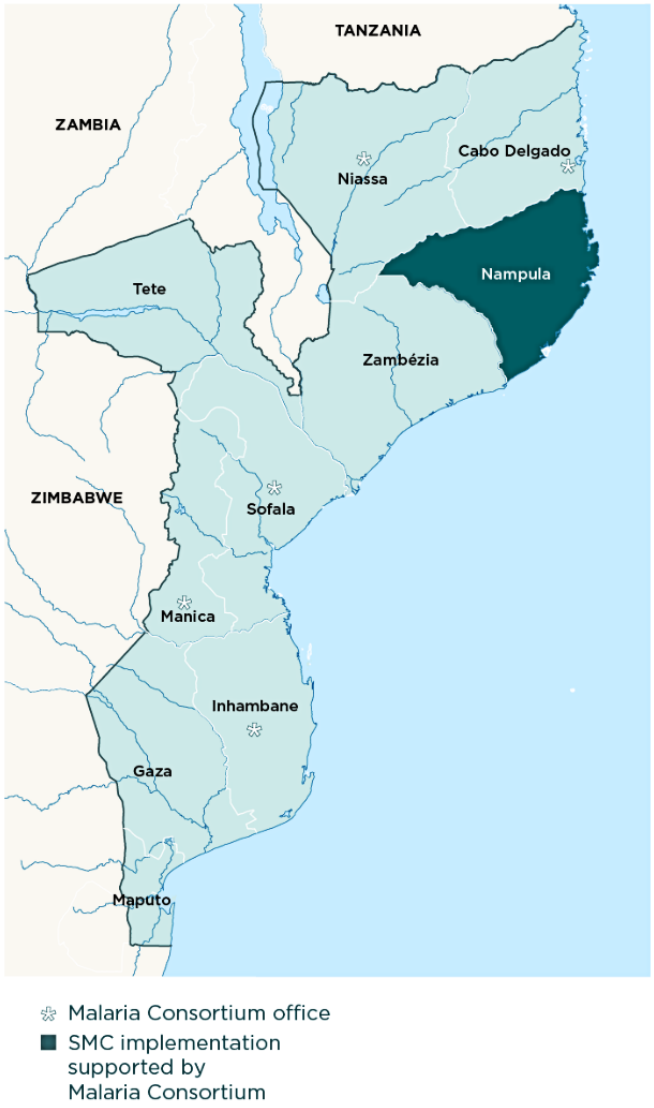
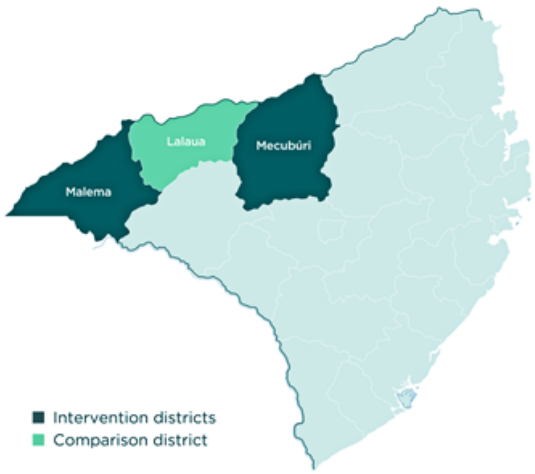


Figure 2. Seasonal malaria chemoprevention intervention and comparison districts.



Study Populations

The study population that is eligible to receive SMC includes afebrile children of either sex, aged 3-59 months, for any of the SMC cycles, residing in Malema and Mecuburi districts. In addition, for the purpose of the end-of-round survey, which includes an indicator measuring the age eligibility of enrolled children, we included children residing in the aforementioned districts, aged 5-10 years, who may inadvertently have received SMC. In addition, health workers who are involved in SMC implementation, caregivers of children aged under 10 years, community leaders, and key stakeholders such as health officials

at different levels of the health system and those involved in SMC implementation will be sampled, according to the study objective, described in more detail in the *Methods* section. The Lalaua district will serve as a control area (see Table 1 for estimated population sizes).

Table 1. Estimated target population of seasonal malaria chemoprevention implementation districts and comparison district by age (2020).

Target population estimates	Population of children aged 3-11 months, n (%)	Population of children aged 12-59 months, n (%)	Total population, n
Intervention area			
Malema	4031 (11.04)	32,438 (88.94)	36,469
Mecuburi	3959 (11.16)	31,515 (88.83)	35,474
Total SMC[a] target population			71,943
Control			
Lalaua	1978 (10.74)	16,425 (89.25)	18,403

[a]SMC: seasonal malaria chemoprevention.

Study Design

We will adopt a type 2 hybrid effectiveness-implementation study design that evaluates the effects of a clinical intervention on relevant outcomes while collecting information on implementation [29]. The hybrid effectiveness-implementation study design supports the pursuit of different lines of research simultaneously, which facilitates the more rapid translation and uptake of study findings for policy makers and implementers [29,30]. This study will use mixed methods to address the aforementioned objectives. Assessments of the protective effect of SPAQ, as delivered as part of SMC implementation, will provide evidence on whether this is appropriate in a region where SP resistance is suspected. Evaluating the implementation of SMC will generate knowledge on the feasibility and acceptability of this intervention in situ, including the challenges, barriers, and facilitators in the local context. Such findings can be useful to inform which intervention components are generalizable and which require local adaptation for other settings [31].

Four monthly cycles of SMC drugs will be distributed door-to-door to eligible children aged between 3 and 59 months by community distributors between November 2020 and February 2021 in 2 districts of Nampula Province. SMC tools and protocols used in Sahelian countries where the Malaria Consortium supports SMC delivery will be adapted to the context in Mozambique for this purpose. A third district will serve as a comparison district (the latter will receive standard malaria prevention, control, and case management). Data collection across the study components was conducted between October 2020 and May 2021 (Figure 3).

The methods are organized according to the study objective, described in more detail below, with an overview provided in Table 2 and Figure 3.

Figure 3. Timeline of seasonal malaria chemoprevention study objectives. Obj: Objective; RCT: randomized controlled trial; SMC: seasonal malaria chemoprevention; SPAQ: sulfadoxine-pyrimethamine and amodiaquine.

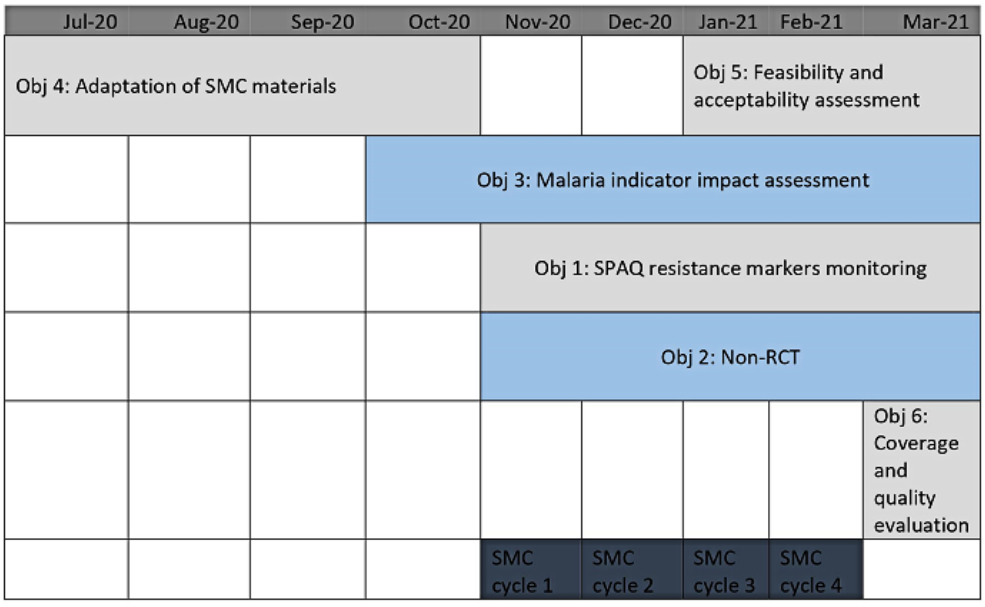


Table 2. Overview of research objectives, methods, and sampling.

Objective	Method	Study population	Inclusion criteria	Exclusion criteria	Sample size (N=3320), n (%)
• SPAQ[a] resistance molecular marker monitoring	Quantitative: molecular analysis	• Eligible children aged 3-59 months on the day 1 of the first SMC[b] cycle	• Aged 3-59 months attending the health facilities in study area with fever or history of fever in preceding 24 hours, with a positive malaria RDT[c] and, with prior informed consent obtained from the parents or guardians	• Presence of any signs or symptoms of severe malaria, refusal to participate	600 (18.07)
• Nonrandomized controlled trial	Quantitative: nonrandomized controlled trial	• Eligible children aged 3-59 months on the day 1 of the first SMC cycle	• Eligible children, visited home for enrollment	• Presence of a severe, chronic illness and a history of a significant adverse reaction to sulfadoxine-pyrimethamine or amodiaquine • Refusal to participate	800 (24.09)
• Assessment of impact of SMC on reported malaria morbidity indicators	Quantitative: DHIS2[d] or SISMA[e] data analysis	• Data quality audit and morbidity analysis of all confirmed malaria cases reported in children aged less than 5 years in the 3 study districts from November 2020 to March or May 2021	• HMIS[f] data on health facility attendance for children aged 0-13 years (inclusive) will be extracted from health facility registers as full line listings, covering November 2020 to May 2021	• Data from children aged >13 years or those falling outside the specified dates	26 health facilities in all 3 study districts
• Process documentation of SMC adaptation	Qualitative: documentation of the adaptation process	• N/A[g]	• N/A	• N/A	N/A
• Feasibility and acceptability assessment	Qualitative: KIIs[h] and FGDs[i]	• Health workers implementing SMC • Caregivers of children aged 3-59 months, community members, and community leaders • Health workers • SMC implementers • Health officials and policy makers (district, provincial, and national)	• Must fall into one of the study population' categories, must consent to participate	• Not categorized into one of the described study populations • Refusal to participate	120 (3.61)
• Coverage and quality evaluation	Quantitative: end-of-round survey	• Eligible children aged 3-119 months who have been a resident in the study location for a minimum of at least one month, during the SMC pilot implementation period. Survey responses will be provided by caregivers	• Households with children aged 3-119 months, resident in the study location >1 month during SMC • Aged 18 years or older with the primary responsibility of feeding and daily care of at least one child aged 3 months to 10 years	• No one aged 18 years or older available at the time of data collection • No children aged 3-119 months present • Refusal to participate	1800 (54.22)

[a]SPAQ: sulfadoxine-pyrimethamine and amodiaquine.

[b]SMC: seasonal malaria chemoprevention.

[c]RDT: rapid diagnostic test.

[d]DHIS2: district health information software.

[e]SISMA: Sistema de informação em Saúde e Monitoria e Avaliação.

[f]HMIS: health management information system.

[g]N/A: not applicable.

[h]KII: key informative interview.

[i]FGD: focus group discussion.

Ethical Considerations

Ethical approval for this study was granted by the Mozambican Ministry of Health National Bioethics Committee on September 15, 2020. Only participants who met the inclusion criteria and provided written informed consent will be included.

Study Objectives and Methods: SPAQ Resistance Molecular Marker Monitoring

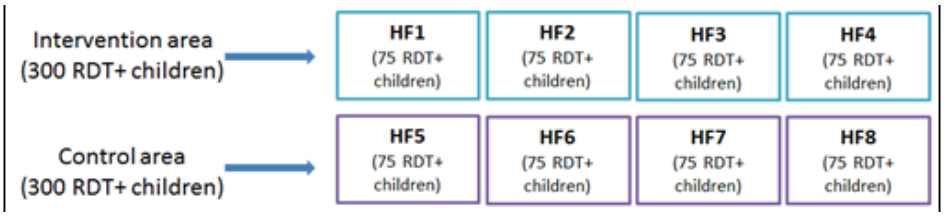
Overview

The purpose of this study is to determine the baseline prevalence of SPAQ resistance markers and any eventual increase after one round (four monthly cycles) of SMC as assessed via molecular markers in the population. Specifically, to detect prevalence over time in the proportion of symptomatic children, using a positive rapid diagnostic test (RDT), residing in 2 districts where SMC will be implemented who carry parasites with *Plasmodium falciparum* dihydrofolate reductase *(dhfr)*, *Plasmodium falciparum* dihydropteroate synthase (*dhps*), *Plasmodium falciparum* chloroquine resistance transporter gene (*pfcrt*) and/or *Plasmodium falciparum* multidrug resistance gene 1 (*pfmdr1*) mutations, compared with children living in a neighboring district with similar epidemiologic characteristics but not receiving SMC. Children enrolled in both areas will be aged 3-59 months and will have similar clinical and parasitological characteristics. Health facility–based cross-sectional surveys will be conducted in October 2020, before the SMC distribution begins (baseline), and in March 2021, after one complete round of SMC (endline), to measure the prevalence of molecular markers associated with resistance to SPAQ in symptomatic children aged less than 5 years with a positive RDT attending selected health facilities in the intervention and control areas. Monitoring the prevalence of alleles associated with drug resistance will be done by collecting blood samples from symptomatic children with evidence of infection. During the surveys, fingerpick blood samples will be collected on Whatman 903 (10534612) filter papers (dried blood spots). Sample collection will be performed in 2 selected first-level health facilities in each district of the intervention area and also in 4 selected health facilities in the comparator district, with a total of 8 health facilities across all 3 districts. The main outcome measure is the prevalence of molecular markers associated with SP (codons 108, 51, and 59 in *dhfr* and 437, 540, and 581 in *dhps*) and AQ (codons 72-76 in *pfcrt* and 86, 184, and 1246 in *pfmdr1*) resistance in blood samples collected from symptomatic children aged less than 5 years with a positive RDT attending the selected health facilities. The prevalence will be assessed in areas with SMC and with no SMC at baseline and at the end of the project.

Indicative Sample Size Calculations

The sample size will be determined using the WHO protocol for drug efficacy testing [32]. The survey's sample size will be calculated to estimate changes in the prevalence of SPAQ resistance markers with sufficient precision to detect a statistically significant difference before and after SMC implementation. It is assumed that the prevalence of *dhfr and dhps* sextuple mutants is 0% [33] in the intervention area. A sample size of 242 samples per survey per arm was estimated to have 90% power to detect a difference at the 5% level (P=.05) between baseline and endline. This will permit confirmation of a prevalence of 5% or higher in *dhfr and dhps* sextuple mutants. Assuming a 10% loss of samples or uninterpretable analysis, the number will be rounded up to 300 samples per area (intervention and comparator districts) per survey per country. Figure 4 shows the estimated sample sizes for each health facility. Samples will be collected in 8 health facilities (4 in the intervention area and 4 in the comparator *control* area).

Figure 4. Estimated sample sizes. Numbers correspond to the children with positive malaria test results. HF: health facility; RDT: rapid diagnostic test.



Selection of Survey Health Facilities

Samples will be collected from selected health facilities from the list of all health facilities in the control and intervention areas, based on attendance of children with fever or history of fever and prevalence of *Plasmodium falciparum* infection among them based on routine data reporting.

Study Population

The study population will include children aged 3-59 months attending the selected health facilities in both the intervention

and comparator districts. The number of children to be screened in each health facility will depend on the proportion of malaria RDT-positive cases over the total number of children meeting the eligibility criteria. Children who do not meet the inclusion criteria, for example, those with a negative RDT result, will be referred within the same health facility for further assessment and appropriate treatment.

Sample Collection and Molecular Analysis

Caregivers of children meeting all the inclusion criteria mentioned earlier will be interviewed using a short paper questionnaire to record personal identifiers of the children such as date of birth, sex, date of interview, and residence location. The study staff will approach them as part of their clinical visits.

A blood sample (4 drops) will be collected through finger prick onto a filter paper (Whatman 3MM) to determine the prevalence of *dhfr*, *dhps*, *pfcrt*, and *pfmdr1* mutations. Other molecular markers of antimalarial resistance will be considered for analysis as comparators. Specimens will be labeled anonymously (unique identifying code, study health facility, and date), dried, stored in individual plastic bags with desiccants, and protected from light, humidity, and extreme temperature until analyzed. All samples will be batched and stored at 4 °Cat the Centro de Investigação em Saúde de Manhiça laboratory (until complete sample collection and analysis). *Dhfr, dhps, pfcrt, and pfmdr1* genotypes will be determined using nested mutation-specific polymerase chain reaction, sequencing, and/or polymerase chain reaction-restriction fragment length polymorphism. The prevalence of *dhfr* mutations at codons 51, 59, and 108 and *dhps* mutations at codons 431, 437, 540, 581, and 613 and *pfcrt* codons 72-76 and *pfmdr1* codons 86, 184, and 1246 will be calculated among the sampled children, and differences in the proportions of samples with each of these mutations between baseline and endline will be tested using the *z* test.

Nonrandomized Controlled Trial

Overview

A nonrandomized controlled trial will be conducted to determine whether the receipt of SPAQ is associated with a reduction in the odds of clinically significant malaria outcomes and to estimate the protective effect of SPAQ. There will be two arms: one (control arm) in the comparator district and the other in one of the SMC intervention districts. Communities will be randomly selected in both the intervention and control districts. Eligible children (aged 3-59 months at the first SMC cycle) will be recruited through random selection. Exclusion criteria include the presence of a severe, chronic illness and a history of a significant adverse reaction to SP or AQ. Selected children will be treated appropriately and retained during the trial. In the control district, communities bordering the intervention district will be avoided because of potential unintended *leakage* of SPAQ across the district boundary.

Sample Size

The study will be powered to have an 80% chance of detecting a 40% reduction in incidence with statistical significance at the 5% level. It is assumed that study participants, in the absence of SMC, would experience 0.2 clinical episodes per child per high-transmission season (corresponding to the SMC round) of sufficient severity to present to a health facility [10]. The sample size calculation, based on the formula for a binary outcome superiority trial, shows that a sample of 654 eligible children (or 327 per arm) is required to provide sufficient statistical power. This multiplies to 818 under the assumption of a 20% loss to follow-up over the four cycles. Therefore, we aim to recruit a minimum of 800 eligible children (400 per arm).

Primary Outcome

The primary outcome of this study will be visits to a health facility for suspected malaria by eligible children and confirmation of malaria diagnosis using an RDT during the 5-month study period, which includes a period of 28 days after the final administration of SPAQ.

Recruitment and Data Collection

Households will be randomly sampled from selected communities in both the control and intervention arms and 1 eligible child recruited at random in each household. A short baseline questionnaire will be administered to collect individual data on each child and to confirm their eligibility after the caregivers provided their consent. In the intervention arm, the questionnaire will be administered before the intake of SPAQ for SMC. The primary end point will be recorded through passive surveillance by study clinicians in both the intervention and comparator areas during the 4-month study period. Children recruited into the study presenting at clinics will be identified using information on SMC record cards, on which a child's information and SMC doses are recorded, and data on health facility visits including suspected malaria cases and results of RDTs will be matched to baseline questionnaire data to build a database for analysis.

Data Analysis

Data will be analyzed using multivariate logistic regression with odds ratios estimated for the association between allocation to the intervention arm and (suspected and confirmed) malaria diagnosis at any point during the study period, converted to a percentage estimate of protective effect. To compensate for the lack of preintervention random allocation of participants to intervention or control groups, covariate adjustment will be made for potential confounders that may influence respondents' odds of experiencing a clinically significant case of malaria. Covariates, measured at baseline, will include sex, age, parental education, and long-lasting insecticidal net use and all of these will be operationalized as categorical variables. Analyses will also use a multivariate Cox proportional hazards model with multiple Cox regression. *Failure* defined as a visit to a health facility for suspected malaria and/or a confirmed case of malaria and timing of this event based on the original date of health facility attendance during the study period and the estimated protective effect calculated.

Assessment of SMC Distribution Impact on Reported Malaria Morbidity Indicators Using Routine Data

We will investigate the impact of SMC on reported malaria morbidity (as a primary end point) in children aged 3-59 months in the study area. Differences in rates of malaria incidence by age at the health facility level will be investigated using a

quasi-experimental design based on regression discontinuity analysis, taking advantage of the discontinuity in eligibility for SMC based on age.

Before obtaining data on malaria indicators at the health facility and district levels, a data quality audit will be conducted to assess the quality of the data that will be used for analysis. The quality of data from districts where SMC is implemented will also be compared with that of data from the comparator district. Health management information system data on health facility attendance for children aged 0-13 years (inclusive) will be extracted from health facility registers as full line listings, covering November 2020 to May 2021 in both implementation districts and the control district by photographing the relevant pages of the registers and entering data directly into Excel tables as appropriate. While monthly suspected malaria cases presenting at each health facility will be calculated, other variables including date of health facility attendance, sex, date of birth (or closest estimate of age in months as a preference, or age in years if this cannot be confirmed from an identity document, previous health facility record, or vaccination or medical card), whether a malaria test was performed, the type of test performed (RDT or microscopy), test results (confirmed malaria or negative test results), malaria mortality, and any other variables collected routinely for all child attendees (eg, nutrition status) will be obtained. Observations from registers will be categorized by children's ages according to the smallest possible increments. Incidence curves [34] for suspected and confirmed malaria cases by age will be modeled from these data (using offset terms to adjust for estimated numbers of children in each age category by health facility catchment area). Incidence curves by age will either be fitted with quadratic or cubic regression terms in Stata 16 (StataCorp) or using a thin plate spline term in R (R Foundation for Statistical Computing; using the mixed gam computation vehicle package). Regression discontinuity analysis [35] using negative binomial models will then be used to assess the reduction in malaria incidence by age-dependent eligibility for SMC. As the primary exposure variable, eligibility will be coded as a binary variable (1=3-59 months 0=0-2 months and 60-155 months) based on age at the start of the SMC round and district. Adjustments will be made for the month of health facility attendance. If possible, random effects will be fitted, with observations of monthly malaria cases nested within clinics. The results will be expressed as rate ratios for the difference in incidence in the eligible age group compared with the expected incidence curve. Models will adjust for sex as an interaction term (considered a moderator for age-dependent malaria susceptibility). Sensitivity analyses may consider the effects of unintended coverage of children aged 5-9 years.

Process Documentation of SMC Adaptation

The purpose of this component is to systematically capture the process of how the SMC model implemented by the Malaria Consortium and partners in West and Central African countries is adapted to the Mozambican context. Specifically, this will take into consideration the existing government health system, structures, personnel, and service delivery at different levels. In view of the current COVID-19 pandemic, all of the aforementioned activities and tools will be appropriately adapted to this outbreak context, which will constitute an additional aspect to be documented as part of the model adaptation. Previous study protocols, implementation reports, tools, and materials from other countries where the Malaria Consortium has implemented SMC will be reviewed and collated. Relevant materials will be adapted and translated for the Mozambican context. All of these adaptations will be captured using a template process documentation tool.

Feasibility and Acceptability Assessment

A key component of investigating the feasibility and efficacy of SMC in Mozambique is understanding the views and experiences of those involved in its implementation and use.

To explore the feasibility and acceptability of implementing SMC, a qualitative assessment using key informant interviews and focus group discussions (FGDs) will be conducted. This study component will examine how SMC is viewed, experienced, and engaged with by different stakeholder groups, including policy makers, implementers, and beneficiaries.

The study population includes health workers and community volunteers who are involved in SMC implementation, caregivers of children aged 3-59 months, community members, community leaders, and key decision makers such as health officials at different levels of the health system. Purposive approaches to sampling will be adopted to include those best able to provide insight into the topic being explored and a range of views and experiences relating to SMC [36]. Participants will fall under four main groups: caregivers of children eligible for SMC; health workers and community volunteers involved in SMC delivery; community members in areas where SMC is implemented; and key informants involved in SMC implementation, program management, and policy making.

Within each participant group, participants with a range of different experiences will be identified, where possible. For example, for caregivers, efforts will be made to include participants of different genders, ages, living in more rural and urban locations; those considered more marginalized, such as adolescents, older caregivers, and people living remotely; and those with different socioeconomic status and education levels. Although we presume that most caregivers will be female, we will attempt to include male caregivers where possible and relevant. We will also aim to include those with different experiences relating to SMC, that is, those who refused and those who agreed to receive SPAQ for their children. For health workers and community-based volunteers, those of different ages and experience and seniority levels will be identified for recruitment. For community members, those with potentially different perspectives will be included, for example, village leaders, older men, older women, and younger women. For key informants, implementing partners and those from district, provincial, and national levels and with a range of different potential insights, for instance, relating to malaria prevention policy making, program management, and drug supply chain management, will be identified for recruitment. In addition to identifying participants purposively, the end-of-round approaches to sampling will be adopted, with the final sample size determined based on evidence of achieving data saturation, when additional participants do not generate new findings relating to the topic of investigation [37,38]. We estimate

recruiting approximately 10-20 participants per group (Table 3) for participation in an in-depth interview. In addition, 6-12 FGDs will be conducted with approximately 6-8 participants per group.

Data will be generated through in-depth interviews and FGDs, based on topic guides, to explore views on SMC, areas relating to SMC acceptability, and reflections on the implementation experience. Topic guides will serve as prompts for the interviewer but will be flexible and participant led. In-depth interviews will aim to encourage participants to elaborate and provide in-depth accounts of their views and experiences relating to SMC, or *thick descriptions* [39], including through using nonverbal and verbal probing. Topic guides will vary the areas of focus, depending on the participant group. For example, interviews with caregivers will explore topics including general views on malaria, malaria prevention options, and SMC, as well as perceived malaria risk, perceived benefits and costs or negatives of SMC, concerns, challenges, and support. Interviews with community distributors will explore topics such as experiences administering SPAQ, how community members respond to SMC, what community distributors themselves think about the pros and cons of SMC and its appropriateness in the region, challenges, and support for engagement with it. Interviews with key informants will explore topics relating to implementation views and experiences, including reflections on the pilot implementation, the appropriateness of SMC for preventing malaria in the region and country, and challenges and opportunities for national rollout.

Table 3. Sampling frame.

Participant group and estimated sample size	Data collection technique
Caregivers	
10-20	IDI[a]
3-6	FGD[b]
Health workers and community-based volunteers	
10-12	IDI
3-6	FGD
Key informants or stakeholders	
10-12	IDI
Community members	
3-6	FGD

[a]IDI: in-depth interview.

[b]FGD: focus group discussion.

FGDs can facilitate an understanding of social norms, providing access to a range of perspectives [40], and the interaction between participants [41]. FGDs will therefore enable the exploration of wider views on SMC acceptability in the communities where the pilot is implemented, as well as views regarding different malaria prevention options, decision-making processes relevant to SMC, and potential barriers and facilitators for SMC implementation. FGDs with community members and caregivers will be homogenized by gender and age to facilitate interaction among participants and the expression of norms and consensus among peers in a grouping that is sensitive to cultural norms. All interviews and FGDs will be audio recorded and then transcribed and translated verbatim. Data collection and analysis will be conducted iteratively, with data analysis beginning at the point of data generation and with participant recruitment and topic focus being adapted as data collection progresses to further test emerging concepts and potential discrepancies from majority themes [42]. Data will be analyzed thematically using coding to identify emergent patterns, concepts, and categories from participants' accounts.

Coverage and Quality Evaluation (End-of-Round Survey)

Overview

The aim of this component is to evaluate the process of SMC implementation in terms of quality, coverage, and adherence to COVID-19 safety guidelines. To evaluate the coverage provided in the SMC pilot, an end-of-round survey will be conducted in March 2021. The objective of the end-of-round survey is to retrospectively determine coverage by surveying caregivers of eligible children aged 3-59 months and ineligible children aged 60-119 months, as leakage into the older age group has been anecdotally observed in other SMC countries [43]. Caregivers will be asked if their children receive the full 3-day course of the SPAQ during each cycle of the SMC round. The key indicators that will be assessed will include (1) the proportion of households with eligible children visited by a community distributor, (2) the proportion of day one SPAQ administered by community distributors to eligible children (in terms of children who received day one SPAQ at least once during 2020-2021 and by monthly cycle), (3) the proportion of eligible children who received a full 3-day course of SPAQ (including day 2 and day 3 AQ, among eligible children who received day one SPAQ), (4) the proportion of SPAQ administered by

community distributors by directly observed treatment (among eligible children who received day one SPAQ), and (5) the proportion of day one SPAQ received per eligible child over the course of the SMC round (including the proportion of children who received day one SPAQ during all four SMC cycles). To measure the quality of SMC coverage, the three key indicators assessed will be the correct age eligibility included, correct directly observed therapy observed, and correct dosage administered. These quality indicators are included along with the coverage indicators in an end-of-round survey tool.

End-of-Round Survey Study Area

This study aims to achieve a representative sample of children aged 3-119 months in households grouped within clusters identified from health facility catchment areas across the 2 intervention districts of the SMC pilot (ie, Malema and Mecuburi).

Study Design

For this objective, the design will be a cross-sectional cluster randomized survey to evaluate the coverage level and quality of SMC piloted in the Malema and Mecuburi districts. Households refusing to participate in the study will be replaced with the next eligible household until the estimated sample size is attained.

Sample Size and Technique

The end-of-round survey will use multistage random samples of households in areas covered by the Malaria Consortium's SMC pilot and will intend to achieve a representative sample of the target population at the district level to estimate the coverage of SMC at the level of individual eligible children. The sampling protocol aims to achieve a self-weighted sample with sampling units selected with a probability proportional to size. Only at the last stage of sampling (ie, at the household level) will a constant number of eligible children (1 child per household) be selected. The survey will be powered to provide an estimate of SMC coverage for children aged 3-59 months with a margin of error of 5%, while also providing a representative sample of children aged 60-119 months. The main sampling frame for the selection process will be a list of villages. Villages will then be randomly selected using the probability proportional to size. Villages will be the primary unit of sampling through which households and eligible children will be selected randomly. This may be reviewed once the study starts if this approach is not feasible in practice. A primary caregiver in this survey refers to any individual, aged at least 18 years, with the primary responsibility of feeding and daily care of at least one child aged less than 5 years, in a household where he or she has been a resident before the start of the SMC pilot or 1 month before the last cycle of SMC. The sample size calculation was performed using Stata 16 using the *svysampsi* command, based on the following assumptions: (1) the assumed intracluster correlation is 0.2; (2) 15 eligible children per cluster (b=cluster size); (3) the (design/cluster effect) = 1 + (b − 1) intracluster correlation = 1 + (15 − 1) 0.2 = 3.8; (4) the coverage rate of SMC in children aged 0-4 years of at least 80% (and in children aged 5-9 years of at most 20%); (5) a margin of error of 5%; (6) finite population adjustment is applied (75,000); (7) nonresponse rate of 5%; and (8) assumed ratio of children aged 5-9 years to those aged 0-4 years of 0.88.

Sampling Procedure

The sample size calculation revealed that a sample of 1842 children was required. It was decided that the survey would include 120 clusters, each comprising 15 children (n=1800), with 60 in each of the two districts. A constant number of households (15) will be randomly sampled from these areas, with the assumption that the populations in each sampling unit were of approximately equal size. One eligible child will be sampled from each compound in the absence of a household-level sampling frame, under the assumption that households contain a similar number of eligible children. Sampling at each stage will be conducted without replacement; once a supervision area or cluster has been selected, it should no longer be eligible for further selection.

Study Tools

The data were collected using a questionnaire developed by the Malaria Consortium. The survey questionnaire will be translated into Portuguese and Macua languages and uploaded into the SurveyCTO software application that will enable direct, field-based computer-aided personal interview and remote capture of the data and transfer to a netbook computer.

Although the coverage surveys will be the main method to determine coverage, two additional data sources will be analyzed and compared with survey results: (1) administrative data based on SMC tally sheets completed by distributors and data compiled via summary forms and end-of-cycle reports, and (2) (coverage=doses delivered/target population) and stock consumption data (coverage=SPAQ coblister packs received before the campaign−SPAQ coblister packs left at the end/target population).

Data Collection

Data will be collected by administering questionnaires to the identified respondents in the sampled compounds within the communities. The survey questionnaires will be administered by a trained research team. All surveys will be administered using SurveyCTO, an electronic data collection platform for smartphones, and data will be uploaded to a remote server after each day of data collection. Interviews will be conducted in local languages using the questionnaires provided by the Malaria Consortium, with data collectors translating from the Portuguese questionnaire on the spot and assigning responses to predefined answer categories in SurveyCTO. For the age eligibility indicator, survey respondents may be asked to present a birth certificate or vaccination card to the data collector to verify the child's date of birth. The duration of data collection is expected to last for 7 days during the first week of March 2021.

Data Analysis

Data analysis will be carried out using Stata 16. Coverage will be calculated using the proportion command. Population size weights will be applied using the svy command as appropriate for estimates of coverage indicators when it is not possible to achieve a self-weighting sample. All indicators of interest will

be calculated as proportions by district and an average across both districts.

Availability of Data and Materials

The associated study protocol and data collection tools will be made available upon request from the corresponding author. Quantitative data sets will be available from the corresponding author upon reasonable request after the completion of primary analyses and dissemination of results. Qualitative study data sets will not be available, as they may include identifiable information that could compromise participant identity.

Results

Data collection and analysis from all six objectives will be completed by September 2021.

Discussion

Principal Findings

This study will provide a unique contribution to the evidence on the prevalence of SPAQ resistance in Mozambique and more broadly in the region, and to what extent it may challenge the protection that SMC confers. Furthermore, this first evaluation of SMC implementation in this context will generate insights on the enablers, challenges, perceptions, feasibility, acceptability, quality, and coverage of this intervention in situ. This study is vital, as it is the first time that SMC is implemented in East and Southern Africa.

Recent evidence from the ACCESS-SMC program showed that the protective effectiveness of each monthly treatment was similar to that observed in randomized controlled trials [44,45]. In 2 countries with district health information software-2 databases established before SMC scale-up (ie, The Gambia and Burkina Faso), estimated reductions of 57% and 42% in the number of malaria deaths in district hospitals were determined for the SMC intervention period, and reductions of 53% and 45% in the number of outpatient cases, respectively [8]. Similar reductions were observed in the number of outpatient malaria cases in other countries [8]. These results represent the first large-scale evaluation of SMC implemented by national programs and provide the first evidence of an impact on malaria deaths. Earlier studies in Burkina Faso and Mali showed effects on prevalence [46,47] and cost-saving benefits [9,48].

Molecular markers of SPAQ resistance occurred at a low prevalence in previous studies in the Sahel, consistent with the effectiveness of SMC observed in several case-control studies. However, there is evidence of selection for resistance to SP in parasites sampled from the same age group in the areas where SMC will be implemented for the first time in Mozambique. Therefore, resistance to both SPAQ needs to be monitored via standardized methods, across all regions in Mozambique where SMC is used, to provide early warning of loss of effectiveness.

Limitations

Leakage of SPAQ to older age groups not targeted by SMC programs raises a concern for the development of drug resistance, as doses administered are unlikely to offer sufficient protection against malaria transmission. This also influences the secondary data analysis in the same way; leakage reduces the apparent effect size in the targeted age group.

Conclusions

This research will be a novel contribution to our understanding of whether SPAQ, when used for SMC, can confer a protective effect against malaria in children aged 3-59 months in a region where malaria transmission is seasonal and SP resistance is expected to be high. In addition, the findings from this study will inform future SMC implementation in Mozambique and other countries and potentially enhance the quality of SMC distribution in terms of quality, coverage, and acceptability. Subsequent phases are expected to provide a more comprehensive assessment of the effectiveness and sustainability of SMCs.

Acknowledgments

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Conflicts of Interest

None declared.

References

1. World Malaria Report 2020. World Health Organization, 2020. URL: https://www.who.int/publications/i/item/9789240015791 [accessed 2020-10-01]
2. High burden to high impact: a targeted malaria response. URL: https://www.who.int/malaria/publications/atoz/high-impact-response/en/ [accessed 2020-10-10]
3. World Health Organization. Global Malaria Program. World Malaria Report 2019:232.

4. Moonasar D, Maharaj R, Kunene S, Candrinho B, Saute F, Ntshalintshali N, et al. Towards malaria elimination in the MOSASWA (Mozambique, South Africa and Swaziland) region. Malar J 2016 Aug 18;15(1):419 [FREE Full text] [doi: 10.1186/s12936-016-1470-8] [Medline: 27538990]
5. Aide P, Candrinho B, Galatas B, Munguambe K, Guinovart C, Luis F, et al. Setting the scene and generating evidence for malaria elimination in Southern Mozambique. Malar J 2019 Jun 06;18(1):190 [FREE Full text] [doi: 10.1186/s12936-019-2832-9] [Medline: 31170984]
6. World Health Organization. World Malaria Program. Seasonal malaria chemoprevention with sulfadoxine-pyrimethamine plus amodiaquine in children: a field guide 2013:56.
7. Meremikwu M, Donegan S, Sinclair D, Esu E, Oringanje C. Intermittent preventive treatment for malaria in children living in areas with seasonal transmission. Cochrane Database Syst Rev 2012 Feb 15(2):CD003756 [FREE Full text] [doi: 10.1002/14651858.CD003756.pub4] [Medline: 22336792]
8. ACCESS-SMC Partnership. Effectiveness of seasonal malaria chemoprevention at scale in west and central Africa: an observational study. Lancet 2020 Dec 05;396(10265):1829-1840 [FREE Full text] [doi: 10.1016/S0140-6736(20)32227-3] [Medline: 33278936]
9. Gilmartin C, Nonvignon J, Cairns M, Milligan P, Bocoum F, Winskill P, et al. Seasonal malaria chemoprevention in the Sahel subregion of Africa: a cost-effectiveness and cost-savings analysis. The Lancet Global Health 2021 Feb;9(2):e199-e208 [FREE Full text] [doi: 10.1016/s2214-109x(20)30475-7]
10. Cairns M, Roca-Feltrer A, Garske T, Wilson AL, Diallo D, Milligan PJ, et al. Estimating the potential public health impact of seasonal malaria chemoprevention in African children. Nat Commun 2012 Jun 06;3:881 [FREE Full text] [doi: 10.1038/ncomms1879] [Medline: 22673908]
11. Greenwood B. New tools for malaria control – using them wisely. Journal of Infection 2017 Jun;74:S23-S26. [doi: 10.1016/s0163-4453(17)30187-1]
12. Mahamar A, Issiaka D, Barry A, Attaher O, Dembele AB, Traore T, et al. Effect of seasonal malaria chemoprevention on the acquisition of antibodies to Plasmodium falciparum antigens in Ouelessebougou, Mali. Malar J 2017 Jul 18;16(1):289 [FREE Full text] [doi: 10.1186/s12936-017-1935-4] [Medline: 28720100]
13. Quelhas D, Puyol L, Quintó L, Serra-Casas E, Nhampossa T, Macete E, et al. Impact of Intermittent Preventive Treatment with Sulfadoxine-Pyrimethamine on Antibody Responses to Erythrocytic-Stage Antigens in Infants in Mozambique. Clin Vaccine Immunol 2008 Aug;15(8):1282-1291 [FREE Full text] [doi: 10.1128/cvi.00044-08]
14. Coldiron ME, Von Seidlein L, Grais RF. Seasonal malaria chemoprevention: successes and missed opportunities. Malar J 2017 Nov 28;16(1):481 [FREE Full text] [doi: 10.1186/s12936-017-2132-1] [Medline: 29183327]
15. Pitt C, Diawara H, Ouédraogo DJ, Diarra S, Kaboré H, Kouéla K, et al. Intermittent preventive treatment of malaria in children: a qualitative study of community perceptions and recommendations in Burkina Faso and Mali. PLoS One 2012 Mar 6;7(3):e32900 [FREE Full text] [doi: 10.1371/journal.pone.0032900] [Medline: 22412946]
16. Ding J, Coldiron ME, Assao B, Guindo O, Blessborn D, Winterberg M, et al. Adherence and Population Pharmacokinetic Properties of Amodiaquine When Used for Seasonal Malaria Chemoprevention in African Children. Clin Pharmacol Ther 2020 May;107(5):1179-1188 [FREE Full text] [doi: 10.1002/cpt.1707] [Medline: 31652336]
17. van Lenthe M, van der Meulen R, Lassovski M, Ouabo A, Bakula E, Badio C, et al. Markers of sulfadoxine-pyrimethamine resistance in Eastern Democratic Republic of Congo; implications for malaria chemoprevention. Malar J 2019 Dec 18;18(1):430 [FREE Full text] [doi: 10.1186/s12936-019-3057-7] [Medline: 31852480]
18. Allen EN, Little F, Camba T, Cassam Y, Raman J, Boulle A, et al. Efficacy of sulphadoxine-pyrimethamine with or without artesunate for the treatment of uncomplicated Plasmodium falciparum malaria in southern Mozambique: a randomized controlled trial. Malar J 2009 Jun 26;8(1):141 [FREE Full text] [doi: 10.1186/1475-2875-8-141] [Medline: 19558654]
19. Gupta H, Macete E, Bulo H, Salvador C, Warsame M, Carvalho E, et al. Drug-Resistant Polymorphisms and Copy Numbers in Plasmodium falciparum, Mozambique, 2015. Emerg Infect Dis 2018 Jan;24(1):40-48 [FREE Full text] [doi: 10.3201/eid2401.170864] [Medline: 29260689]
20. Grais R, Laminou IM, Woi-Messe L, Makarimi R, Bouriema SH, Langendorf C, et al. Molecular markers of resistance to amodiaquine plus sulfadoxine-pyrimethamine in an area with seasonal malaria chemoprevention in south central Niger. Malar J 2018 Feb 27;17(1):98 [FREE Full text] [doi: 10.1186/s12936-018-2242-4] [Medline: 29486766]
21. Chico RM, Cano J, Ariti C, Collier TJ, Chandramohan D, Roper C, et al. Influence of malaria transmission intensity and the 581G mutation on the efficacy of intermittent preventive treatment in pregnancy: systematic review and meta-analysis. Trop Med Int Health 2015 Dec 30;20(12):1621-1633 [FREE Full text] [doi: 10.1111/tmi.12595] [Medline: 26325263]
22. Gutman J, Kalilani L, Taylor S, Zhou Z, Wiegand RE, Thwai KL, et al. The A581G Mutation in the Gene Encoding Plasmodium falciparum Dihydropteroate Synthetase Reduces the Effectiveness of Sulfadoxine-Pyrimethamine Preventive Therapy in Malawian Pregnant Women. J Infect Dis 2015 Jun 15;211(12):1997-2005 [FREE Full text] [doi: 10.1093/infdis/jiu836] [Medline: 25564249]
23. Harrington W, Mutabingwa TK, Kabyemela E, Fried M, Duffy PE. Intermittent treatment to prevent pregnancy malaria does not confer benefit in an area of widespread drug resistance. Clin Infect Dis 2011 Aug 01;53(3):224-230 [FREE Full text] [doi: 10.1093/cid/cir376] [Medline: 21765070]

24. Desai M, Gutman J, Taylor SM, Wiegand RE, Khairallah C, Kayentao K, et al. Impact of Sulfadoxine-Pyrimethamine Resistance on Effectiveness of Intermittent Preventive Therapy for Malaria in Pregnancy at Clearing Infections and Preventing Low Birth Weight. Clin Infect Dis 2016 Feb 01;62(3):323-333 [FREE Full text] [doi: 10.1093/cid/civ881] [Medline: 26486699]
25. Okell L, Griffin JT, Roper C. Mapping sulphadoxine-pyrimethamine-resistant Plasmodium falciparum malaria in infected humans and in parasite populations in Africa. Sci Rep 2017 Aug 07;7(1):7389 [FREE Full text] [doi: 10.1038/s41598-017-06708-9] [Medline: 28785011]
26. National Malaria Control Programme MOHM. Procedure Manual. Routine analysis of National Malaria Control Programme data quality 2019:55.
27. World Health Organization. Seasonal malaria chemoprevention (SMC) for plasmodium falciparum malaria control in highly seasonal transmission areas of the Sahel sub-region of Africa. WHO Policy Recommendation 2012:4 [FREE Full text]
28. Antwi GD, Bates LA, King R, Mahama PR, Tagbor H, Cairns M, et al. Facilitators and Barriers to Uptake of an Extended Seasonal Malaria Chemoprevention Programme in Ghana: A Qualitative Study of Caregivers and Community Health Workers. PLoS One 2016 Nov 29;11(11):e0166951 [FREE Full text] [doi: 10.1371/journal.pone.0166951] [Medline: 27898699]
29. Curran GM, Bauer M, Mittman B, Pyne JM, Stetler C. Effectiveness-implementation hybrid designs: combining elements of clinical effectiveness and implementation research to enhance public health impact. Med Care 2012 Mar;50(3):217-226 [FREE Full text] [doi: 10.1097/MLR.0b013e3182408812] [Medline: 22310560]
30. Wolfenden L, Williams CM, Wiggers J, Nathan N, Yoong SL. Improving the translation of health promotion interventions using effectiveness-implementation hybrid designs in program evaluations. Health Promot J Austr 2016 Feb;27(3):204-207. [doi: 10.1071/HE16056] [Medline: 29241482]
31. Lauria M, Fiori KP, Jones HE, Gbeleou S, Kenkou K, Agoro S, et al. Assessing the Integrated Community-Based Health Systems Strengthening initiative in northern Togo: a pragmatic effectiveness-implementation study protocol. Implement Sci 2019 Oct 16;14(1):92 [FREE Full text] [doi: 10.1186/s13012-019-0921-3] [Medline: 31619250]
32. World Health Organization. World Malaria Program. Minutes of the Technical Expert Group on Drug Efficacy and Response 2017 Jun 01:35 [FREE Full text]
33. Centro de Investigação em Saúde de Manhiça. Unpublished data. Unpublished data 2020:1.
34. Ross A, Smith T. Interpreting malaria age-prevalence and incidence curves: a simulation study of the effects of different types of heterogeneity. Malar J 2010 May 17;9:132 [FREE Full text] [doi: 10.1186/1475-2875-9-132] [Medline: 20478060]
35. Venkataramani AS, Bor J, Jena AB. Regression discontinuity designs in healthcare research. BMJ 2016 Mar 14;352:i1216 [FREE Full text] [doi: 10.1136/bmj.i1216] [Medline: 26977086]
36. Marshall M. Sampling for qualitative research. Fam Pract 1996 Dec;13(6):522-525 [FREE Full text] [doi: 10.1093/fampra/13.6.522] [Medline: 9023528]
37. Green J. In: Thorogood N, editor. Qualitative Methods for Health Research. London: Sage Publications; 2009.
38. O'Reilly M, Parker N. 'Unsatisfactory Saturation': a critical exploration of the notion of saturated sample sizes in qualitative research. Qualitative Research 2012 May 17;13(2):190-197 [FREE Full text] [doi: 10.1177/1468794112446106]
39. Rapley TJ. The art(fulness) of open-ended interviewing: some considerations on analysing interviews. Qualitative Research 2016 Nov 07;1(3):303-323 [FREE Full text] [doi: 10.1177/146879410100100303]
40. Arskey H, Knight P. Interviewing for social scientists. London: Sage Publications; 1999.
41. Brocki J, Wearden A. A critical evaluation of the use of interpretative phenomenological analysis (IPA) in health psychology. Psychology & Health 2007 Feb 01;21(1):87-108 [FREE Full text] [doi: 10.1080/14768320500230185]
42. Corbin J, Strauss A. Basics of qualitative research: Techniques and procedures for developing grounded theory. Los Angeles: Sage Publications; 2008.
43. Compaoré R, Yameogo MWE, Millogo T, Tougri H, Kouanda S. Evaluation of the implementation fidelity of the seasonal malaria chemoprevention intervention in Kaya health district, Burkina Faso. PLoS One 2017;12(11):e0187460 [FREE Full text] [doi: 10.1371/journal.pone.0187460] [Medline: 29186137]
44. Konaté AT, Yaro JB, Ouédraogo AZ, Diarra A, Gansané A, Soulama I, et al. Intermittent preventive treatment of malaria provides substantial protection against malaria in children already protected by an insecticide-treated bednet in Burkina Faso: a randomised, double-blind, placebo-controlled trial. PLoS Med 2011 Feb 01;8(2):e1000408 [FREE Full text] [doi: 10.1371/journal.pmed.1000408] [Medline: 21304925]
45. Dicko A, Diallo AI, Tembine I, Dicko Y, Dara N, Sidibe Y, et al. Intermittent Preventive Treatment of Malaria Provides Substantial Protection against Malaria in Children Already Protected by an Insecticide-Treated Bednet in Mali: A Randomised, Double-Blind, Placebo-Controlled Trial. PLoS Med 2011 Feb 1;8(2):e1000407. [doi: 10.1371/journal.pmed.1000407]
46. Diawara F, Steinhardt LC, Mahamar A, Traore T, Kone DT, Diawara H, et al. Measuring the impact of seasonal malaria chemoprevention as part of routine malaria control in Kita, Mali. Malar J 2017 Aug 10;16(1):325 [FREE Full text] [doi: 10.1186/s12936-017-1974-x] [Medline: 28797263]
47. Druetz T, Corneau-Tremblay N, Millogo T, Kouanda S, Ly A, Bicaba A, et al. Impact Evaluation of Seasonal Malaria Chemoprevention under Routine Program Implementation: A Quasi-Experimental Study in Burkina Faso. Am J Trop Med Hyg 2018 Feb;98(2):524-533 [FREE Full text] [doi: 10.4269/ajtmh.17-0599] [Medline: 29260654]

48. Nonvignon J, Aryeetey GC, Issah S, Ansah P, Malm KL, Ofosu W, et al. Cost-effectiveness of seasonal malaria chemoprevention in upper west region of Ghana. Malar J 2016 Jul 16;15:367 [FREE Full text] [doi: 10.1186/s12936-016-1418-z] [Medline: 27423900]

Abbreviations

ACCESS-SMC: Achieving Catalytic Expansion of SMC in the Sahel
AQ: amodiaquine
dhfr: dihydrofolate reductase
dhps: dihydropteroate synthetase
FGD: focus group discussion
pfcrt: Plasmodium falciparum chloroquine resistance transporter gene
pfmdr1: Plasmodium falciparum multidrug resistance gene 1
RDT: rapid diagnostic test
SMC: seasonal malaria chemoprevention
SP: sulfadoxine-pyrimethamine
SPAQ: sulfadoxine-pyrimethamine and amodiaquine
WHO: World Health Organization

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Protocol

Development and Evaluation of a Decision Aid to Support Patients' Participatory Decision-Making for Tumor-Specific and Palliative Therapy for Advanced Cancer: Protocol for a Pre-Post Study

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Abstract

Background: To support advanced cancer patients and their oncologists in therapeutic decisions, we aim to develop a decision aid (DA) in a multiphased, bicentric study. The DA aims to help patients to better understand risks and benefits of the available treatment options including the options of standard palliative care or cancer-specific treatment (ie, off-label drug use within an individual treatment plan).

Objective: This study protocol outlines the development and testing of the DA in a pre-post study targeting a heterogeneous population of advanced cancer patients.

Methods: In the first step, we will assess patients' information and decisional needs as well as the views of the health care providers regarding the content and implementation of the DA. Through a scoping review, we aim to analyze specific characteristics of the decision-making process and to specify the treatment options, outcomes, and probabilities. An interdisciplinary research group of experts will develop and review the DA. In the second step, testing of the DA (design and field testing) with patients and oncologists will be conducted. As a last step, we will run a pre-post design study with 70 doctor-patient encounters to assess improvements on the primary study outcome: patients' level of decisional conflict. In addition, the user acceptance of all involved parties will be tested.

Results: Interviews with cancer patients, oncologists, and health care providers (ie, nurses, nutritionists) as well as a literature review from phase I have been completed. The field testing is scheduled for April 2021 to August 2021, with the final revision scheduled for September 2021. The pre-post study of the DA and acceptance testing are scheduled to start in October 2021 and shall be finished in September 2022.

Conclusions: A unique feature of this study is the development of a DA for patients with different types of advanced cancer, which covers a wide range of topics relevant for patients near the end of life such as forgoing cancer-specific therapy and switching to best supportive care.

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KEYWORDS

decision aid; neoplasms; palliative care; clinical trials; longitudinal study

Introduction

Background

Patients with advanced cancer, when most standard therapies have been administered, are confronted with complex decisions about the further course of their treatment. They might face such decisions as (1) forgoing cancer-specific treatment and focusing on best supportive care or (2) off-label treatment within an individual treatment plan or possible inclusion in early clinical trials (ie, phase I and II studies).

Such decisions are complex and require the consideration of patients' decision-making values and treatment preferences as well as weighing different factors such as patients' quality of life, therapy side effects, and uncertainty about possible treatment outcomes [1,2]. We use the term decision-making values for the importance that patients place on the options' positive and negative aspects when considering a specific decision. Treatment preferences refer to the degree to which each patient prefers each treatment option [3]. Treatment preferences (ie, regarding family involvement in decisions or the extent of participation in decision making) and patients' decision-making values (ie, for quality or length of life) might differ considerably [3]. Current guidelines on advanced care planning [4] emphasize the importance of consideration and timely integration of patients' treatment preferences and decision-making values in decision making in advanced cancer [3,5,6].

Furthermore, compounding the decisional process is that, on the one hand, oncologists often avoid prognosticating and eliciting patients' treatment preferences for or against anticancer therapy and decision-making values [5-9]; on the other hand, many patients tend to have an inaccurate perception of the curability of their cancer [5,10-13]. A multicenter international study conducted with 1390 patients with advanced cancer demonstrated that 55% of patients receiving palliative care thought that their cancer was curable [10]. The same is true of patients participating in clinical trials. Many of them tend to have therapeutic misconception. They misunderstand a trial's purpose and express "unrealistic optimism" regarding its benefits [14-18]. A study with 301 cancer patients with gastrointestinal, gynecological, and lung cancers showed that more than 80% of patients in phase 1 clinical trials expected clinical benefits (ie, tumor shrinkage) and 10% even hoped for a cure [18].

Against this background, shared decision making (SDM), an approach based on patients' engagement in the decisional process, becomes of particular importance in advanced cancer planning [11]. SDM has been increasingly advocated as it elicits patients' decision-making values and treatment preferences. It permits informing patients about treatment benefits and harms and involving patients more actively in care planning, helping them weigh information based on their preferences [2].

Despite the fact that patients with advanced cancer might differ in their coping with disease [12], need for information, and preferred level of involvement in decisions [13,19], there is an urgent need to facilitate SDM and systematically support patients and oncologists in arriving at evidence-informed and value-congruent decisions as these decisions have a major impact on patients' last months of life [2].

One of the existing possible ways to facilitate SDM is using patient decision aids (DAs). DAs are tools (pamphlets, videos, web-based or paper-based materials) that aim to help patients to participate in decision making. They provide information about different treatment options and patient-related advantages and disadvantages, help patients clarify their health care goals, and elicit and integrate their decision-making values in the decision-making process [20,21].

Various systematic literature reviews on DAs for people facing treatment or screening decisions demonstrated that the use of DAs can improve SDM, aligning decisions with the preferences of patients without negative impact on clinical outcomes. DAs have been shown to increase patients' involvement in decision making in various clinical domains as well as to improve patients' informed choices and to facilitate challenging discussions about goals of care and advanced care planning. Studies show that using DAs can contribute significantly to reducing decisional conflict and make patients feel more confident to make decisions [20,22-24]. The use of DAs has been shown to be associated with patients' increased knowledge of treatment options [20]. Patients who used DAs had a more accurate risk perception and more realistic expectations of therapy outcomes [18,25,26]. For example, a study conducted with 40 hospitalized patients with advanced cancer demonstrated that a video DA reduced patients' decisional uncertainty while increasing patients' knowledge and readiness for palliative radiation therapy [27]. Furthermore, they could contribute to patients' satisfaction with decisions and minimize patients and caregivers' regret and blame on physicians [20,26,28-31].

However, many of the available DAs target patients considering therapy for early-stage cancer, cancer screening, or decisions about genetic testing and rarely target patients considering the management of advanced cancer [26,32-35].

There are only a few DAs for advanced cancer patients even though recommendations for their systematic development have been published [21]. Existing DAs are limited in their use by a certain type of cancer (ie, colorectal cancer or prostate cancer [36,37]) or target certain treatment scenarios (ie, participation in early phase clinical trials [2], use of standard systemic cancer therapies [38,39], or initial treatment after diagnoses [40]). To our knowledge, one patient communication aid in the Dutch language has been developed that targets clarification of patients' preferences and encompasses a question prompt list that can be used by patients with advanced cancer regardless of tumor type when talking to their oncologist [11].

Study Objectives

Against this background, we aim to develop a patient DA with a patient-centered design to support advanced cancer patients

and their oncologists in decision making about anticancer treatment in situations where standard anticancer treatment lines have been exhausted. The DA will be aimed at a heterogeneous population of cancer patients, independently of cancer type as it will focus on situations that are generic for patients when standard treatment options are about to be exhausted. These decisions are typically similar for all cancer types and are about forgoing cancer-specific therapy and switching to best supportive care. The alternative is an additional tumor-specific treatment as off-label treatment, experimental individual treatment plan, or treatment within a clinical trial. With such a generic DA, we aim to facilitate routine initiation of the end-of-life discussions that still occur too late in the course of disease. Second, we aim to develop a clinically feasible implementation plan for the DA.

Furthermore, we aim to assess the acceptance and test potential effects of the developed DA on (1) oncologist-patient interaction (ie, satisfaction with the oncologist-patient interaction), (2) patient involvement in decision making, and (3) level of decisional conflict and uncertainties about choices.

Conceptional Framework

The novelty of this study and the planned DA is that it targets patients with different types of advanced cancer in order to provide them with information and help them decide about the continuation or forgoing of tumor-specific therapy in clinical situations, in which there is no further standard tumor-specific therapy available but treatment is available as off-label treatment or part of a trial. Hence, the DA aims to facilitate SDM, which is essentially the communication of the best-available research evidence on benefits and harms of options and the clarification of patients' treatment preferences in relation to this information [41]. Based on a consensus of experts in the field [41], SDM has been defined in terms of 3 broad phases: (1) team talk: work together, describe choices, offer support, and ask about patients' goals; (2) option talk: discuss alternatives using risk communication principles; and (3) decision talk: get to informed preferences, make preference-based decisions.

The DA in our project is used to influence phase 1 of the SDM, which will probably affect the health care provider-patient communication in phases 2 and 3 as well. Based on the available body of randomized trials on clinical DAs [20], we primarily expect decreased patient decisional conflict and an increased feeling of being informed. Although the impact of DAs on professional performance seems limited overall, the use of the DA with patients with advanced cancer may also reduce intensive treatment. While we will measure quality of life in our study, we do not expect changes as a result of the use of the DA based on the available research evidence [20]. Given the practice-based character of the study, we did not specify and measure psychological factors and processes that may be affected by the DA, such as coping mechanisms.

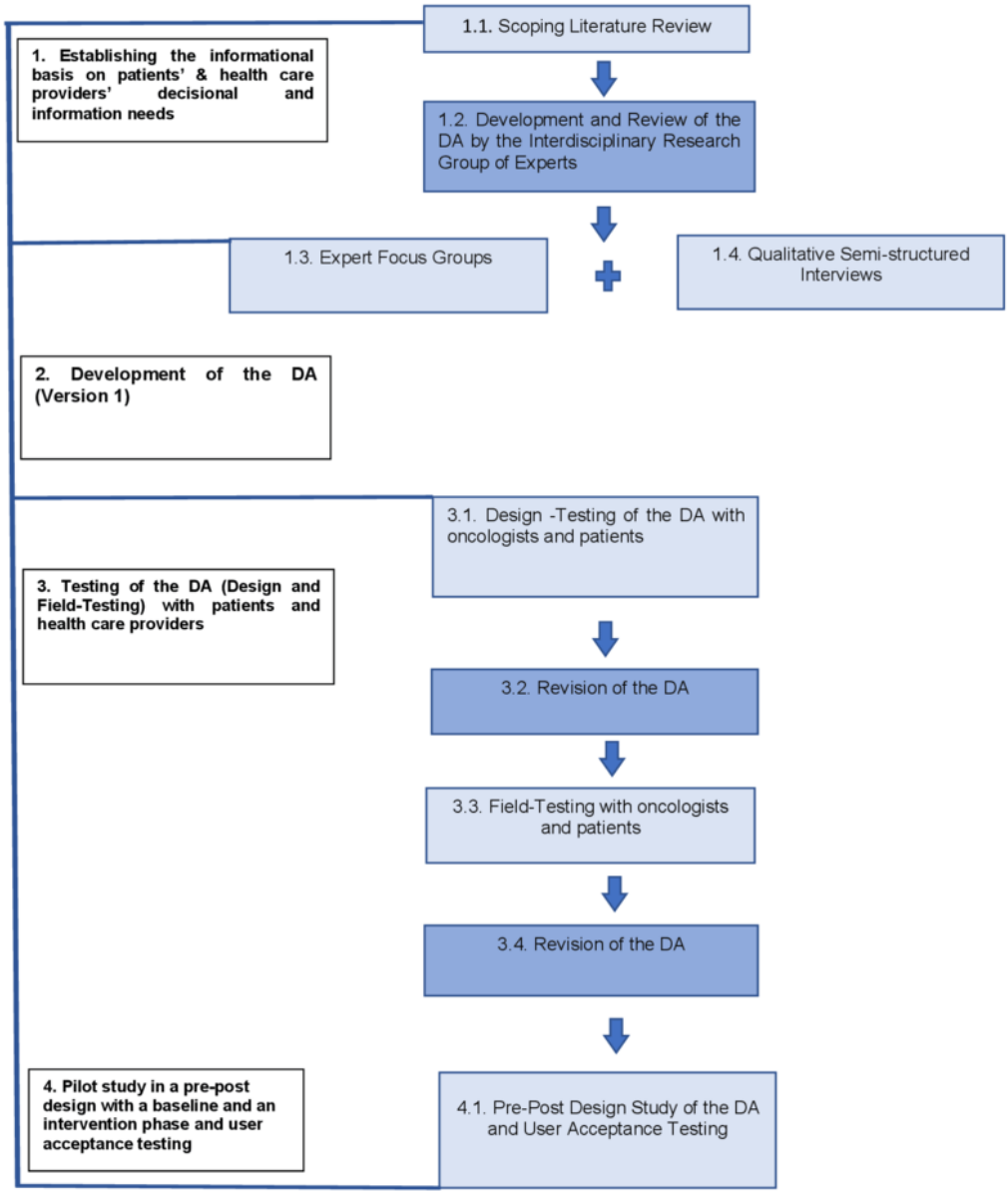
Methods

Overview

We will use a systematic stepwise development process for the DA based on the International Patient Decision Aid Standards (IPDAS) collaboration guidelines, which are particularly relevant to "preference-sensitive" decisions [21,42]. The process will include the following key steps of DA development and testing: (1) establishing the informational basis for patients' and health care providers' decisional and information needs, (2) development and review of the DA by the interdisciplinary research group and presenting it in research colloquiums, (3) testing of the DA (design and field testing) with patients and health care providers (understandability, acceptance, usability, and feasibility testing) as well as usage instruction with health care providers, (4) pilot study in a pre-post design with baseline and intervention phases to evaluate the DA with regard to 3 objectives of feasibility and pilot research [43]: testing procedures, estimating recruitment and retention, and determining sample size. The first 2 objectives primarily relate to feasibility, while the third objective relates to the effectiveness of the intervention (the smaller the potential effects, the higher the sample size in a definitive trial needs to be). For the third objective, we have included patient-related outcomes and have planned to explore the potential effects of the DA in a pre-post comparison. The intervention phase will include user acceptance testing with oncologists and patients.

The model of the DA development process based on the model by Coulter et al [44] is presented in Figure 1.

Figure 1. Overview of the decision aid (DA) development process based on the model by Coulter et al [44].



Study Setting

The study is bicentric and will be carried out at the Department of Medical Oncology, National Center for Tumor Diseases (NCT), Heidelberg University Hospital, Heidelberg, Germany and at the Department of Internal Medicine II (Palliative Care), University of Jena, Jena Germany. Patients will be recruited in Heidelberg (oncology) and Jena (specialized palliative care). This study was approved by the Ethics Committee of the Medical Faculty of the University of Heidelberg and University of Jena.

Establishing the Informational Basis on Patients' and Care Providers' Decisional and Information Needs

As a first step in our study, we plan on assessing patients' and care providers' decisional and information needs as well as care providers' and patients' decision-making pathways. We aim to analyze specific characteristics of the decision-making process in patients with advanced cancer, to work out the content, features, and best way to deliver the DA.

Scoping Literature Review

Substantial evidence is already available on the content of decisions made by advanced cancer patients and their caregivers, as well as on their treatment preferences that influence such decisions. In addition, as mentioned earlier, some DAs have already been developed for this context. To provide an overview of the current state of research, we aim to conduct a scoping review as a first step in this study.

The objective of this scoping review is twofold: first, to assess the current state of research literature, as well as the grey literature, on patients and caregivers and their priorities regarding choices on advanced cancer management in the last

months of life. This will also involve examining already existing DAs in this particular field. Second, we aim to systematically analyze studies on DAs for patients with advanced cancer in order to gather information on technical issues, such as the design of DAs or information on the facilitating and inhibiting factors in design and implementation. For this purpose, both development and evaluation studies on DAs will be reviewed and their quality assessed using the criteria from the IPDAS Collaboration [21].

The scoping review will be conducted jointly by research associates from the department of Health Economics and Health Care Management of Bielefeld University, Institute for History and Ethics of Medicine of Martin Luther University Halle-Wittenberg, and Department of Medical Oncology of the NCT, to ensure that value-related aspects of decision making will be covered as part of the review. We will search pertinent databases (Medline, PsycInfo, Web of Science, DIMDI, Euroethics) up to December 2019 for relevant publications in the English or German language. Various keywords for synonyms of decision making as well as cancer and end-of-life care will be used to include relevant studies. The findings of this scoping review will be reported according to the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-analysis Extension for Scoping Reviews) guidelines [45].

In order to ensure transparency and consistency in the reporting of results, this scoping review will follow the methodological framework for scoping reviews developed by Arksey and O'Malley [46] with the proposed improvements by Levac et al [47] and Peters et al [48]. This framework consists of the following stages: (1) identifying the research question; (2) identifying relevant studies; (3) selecting studies; (4) charting the data; (5) collating, summarizing, and reporting the results; (6) expert consultation.

The insights from this scoping review will inform the subsequent focus groups with clinical experts and semistructured interviews with patients.

Establishment of the Interdisciplinary Research Group of Experts

The expert group will consist of the team members of our research group (n=4) who will have mostly a supervision function and advisory function. It will include an oncologist, leader of 1 palliative care unit, leader of a medical ethics department, and leader of a department in health service research. Members of this group will not conduct the field research but will serve as active research team members who guide, review, edit, and approve each step of the research process. Their major role is to guide the overall study and to ensure the patient DA will be patient-centered, meaningful, understandable, usable, and feasible for rapid implementation.

Expert Focus Groups

As a second step, we plan to conduct 3 focus group discussions. A focus group interview is a semistructured discussion with a group of experts where different topics can be explored in participants' interactions with each other [49]. The successful implementation and follow-up use of the DA depend on oncologists' willingness to discuss the DA together with the patients during the consultations. Furthermore, based on their experiences, oncologists can shed light on many important aspects of patients' decision making. Thus, their perspectives seem to be essential for the development of the DA.

The major aim of our focus group interviews is to identify existing difficulties in discussing tumor-specific and palliative therapy with patients, implementation strategies, and possible barriers as well as the best timing for using the DA.

The focus group interviews will be used to generate information on potential factors relevant to the sampling and content of the semistructured face-to face interviews with patients. When planning the focus groups and later reporting on the results, we will refer to the COREQ (consolidated criteria for reporting qualitative research) checklist for in-depth interviews and focus groups that covers all important components of a focus group study design [49].

Participants, Setting, and Data Collection

Participants (5-8 persons per focus group) will be recruited at both study sites (Jena and Heidelberg). Three focus groups are planned: 2 focus groups will include oncologists with different levels of working experience, and the other will be conducted with a multidisciplinary team of support services. We plan to include nurses, specialists from an ambulatory palliative care team, nutrition, counseling social work, and psycho-oncology for this focus group. Participants will be purposely sampled to represent different levels of working experience, age, and gender to reflect a wide range of opinions. Participants will be approached by telephone by a study nurse. The focus groups will last approximately 90 minutes (each focus group).

Development of the Interview Guide

An interview discussion guide will be developed by a multidisciplinary team including expertise from clinical oncology, social sciences, and medicine ethics and pretested with 2 oncologists and 2 nurses before being used in the subsequent focus groups. The primary results of the literature review will be incorporated into the development of the interview guide. Three major topics for the focus groups will encompass the most important aspects that could be helpful for the development of the DA. Every topic will have several questions in order to gain deep insight into the decision-making process in advanced cancer regarding the context, use, and implementation of DAs. Furthermore, based on the literature review, we decided to develop a preliminary DA prototype in order to discuss it at the end of each focus group. This preliminary prototype will include the most important aspect of a DA and will be used as a trigger for a discussion about the implementation and development of our DA. The aim is to figure out which aspects identified in the literature review might be useful for our DA. An iterative process will be used so that the information derived from the first focus group will be analyzed and the interview guide will be revised and adjusted for the next focus groups.

The interview guide topics are presented in Textbox 1.

Textbox 1. Focus group topics.

1. Questions on the decision-making process in advanced cancer about:
   - limiting cancer-specific treatment, possible off-label drug use, and integration of supportive care
   - patients' inclusion in early clinical studies (important factors for oncologists and patients)
   - clinical scenarios in advanced cancer care
2. Questions on the decision aid (DA), including:
   - context and form of the DA
   - time of use
   - implementation barriers and implementation strategy
3. Discussion of the DA prototype (a DA prototype has been developed before the focus group interviews and will be shown at the end of the focus group for discussion)

Analysis of the Focus Groups

Interviews will be audiotaped, transcribed verbatim, and analyzed according to qualitative inductive content analysis as described by Sandelowski [50]. We decided to use this approach as there is not much research on DAs that are not limited to a certain cancer type in advanced cancer near the end of life [21,36,37]. As this content might differ considerably from usual cancer DAs, we favored a more open approach without using the pre-existing categories for analysis as suggested by deductive content analysis. Inductive content analysis includes open coding, creating categories, and themes.

In the first step of open coding, interviews will be analyzed "sentence by sentence" while codes will be written in the text. In the next step, the codes will be categorized. After this, the lists of categories will be grouped into themes [51]. The coding will be conducted by 2 researchers (KL and BS) who will discuss coding disagreements and refine the coding system. To minimize the personal bias and reflexivity of 2 single researchers, we plan to discuss results from every coding round in our interdisciplinary research team. Furthermore, the final results and possible input for the development of the DA and for the patients' interviews will be discussed in our research team. This analysis will be conducted with the help of the data analysis software MAXQDA (VERBI GmbH, Berlin, Germany).

Qualitative Semistructured Interviews

The aim of qualitative interviews is the assessment of patients' decision-making values and treatment preferences associated with the decision-making process when standard systemic therapies have been exhausted, as well as factors contributing to the decisional conflict. As the interview topics are about forgoing cancer-specific treatment and are very sensitive for patients, a qualitative approach has been selected as it mostly suited for exploring sensitive topics [52]. In spite of the fact that family members play an important role in decision making in advanced cancer, we decided to exclude them from interviews due to difficulties in the recruitment process.

Participants, Setting, and Data Collection

Patients will be recruited at the NCT (University Hospital Heidelberg) in the in- and outpatient settings. We will include adult patients with incurable, stage IV disease (prostate, breast, pancreatic, stomach, or colorectal cancer) in an advanced treatment stage (prognosis <12 months and/or standard palliative care only is considered). These entities cover a large proportion of cancer burden. In addition, these are the entities covered by the outpatient clinics of the Department of Medical Oncology of the NCT. These inclusion criteria make it possible to interview patient groups who are potential users of a DA at an advanced cancer stage when decisions about forgoing cancer-specific treatment are usually discussed with patients. Furthermore, we will try to include patients who have already made at least 1 of the 3 decisions. However, the focus will be on the orientation towards the physical and mental condition of patients. An experienced oncologist will be in charge for the recruitment and will decide if patients' psychological states will allow them to participate in the interview. If a patient has physical symptoms (ie, pain) or his or her physical condition worsens, he or she will not be asked to participate in the interview. Included patients will be monitored by their oncologists after the interview, and if necessary, in case of distress, a psycho-oncology team will be contacted to support the patient. Patients must have an adequate level of the German language and be willing and able to give informed consent for participation in the study.

Patients that already are under standard palliative care only, are cognitively impaired, have extreme anxiety or distress, or have a severe comorbid illness, excluding antitumor treatment as assessed by the treating oncologist, will be excluded from the study.

Interviews will be conducted until informational saturation will be reached. We will transcribe and code interviews one by one in order to control the process data acquisition and if necessary, we will adjust the interview guide. Furthermore, this will allow us to control whether saturation has been reached. Regarding saturation, we understand this as the point in our research process when little or no new information emerge in from the data collection and analysis [53]. We opted for this prolonged process as the research is conducted with a very vulnerable patient group who are near the end of life and who have different health conditions.

Thereby, we aim to maximize variation in the purposeful sampling, considering relevant factors that might have an impact on interview results: age, level of education, gender, residential environment (eg, living alone), physical distress related to prior treatment, treatment duration, and availability of experimental treatment. A minimum number of 20 interviews will be performed to address the likely heterogeneity of the underlying cancer entities.

Development of the Interview Guide

Based on the results of the scoping review and focus groups, the semistructured interview guide will be developed jointly with the researcher of medical ethics and health economics and health care management and involve representatives from oncology to ensure that ethically relevant as well as clinical aspects will be included. As this patient group is very vulnerable due to their far advanced cancer disease and being near the end of life, the interview needs a sensitive approach. We will work with a case scenario in which a similar treatment situation for an advanced cancer patient will be described. Working with a case scenario will help to avoid confronting patients directly with sensitive questions that they might not feel comfortable disclosing or might even escape their own awareness but at the same time will help to explore patients' treatment preferences as well as knowledge about decision alternatives and corresponding values. For practical reasons, we decided to use only one case scenario in order not to burden patients with interviews that are too long. The wording will be as neutral as possible in order to avoid potential influences on the patients' thinking processes. We aim to use the case scenario as an entry point into the interview and then ask the patients about their own decision making if they demonstrate a willingness to do so during the interview.

The case scenario and the interview topics are presented in Textbox 2. The questions for the interviews will be formulated to ensure patient-centered and literary-sensitive language and will be pretested in pilot interviews with some patients (n=3). After a test with patients and discussion of the results in our expert groups, the interview guide will be improved so that the interview guide can be elaborated based on the patients' viewpoints and experiences. Trained research personnel in social sciences and medical ethics will conduct the face-to-face interviews. The interviews will last approximately 30-60 minutes each.

Textbox 2. Topics for patients' interviews.

Case scenario about an advanced cancer patient facing decision of treatment limitation: "A 64-year-old female patient received a diagnosis of colorectal cancer with metastasis 4 years ago. The tumor was operated but, in some time, came back. At the moment — like nearly continuously for 3.5 years — she has been treated with chemotherapy. Now the patient has found out that the cancer has gotten worse and that the therapy is not effective anymore. Further cancer-specific treatment could be off-label drug use within an individual treatment plan or inclusion of the patient in an early clinical trial, where a new drug will be tested. However, these treatment options have uncertain outcomes and unclear risks."

There are the following possible scenarios for this patient: (1) forgoing cancer-specific treatment and switching to standard palliative care or (2) individual off-label drug use or inclusion in a clinical trial.

1. Questions on this case scenario regarding the decision-making process about forgoing cancer-specific therapy (ie, If you put yourself in the position of the patient, what information would you need to make a decision?)
2. Questions on patients' treatment preferences and decision-making values
3. Questions on the decision aid: context, form, and time of use of a decision aid

Analysis of Qualitative Interviews

The analysis of the qualitative interviews will be conducted analogous to the focus groups (see Analysis of the Focus Groups).

Development of a DA (Version 1)

Based on the scoping literature review, expert focus groups, and qualitative semistructured interviews, a prototype version of the DA will be developed following the criteria for developing DAs provided by the IPDAS [21]: assessment of users' needs to discuss options (results of the literature review, focus groups, and interviews), presenting information in a balanced manner, using plain language (design testing), and field testing [21]. It should be emphasized that deviations from the IPDAS could be possible following the qualitative part of our study.

We anticipate that the DA will encompass treatment options (cancer-specific treatment [ie, off-label use of therapies] vs standard palliative care) with risks and benefits as well as preferences and other factors that are associated with decisions in advanced cancer care.

Due to the proposed generic use of the DA (various tumor entities with a respective variance of options), the rapid development of therapies, and evolving clinical and scientific knowledge, we refrained from providing explicit evidence in the DA. The prognostic information will be added personally by oncologists during the patient-oncologist consultation. To guide the decision conversation and allow for an individually tailored approach, the preference of patients about how much information they like to receive and how much they like to be involved in the decision is assessed as part of the DA.

We are planning a paper-based DA that is introduced to the patient and his or her relatives by an oncologist at the moment that a decision needs to made for or against (continued) oncological treatment in the trajectory of advanced cancer patients. This first draft will be reviewed by the steering group, consisting of 3-5 experts from oncology, medical ethics, and the social sciences to assess the DA in terms of its content and design.

Furthermore, we plan to develop a usage instruction for oncologists. It aims to give indications for oncologists about the timing for DA use, discussion of the DA with patients, and the documentation of the discussion with patients.

Testing of the DA (Design and Field Testing) With Patients and Health Care Providers

The testing of the DA will include 2 steps. In the first step, we will test the design of the DA with potential users in a controlled environment. In the second step, the DA will be field-tested with patients and oncologists in a real clinical situation, and we will focus on confirming the feasibility of the DA as used in clinical practice. Additionally, the DA usage instruction will be tested with oncologists.

Design Testing of the DA

In the second project phase, the developed prototype of the DA will undergo a design test. The aim of this testing is to assess the understandability, acceptability, feasibility, and attractiveness of the prototype. Testing will be conducted using face-to face interviews with oncologists (at least 2-3) and cancer patients (at least 6-8) who have been faced with the decision of continuing tumor-specific therapy in the past. Using a think-aloud technique [54] with participants going through the DA as if in the actual decision situation, information about comprehensibility of terms and diagrams used, attractiveness, and manageability of the DA will be elicited from participants' reactions. Additional questions cover the participants' opinions of the length, design, and understandability as well as the content of the DA. Moreover, participants will be asked to provide recommendations for possible improvements of the DA. The interview will last approximately 20-30 minutes. Interviews are conducted in the preferred place of the participants (eg, clinic, home) to ensure a comfortable environment where participants can concentrate on the task. Interviews are conducted once with each participant.

Revision of the DA

Based on the results obtained in the alpha testing, we aim to optimize the prototype draft. After every 2-3 interviews, the DA will be updated based on the feedback of the participants. Alpha testing is completed if there are no further adaptations necessary.

Field Testing

In the field-testing phase, the feasibility of the DA will be evaluated in "real-world" settings by 16-20 patients and 4-6 oncologists who were not involved in the design phase. Feasibility is operationalized in terms of (1) time required for use and (2) acceptability for patients and oncologists. We will conduct qualitative interviews with patients and oncologists using the following questions:

- What is the best time to use this DA?
- What is the best way to use the DA by oncologists and patients?
- Was the DA helpful to make a treatment decision?
- What did you find good about the DA?
- How do you think the DA could be improved?
- What impact did the DA have on the length of the consultation?
- Would you recommend using this DA? (patients); When would you use the DA in the future? (oncologists)

Each interview will last approximately 20-30 minutes. Qualitative data will be thematically analyzed. The analysis will be conducted analogous to the qualitative analyses described in the qualitative interviews and focus groups.

Revision of the DA

After every 3-4 interviews, the DA will be revised based on the feedback from the participants. Additionally, relevant observations and feedback are summarized in a guide for use. If necessary, another round of field testing will be conducted. Field testing is completed if, based on the feedback after at least 3 rounds, there are no further adaptations of the DA necessary. Based on the results from field testing, the DA will be revised once again by an expert group, and a final version will be developed.

Pre-Post Study of the DA and its Acceptance Testing

In the last project phase, we will run a pre-post study of the DA. It has 2 measurement phases: baseline and intervention. The aim of this study is to examine the potential effects of the DA on patients' knowledge, behavioral changes, and clinical outcomes and to test its acceptance. The Medical Research Council Framework for developing and evaluating complex interventions, which has guided our study, specifies 3 objectives for feasibility and pilot research [43]: (1) testing procedures, (2) estimating recruitment and retention, and (3) determining the sample size. The first 2 objectives primarily relate to feasibility, while the third objective relates to the effectiveness of the intervention (the smaller the potential effects, the higher the sample size needs to be in a definitive trial). For the third objective, we have included patient-related outcomes and plan to explore the potential effects of the DA in a pre-post comparison.

Design and Settings

First, patients will be recruited in a baseline phase lasting 4 months to observe usual care without using the DA. It means that oncologists will inform patients about further treatment options for cancer-specific therapy, side effects, and potential benefit, but they will not explicitly address that best supportive care would also be an option and will not use a decision support tool for eliciting patient preferences and assisting in decision making. The baseline phase will be followed by an intervention phase lasting 6 months. Oncologists and patients will use the DA in the same situation (change of treatment needs to be discussed with the patient because of disease progression, treatment toxicity, or other reasons). A minimum of 40 doctor-patient encounters will be included in the 4-month baseline, and 40 doctor-patient encounters will also be included in the 6-month DA intervention phase. The whole sample will encompass 80 doctor-patient encounters. The planned sample size is largely determined by the feasibility of recruiting patients within the available project duration.

Measurements

The potential effect of the DA will be evaluated by testing the improvements on the primary outcome for our study level of decisional conflict. Level of decisional conflict will be measured with the Decision Conflict Scale [55] that assesses patients' perceptions of uncertainty, modifiable factors contributing to uncertainty, and ultimate satisfaction with the choice. It is one of the most robust and validated instruments to test the impact of DAs in end-of-life decision making [56]; We assume that the Decisional Conflict Scale score will decrease for the patients who use the DA.

Furthermore, we aim to assess the patients' involvement in decision making, certainty about choice, and satisfaction with the oncologist-patient interaction as exploratory endpoints. Patients' involvement in decision making will be assessed with the German questionnaire on shared decision making (PEF-FB-9) [57]. The trade-off between patients' preferences for quality and length of life will be assessed with the validated German version of the Quality-Quantity Questionnaire [1]. The preferred role of the patient in decision making will be assessed with the German version of the Control Preference Scale [58]. Satisfaction with the oncologist-patient interaction will be assessed using the validated Questionnaire on the Quality of Physician-Patient Interaction (QQPPI) [59]. Effect on hope (German version of the Herth Hope Index [60]), anxiety (EQ-5D-5L [61]), quality of life (EORTC QLQ-C30 [62]), and documentation of patient preferences will be measured.

Description of the measures and their psychometric properties, scoring, and interpretation are provided in Table 1.

Such determinants of quality of palliative care as time of integration of specialized palliative services into care, aggressiveness of therapy (anticancer treatment <14 days before death), and place of death will be recorded.

During data collection, patients might have changes in mental status (ie, develop depression or cognitive problems) as well as experience changes in decision making. The study physician involved with data collection will document all possibly relevant factors.

The questionnaires will be completed by patients and oncologists before and after the intervention and will take approximately 15-20 minutes to complete. All assessments will be conducted in German.

Table 1. Description of the measures and their psychometric properties, scoring, and interpretation.

Outcome	Instrument	Scoring and interpretation
Level of decisional conflict	Decision Conflict Scale	The German version of the Decision Conflict Scale demonstrated good psychometric properties. The internal consistency was found to be high (Cronbach=.96). It has 5 subscales with a total of 16 items and 5 response categories, ranging from 0 (strongly agree) to 4 (strongly disagree). The total score is calculated in the following way: The 16 Items are (1) summed, (2) divided by 16, and (3) multiplied by 25. Scores range from 0, no decisional conflict, to 100, extremely high decisional conflict.
Patients' involvement in decision making	Questionnaire for participatory decision making (PEF-FB-9)	The German questionnaire on shared decision making "Der Fragebogen zur Partizipativen Entscheidungsfindung" (PEF-FB-9) demonstrated high internal consistency (Cronbach=.93). It has 9 items scored on a 6-point Likert scale, ranging from 0 (not at all) to 6 (fully correct). The score is created by adding all items (range 0-45 points). A higher score means more shared decision making.
Trade-off between patients' preferences for quality and length of life	Quality-Quantity Questionnaire	The validated German version of the Quality-Quantity Questionnaire consists of 9 items in 2 preference dimensions: Q(uality) of life (QL) and L(ength) of life (LL). The scales demonstrated good and acceptable internal consistency (Cronbach=0.71 for LL and .59 for QL). Patients indicate how strongly they agree or disagree with the statements on a 5-point Likert scale. High scores on the quantity or quality scale indicate the importance of the length or quality of life, respectively.
Preferred role of the patient in decision making	Control Preference Scale (CPS)	The preferred role of the patient in decision making will be assessed with the German version of the CPS. It is a valid and reliable measure of preferred roles in medical decision making. It consists of 5 statements (A, B, C, D, E) that each portrays a different role in treatment decision making. For analysis, a categorical variable, which is the person's most preferred role in treatment decision making, will be created. Preference orders will be reclassified into Active (A, B), Collaborative (C), and Passive (D, E).
Satisfaction with the oncologist-patient interaction	Quality of Physician-Patient Interaction (QQPPI)	The German version of the validated QQPPI — "Fragebogen zur Arzt-Patienten-Interaktion" (FAPI) — showed very good reliability (Cronbach=.97). It has 14 items rated on a 5-point scale (range: 1 [I do not agree] to 5 [I fully agree]). The total score is calculated as a mean of all 14 items. The lowest score (1) indicates the lowest quality of physician-patient interaction, and the highest (14) indicates the highest quality of physician-patient interaction.
Effect on hope	German version of the Herth Hope Index (HHI-D)	The HHI-D has satisfactory reliability (Cronbach=.82). It has 12 items rated on a 4-point Likert scale that ranges from 1 (strongly disagree) to 4 (strongly agree), with items #3 and #6 reverse-coded. The scale has 1 global score that ranges from 12 to 48. Higher scores indicate more hope.
Effect on patients' quality of life	EORTC QLQ-C30	The EORTC QLQ-C30 questionnaire is widely used to measure the quality of life of cancer patients. The QLQ-C30 has a global health status scale, 5 functional scales, and 3 symptom scales. High scores on the functional scales mean healthy functioning. A high score for global health status means a higher quality of life. A high score on the symptom scales indicates a high level of problems. Scores for all scales and single items range from 0 to 100. The questionnaires will be interpreted following the official guidelines of the EORTC.
Effect on patients' anxiety	Anxiety EQ-5D-5L	The EQ-5D-5L, a preference-based measure of general health status, consists of 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), each with 5 levels of problems: 1=no, 2=slight, 3=moderate, 4=severe, and 5=extreme or unable to perform the task. The anxiety/depression dimension of the EQ-5D-5L will be used to detect anxiety and depressive symptoms.

User Acceptance Testing With Oncologists and Patients

A variety of factors can affect users' acceptance of a DA. Among these factors, users' perceptions and expectations are the key factors that influence their acceptance. Therefore, we aim to survey the oncologists' and patients' acceptance of the DA. The acceptance testing will be conducted during the intervention phase with patients and oncologists who will be caring for the patients in the pre-post study. The major aim is to assess oncologists' perceptions of the usefulness (how useful oncologists find the DA), willingness to use the DA in daily routine with patients (how comfortable they would be to use the DA with patients), willingness or readiness to use it in clinical practice (how likely they would use it within the next 5 months), and perceived need for the DA. In addition, the patients' perceptions of usefulness and willingness to use the DA during consultations with their oncologists will be assessed. The oncologists who were involved in the development of DA will be excluded from acceptance testing.

Measurements

In order to access oncologists' acceptance of the DA, we plan to use the German version of the Ottawa Acceptability of Decision Rules Instrument (OADRI) [63]. It is a 12-item instrument developed to measure the acceptability of and willingness to use clinical decision rules in the future [64].

Patients' acceptability will be measured with a question (whether the patient found the DA useful for their decisions) from the DA feedback questionnaire developed by Juraskova et al [65]. Our research team will translate it into German. We refrain from

using long questionnaires for patients as they already have to fulfill the set of questionnaires from the pre-post design study.

Sample Characteristics

Patients will be recruited at participating study sites (Jena, Heidelberg) in inpatient and outpatient settings. Patients will be identified by a study nurse via the electronic health record of patients scheduled in the outpatient or inpatient clinic and approached for participation if they fulfill the inclusion criteria.

We will include adult patients with incurable, stage IV disease (prostate, breast, pancreatic, stomach, or colorectal cancer) in an advanced treatment stage (prognosis <12 months or standard palliative care only is considered). The patient must have an adequate level of the German language to complete the questionnaire and is willing and able to give informed consent for participation in the study.

We will exclude patients from the study who are already under standard palliative care only, are cognitively impaired, have extreme anxiety or distress, or have a severe comorbid illness, excluding antitumor treatment as assessed by the treating oncologist.

The influence of implicit bias will be reduced by recruitment of patients both in Heidelberg and Jena. In addition, the use of a trained study nurse at both sites will reduce implicit bias in recruitment. Drop-out reasons will be documented.

Oncologists will be recruited from the participating study sites (Jena, Heidelberg). They will be identified by a study nurse and invited to participate in the study via phone. We will include oncologists with different levels of working experience and of varying ages. The oncologists who participated in the development of the DA will be excluded from participation in the study.

Data Analysis

Analyses will be performed using SPSS v.20.0. A descriptive analysis of the sample will be performed. According to the level of variables, means, SDs, medians, minimum and maximum, and absolute or relative frequencies will be reported.

Clinically significant decisional conflict will be calculated and defined by a score of ≥25/100 on the Decision Conflict Scale, which is the most commonly used threshold to distinguish a harmful level of decisional conflict [62-64].

We will compare primary and exploratory outcome measures between the 2 patient groups (baseline and intervention) using Student *t* tests or analysis of variance. Parametric or nonparametric statistics (depending on the distribution of the data) will be used for the analysis of the patient groups from the baseline and intervention phases.

We will compare clinical confounders (time of integration of specialized palliative services into care; aggressiveness of therapy [anticancer treatment <14 days before death and place of death]) between the 2 patient groups (baseline and intervention) by comparing mean values. Measures of variability (SD) will be calculated.

Given the practice-based character and the small sample size of the study, we refrain from extensive measurement and multivariate analysis of mediators and moderators of the intervention effects. For the latter reason, we do not plan to use multiple imputation of missing values. Missing values will be handled by allowing a maximum of 35% missing in the calculation of scale scores.

P values of the corresponding statistical tests comparing treatment groups (ie, 2-sample *t* tests for continuous variables and chi-square tests for categorical data) will be given. Statistical significance will be assessed at the level of α=.05 (two-sided).

Timeline of the Study

The study will be conducted over a period of 3 years, with 12 months for conducting focus groups, interviews, and developing the first version of the DA. In a further 12 months, DA testing will follow as well as the completion of the DA. In the last 12 months of the study, a pre-post study and acceptance analysis will be conducted.

Results

We anticipate that this study will provide evidence about the developmental process, acceptance, and potential effects of a DA to support advanced cancer patients' decision making in relation to the limitation of cancer-specific treatment near the end of life. The results will be disseminated through publications in peer-reviewed scientific journals and via presentations at academic conferences. The scoping literature review will provide information on the possible content, features, structure of DAs, and information on fostering and hindering factors in design and implementation strategies. The focus groups will identify factors influencing the decision-making process in advanced cancer, timing, and possible ways of delivery of the DA. Interviews with patients will provide information about patients' decisional and informational needs, important factors for the decision-making process, and patient preferences and wishes regarding a DA.

Design and field testing will produce an optimized prototype of the DA for further testing. The pre-post study will test the potential effects of the DA on patients' knowledge, behavioral changes, and clinical outcomes as well as its acceptance.

The field testing is scheduled for April 2021 to August 2021, with the final revision scheduled for September 2021. The pre-post study of the DA and acceptance testing is scheduled to start in October 2021 and shall be finished in September 2022.

Discussion

The key strength of this study is that it aims at developing a DA that can be effectively used across different types of cancer. Furthermore, a wide range of topics relevant for advanced cancer near the end of life such as forgoing cancer-specific therapy and patients' inclusion in clinical trials will be covered. To our knowledge, it will be the first DA of its kind.

In trying to develop a DA that is suitable for patients with any cancer type, this certainly will create a number of challenges

(in terms of synthesizing the evidence on advanced cancer treatment options and presenting the benefits and risks and choices available). To face this challenge, 2 extensive validation validity phases will be included (review and re-draft of prototype versions 2 and 3), during which the DA will undergo review from advanced cancer patients, oncologists, and other experts from medical ethics and social sciences.

A further strength of this study is that we do not focus solely on the development of a DA but also on testing its impact on clinical practice and on patients' health outcomes. Additionally, we will evaluate the acceptance of the DA within the implementation study.

Furthermore, for all phases of the DA development and testing, interdisciplinary experts from psycho-oncology, sociology, oncology, palliative medicine, and medical ethics will be involved, enabling a better framework for this process.

This study has several limitations. One of the limitations is that developing and subsequent testing of the DA will take place mainly at the NCT in Heidelberg. The NCT is a national innovative tumor center, combining patient-oriented research, care, and a multidisciplinary approach. It offers a wide spectrum of consulting services for patients such as nutrition, psycho-oncology, pain therapy, pastoral care, self-help, social service, sports, and physical activity. It means that patients have additional services and a more individualized care approach in comparison to other hospitals.

Although the perspective of another hospital (palliative care unit in Jena) will be taken into consideration, it is likely that future multicentric research evaluating our DA's impact on patients' outcomes as well as process evaluation of the DA implementation may therefore also be needed.

Furthermore, due to recruitment difficulties, we decided not to interview patients' family members, who usually are involved in these decisions. Missing this important perspective might have an impact on the results of our study.

In patient interviews, we used a case scenario that might increase social matching bias. Furthermore, there can be a difference between what people think they would do in a described situation and their actual behavior. Furthermore, the interview guide had to be modified and customized according to the patients' current physical and mental status. This could lead to decreased generalizability of the results.

Our sample size in the pre-post study is relatively small due to the severe conditions of the patients who are near the end of life. This leads to difficulties in recruitment and can restrict the interpretation of the results.

Furthermore, given the relatively small sample size of the planned study, we can only explore the diversity of patients and health care professionals to a specific degree.

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Conflicts of Interest

None declared.

References

1. Laryionava K, Sklenarova H, Heußner P, Haun MW, Stiggelbout AM, Hartmann M, et al. Cancer patients' preferences for quantity or quality of life: German translation and validation of the quality and quantity questionnaire. Oncol Res Treat 2014;37(9):472-478. [doi: 10.1159/000366250] [Medline: 25231687]
2. van Lent LGG, Stoel NK, van Weert JCM, van Gurp J, de Jonge MJA, Lolkema MP, et al. Realizing better doctor-patient dialogue about choices in palliative care and early phase clinical trial participation: towards an online value clarification tool (OnVaCT). BMC Palliat Care 2019 Nov 29;18(1):106 [FREE Full text] [doi: 10.1186/s12904-019-0486-6] [Medline: 31783851]
3. Llewellyn-Thomas HA, Crump RT. Decision support for patients: values clarification and preference elicitation. Med Care Res Rev 2013 Mar 01;70(1 Suppl):50S-79S. [doi: 10.1177/1077558712461182] [Medline: 23124615]
4. Schrijvers D, Cherny NI, ESMO Guidelines Working Group. ESMO Clinical Practice Guidelines on palliative care: advanced care planning. Ann Oncol 2014 Sep;25 Suppl 3:iii138-iii142 [FREE Full text] [doi: 10.1093/annonc/mdu241] [Medline: 25210082]
5. Baile WF, Lenzi R, Parker PA, Buckman R, Cohen L. Oncologists' attitudes toward and practices in giving bad news: an exploratory study. J Clin Oncol 2002 Apr 15;20(8):2189-2196. [doi: 10.1200/JCO.2002.08.004] [Medline: 11956281]
6. Baile WF, Buckman R, Lenzi R, Glober G, Beale EA, Kudelka AP. SPIKES-A six-step protocol for delivering bad news: application to the patient with cancer. Oncologist 2000;5(4):302-311 [FREE Full text] [doi: 10.1634/theoncologist.5-4-302] [Medline: 10964998]
7. Hancock K, Clayton JM, Parker SM, Wal der S, Butow PN, Carrick S, et al. Truth-telling in discussing prognosis in advanced life-limiting illnesses: a systematic review. Palliat Med 2007 Sep;21(6):507-517. [doi: 10.1177/0269216307080823] [Medline: 17846091]

8. Habib AR, Cronin AM, Earle CC, Tulsky JA, Mack JW, Abel GA, et al. How Do Blood Cancer Doctors Discuss Prognosis? Findings from a National Survey of Hematologic Oncologists. J Palliat Med 2019 Jun;22(6):677-684 [FREE Full text] [doi: 10.1089/jpm.2018.0441] [Medline: 30907686]
9. Gilligan T, Bohlke K, Baile WF. Patient-Clinician Communication: American Society of Clinical Oncology Consensus Guideline Summary. JOP 2018 Jan;14(1):42-46. [doi: 10.1200/jop.2017.027144]
10. Yennurajalingam S, Rodrigues LF, Shamieh O, Tricou C, Filbet M, Naing K, et al. Perception of Curability Among Advanced Cancer Patients: An International Collaborative Study. Oncologist 2018 Apr;23(4):501-506 [FREE Full text] [doi: 10.1634/theoncologist.2017-0264] [Medline: 29158371]
11. Henselmans I, Brugel SD, de Haes HCJM, Wolvetang KJA, de Vries LM, Pieterse AH, et al. Promoting shared decision making in advanced cancer: Development and piloting of a patient communication aid. Patient Educ Couns 2019 May;102(5):916-923. [doi: 10.1016/j.pec.2018.12.018] [Medline: 30591283]
12. Chen CH, Kuo SC, Tang ST. Current status of accurate prognostic awareness in advanced/terminally ill cancer patients: Systematic review and meta-regression analysis. Palliat Med 2017 May;31(5):406-418. [doi: 10.1177/0269216316663976] [Medline: 27492160]
13. Elkin EB, Kim SHM, Casper ES, Kissane DW, Schrag D. Desire for information and involvement in treatment decisions: elderly cancer patients' preferences and their physicians' perceptions. J Clin Oncol 2007 Nov 20;25(33):5275-5280. [doi: 10.1200/JCO.2007.11.1922] [Medline: 18024875]
14. Garrett SB, Koenig CJ, Trupin L, Hlubocky FJ, Daugherty CK, Reinert A, et al. What advanced cancer patients with limited treatment options know about clinical research: a qualitative study. Support Care Cancer 2017 Oct;25(10):3235-3242 [FREE Full text] [doi: 10.1007/s00520-017-3734-4] [Medline: 28488050]
15. Politi MC, Kuzemchak MD, Kaphingst KA, Perkins H, Liu J, Byrne MM. Decision Aids Can Support Cancer Clinical Trials Decisions: Results of a Randomized Trial. Oncologist 2016 Dec;21(12):1461-1470 [FREE Full text] [doi: 10.1634/theoncologist.2016-0068] [Medline: 27511904]
16. Schildmann J, Bruns F. Informed Consent and Phase I Trials: Cognitive Failure and Additional Challenges to Informed Decision Making. J Clin Oncol 2019 Jan 10;37(2):169. [doi: 10.1200/JCO.18.01136] [Medline: 30433847]
17. Rezash V, Reed J, Gedeon B, Parsons E, Siedlecki S, Daniels B, et al. Who Needs What? Perceptions of Patients and Caregivers in Oncology Phase 1 Trials. J Patient Exp 2020 Mar;7(1):27-33 [FREE Full text] [doi: 10.1177/2374373519830743] [Medline: 32128368]
18. Dolly SO, Kalaitzaki E, Puglisi M, Stimpson S, Hanwell J, Fandos SS, et al. A study of motivations and expectations of patients seen in phase 1 oncology clinics. Cancer 2016 Nov 15;122(22):3501-3508 [FREE Full text] [doi: 10.1002/cncr.30235] [Medline: 27716902]
19. Laryionava K, Winkler EC. Patients' Preferences in Non-Curable Cancer Disease. Oncol Res Treat 2019;42(1-2):31-34 [FREE Full text] [doi: 10.1159/000496120] [Medline: 30661068]
20. Stacey D, Légaré F, Lewis K, Barry MJ, Bennett CL, Eden KB, et al. Decision aids for people facing health treatment or screening decisions. Cochrane Database Syst Rev 2017 Apr 12;4(4):CD001431 [FREE Full text] [doi: 10.1002/14651858.CD001431.pub5] [Medline: 28402085]
21. Elwyn G, O'Connor A, Stacey D, Volk R, Edwards A, Coulter A, International Patient Decision Aids Standards (IPDAS) Collaboration. Developing a quality criteria framework for patient decision aids: online international Delphi consensus process. BMJ 2006 Aug 26;333(7565):417 [FREE Full text] [doi: 10.1136/bmj.38926.629329.AE] [Medline: 16908462]
22. Lam WWT, Chan M, Or A, Kwong A, Suen D, Fielding R. Reducing treatment decision conflict difficulties in breast cancer surgery: a randomized controlled trial. J Clin Oncol 2013 Aug 10;31(23):2879-2885. [doi: 10.1200/JCO.2012.45.1856] [Medline: 23835709]
23. Osaka W, Nakayama K. Effect of a decision aid with patient narratives in reducing decisional conflict in choice for surgery among early-stage breast cancer patients: A three-arm randomized controlled trial. Patient Educ Couns 2017 Mar;100(3):550-562. [doi: 10.1016/j.pec.2016.09.011] [Medline: 28277290]
24. Eden KB, Scariati P, Klein K, Watson L, Remiker M, Hribar M, et al. Mammography Decision Aid Reduces Decisional Conflict for Women in Their Forties Considering Screening. J Womens Health (Larchmt) 2015 Dec;24(12):1013-1020 [FREE Full text] [doi: 10.1089/jwh.2015.5256] [Medline: 26360918]
25. O'Connor A. Using patient decision aids to promote evidence-based decision making. ACP J Club 2001;135(1):A11-A12. [Medline: 11471526]
26. McAlpine K, Lewis KB, Trevena LJ, Stacey D. What Is the Effectiveness of Patient Decision Aids for Cancer-Related Decisions? A Systematic Review Subanalysis. JCO Clin Cancer Inform 2018 Dec;2:1-13 [FREE Full text] [doi: 10.1200/CCI.17.00148] [Medline: 30652610]
27. Dharmarajan KV, Walters CB, Levin TT, Milazzo CA, Monether C, Rawlins-Duell R, et al. A Video Decision Aid Improves Informed Decision Making in Patients With Advanced Cancer Considering Palliative Radiation Therapy. J Pain Symptom Manage 2019 Dec;58(6):1048-1055.e2 [FREE Full text] [doi: 10.1016/j.jpainsymman.2019.08.014] [Medline: 31472276]
28. Härter M, Moumjid N, Cornuz J, Elwyn G, van der Weijden T. Shared decision making in 2017: International accomplishments in policy, research and implementation. Z Evid Fortbild Qual Gesundhwes 2017 Jun;123:1-5. [doi: 10.1016/j.zefq.2017.05.024] [Medline: 28546053]

29. O'Connor AM, Stacey D, Entwistle V, Llewellyn-Thomas H, Rovner D, Holmes-Rovner M, et al. Decision aids for people facing health treatment or screening decisions. Cochrane Database Syst Rev 2003(2):CD001431. [doi: 10.1002/14651858.CD001431] [Medline: 12804407]
30. Bailey RA, Pfeifer M, Shillington AC, Harshaw Q, Funnell MM, VanWingen J, et al. Effect of a patient decision aid (PDA) for type 2 diabetes on knowledge, decisional self-efficacy, and decisional conflict. BMC Health Serv Res 2016 Jan 14;16:10 [FREE Full text] [doi: 10.1186/s12913-016-1262-4] [Medline: 26762150]
31. Légaré F, Adekpedjou R, Stacey D, Turcotte S, Kryworuchko J, Graham ID, et al. Interventions for increasing the use of shared decision making by healthcare professionals. Cochrane Database Syst Rev 2018 Jul 19(7):CD006732 [FREE Full text] [doi: 10.1002/14651858.CD006732.pub4] [Medline: 30025154]
32. Elit LM, Levine MN, Gafni A, Whelan TJ, Doig G, Streiner DL, et al. Patients' preferences for therapy in advanced epithelial ovarian cancer: development, testing, and application of a bedside decision instrument. Gynecol Oncol 1996 Sep;62(3):329-335. [doi: 10.1006/gyno.1996.0244] [Medline: 8812525]
33. Fiset V, O'Connor AM, Evans W, Graham I, Degrasse C, Logan J. Development and evaluation of a decision aid for patients with stage IV non-small cell lung cancer. Health Expect 2000 Jun;3(2):125-136 [FREE Full text] [doi: 10.1046/j.1369-6513.2000.00067.x] [Medline: 11281919]
34. Leighl NB, Butow PN, Tattersall MHN. Treatment decision aids in advanced cancer: when the goal is not cure and the answer is not clear. J Clin Oncol 2004 May 01;22(9):1759-1762 [FREE Full text] [doi: 10.1200/JCO.2004.02.166] [Medline: 15118002]
35. A to Z Inventory of Decision Aids. The Ottawa Hospital Research Institute. 2019. URL: https://decisionaid.ohri.ca/azinvent.php [accessed 2021-07-30]
36. Ankolekar A, Vanneste BGL, Bloemen-van Gurp E, van Roermund JG, van Limbergen EJ, van de Beek K, et al. Development and validation of a patient decision aid for prostate Cancer therapy: from paternalistic towards participative shared decision making. BMC Med Inform Decis Mak 2019 Jul 11;19(1):130 [FREE Full text] [doi: 10.1186/s12911-019-0862-4] [Medline: 31296199]
37. Leighl NB, Shepherd HL, Butow PN, Clarke SJ, McJannett M, Beale PJ, et al. Supporting treatment decision making in advanced cancer: a randomized trial of a decision aid for patients with advanced colorectal cancer considering chemotherapy. J Clin Oncol 2011 May 20;29(15):2077-2084. [doi: 10.1200/JCO.2010.32.0754] [Medline: 21483008]
38. Smith TJ, Dow LA, Virago EA, Khatcheressian J, Matsuyama R, Lyckholm LJ. A pilot trial of decision aids to give truthful prognostic and treatment information to chemotherapy patients with advanced cancer. J Support Oncol 2011;9(2):79-86 [FREE Full text] [doi: 10.1016/j.suponc.2010.12.005] [Medline: 21542415]
39. Spronk I, Meijers MC, Heins MJ, Francke AL, Elwyn G, van Lindert A, et al. Availability and effectiveness of decision aids for supporting shared decision making in patients with advanced colorectal and lung cancer: Results from a systematic review. Eur J Cancer Care (Engl) 2019 May;28(3):e13079. [doi: 10.1111/ecc.13079] [Medline: 31066142]
40. Shirai Y, Fujimori M, Ogawa A, Yamada Y, Nishiwaki Y, Ohtsu A, et al. Patients' perception of the usefulness of a question prompt sheet for advanced cancer patients when deciding the initial treatment: a randomized, controlled trial. Psychooncology 2012 Jul;21(7):706-713. [doi: 10.1002/pon.1955] [Medline: 21425387]
41. Elwyn G, Durand MA, Song J, Aarts J, Barr PJ, Berger Z, et al. A three-talk model for shared decision making: multistage consultation process. BMJ 2017 Nov 06;359:j4891 [FREE Full text] [doi: 10.1136/bmj.j4891] [Medline: 29109079]
42. Volk RJ, Llewellyn-Thomas H, Stacey D, Elwyn G. Ten years of the International Patient Decision Aid Standards Collaboration: evolution of the core dimensions for assessing the quality of patient decision aids. BMC Med Inform Decis Mak 2013;13 Suppl 2:S1 [FREE Full text] [doi: 10.1186/1472-6947-13-S2-S1] [Medline: 24624947]
43. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M, Medical Research Council Guidance. Developing and evaluating complex interventions: the new Medical Research Council guidance. BMJ 2008 Sep 29;337:a1655 [FREE Full text] [doi: 10.1136/bmj.a1655] [Medline: 18824488]
44. Coulter A, Stilwell D, Kryworuchko J, Mullen PD, Ng CJ, van der Weijden T. A systematic development process for patient decision aids. BMC Med Inform Decis Mak 2013;13 Suppl 2:S2 [FREE Full text] [doi: 10.1186/1472-6947-13-S2-S2] [Medline: 24625093]
45. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Ann Intern Med 2018 Oct 02;169(7):467-473 [FREE Full text] [doi: 10.7326/M18-0850] [Medline: 30178033]
46. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. International Journal of Social Research Methodology 2005 Feb;8(1):19-32 [FREE Full text] [doi: 10.1080/1364557032000119616] [Medline: 20854677]
47. Levac D, Colquhoun H, O'Brien KK. Scoping studies: advancing the methodology. Implement Sci 2010 Sep 20;5:69 [FREE Full text] [doi: 10.1186/1748-5908-5-69] [Medline: 20854677]
48. Peters MDJ, Godfrey CM, Khalil H, McInerney P, Parker D, Soares CB. Guidance for conducting systematic scoping reviews. Int J Evid Based Healthc 2015 Sep;13(3):141-146. [doi: 10.1097/XEB.0000000000000050] [Medline: 26134548]
49. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. Int J Qual Health Care 2007 Dec;19(6):349-357. [doi: 10.1093/intqhc/mzm042] [Medline: 17872937]

50. Sandelowski M. Whatever happened to qualitative description? Res Nurs Health 2000 Aug;23(4):334-340. [doi: 10.1002/1098-240x(200008)23:4<334::aid-nur9>3.0.co;2-g] [Medline: 10940958]
51. Elo S, Kyngäs H. The qualitative content analysis process. J Adv Nurs 2008 Apr;62(1):107-115. [doi: 10.1111/j.1365-2648.2007.04569.x] [Medline: 18352969]
52. Dempsey L, Dowling M, Larkin P, Murphy K. Sensitive Interviewing in Qualitative Research. Res Nurs Health 2016 Dec;39(6):480-490. [doi: 10.1002/nur.21743] [Medline: 27434172]
53. Guest G, Bunce A, Johnson L. How Many Interviews Are Enough? Field Methods 2016 Jul 21;18(1):59-82. [doi: 10.1177/1525822x05279903]
54. Boren T, Ramey J. Thinking aloud: reconciling theory and practice. IEEE Trans. Profess. Commun 2000;43(3):261-278. [doi: 10.1109/47.867942]
55. O'Connor AM. Validation of a decisional conflict scale. Med Decis Making 1995;15(1):25-30. [doi: 10.1177/0272989X9501500105] [Medline: 7898294]
56. Song M, Sereika SM. An evaluation of the Decisional Conflict Scale for measuring the quality of end-of-life decision making. Patient Educ Couns 2006 Jun;61(3):397-404. [doi: 10.1016/j.pec.2005.05.003] [Medline: 15970420]
57. Kriston L, Scholl I, Hölzel L, Simon D, Loh A, Härter M. The 9-item Shared Decision Making Questionnaire (SDM-Q-9). Development and psychometric properties in a primary care sample. Patient Educ Couns 2010 Jul;80(1):94-99. [doi: 10.1016/j.pec.2009.09.034] [Medline: 19879711]
58. Degner LF, Sloan JA, Venkatesh P. The Control Preferences Scale. Can J Nurs Res 1997;29(3):21-43. [Medline: 9505581]
59. Bieber C, Nicolai J, Müller K, Eich W. Der Fragebogen zur Arzt-Patient-Interaktion (FAPI) – Validierung und psychometrische Optimierung anhand einer Stichprobe chronischer Schmerzpatienten. Klin Diagnostik Evaluation 2011;4:78-93 [FREE Full text]
60. Geiser F, Zajackowski K, Conrad R, Imbierowicz K, Wegener I, Herth KA, et al. The German Version of the Herth Hope Index (HHI-D): Development and Psychometric Properties. Oncol Res Treat 2015;38(7-8):356-360. [doi: 10.1159/000435900] [Medline: 26278579]
61. Herdman M, Gudex C, Lloyd A, Janssen M, Kind P, Parkin D, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). Qual Life Res 2011 Dec;20(10):1727-1736 [FREE Full text] [doi: 10.1007/s11136-011-9903-x] [Medline: 21479777]
62. Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst 1993 Mar 03;85(5):365-376. [doi: 10.1093/jnci/85.5.365] [Medline: 8433390]
63. Faller N, Stalder O, Limacher A, Bassetti S, Beer JH, Genné D, et al. Frequency of use and acceptability of clinical prediction rules for pulmonary embolism among Swiss general internal medicine residents. Thromb Res 2017 Dec;160:9-13. [doi: 10.1016/j.thromres.2017.09.028] [Medline: 29080550]
64. Brehaut JC, Graham ID, Wood TJ, Taljaard M, Eagles D, Lott A, et al. Measuring acceptability of clinical decision rules: validation of the Ottawa acceptability of decision rules instrument (OADRI) in four countries. Med Decis Making 2010;30(3):398-408. [doi: 10.1177/0272989X09344747] [Medline: 20042533]
65. Juraskova I, Butow P, Fisher A, Bonner C, Anderson C, Bu S, et al. Development and piloting of a decision aid for women considering participation in the Sentinel Node Biopsy versus Axillary Clearance 2 breast cancer trial. Clin Trials 2015 Aug;12(4):409-417. [doi: 10.1177/1740774515586404] [Medline: 26033878]

Abbreviations

COREQ: consolidated criteria for reporting qualitative research
DA: decision aid
IPDAS: International Patient Decision Aid Standards
NCT: National Center of Tumor Diseases
OADRI: Ottawa Acceptability of Decision Rules Instrument
PRISMA-ScR: Preferred Reporting Items for Systematic Reviews and Meta-analysis Extension for Scoping Reviews
QQPPI: Questionnaire on the Quality of Physician-Patient Interaction
SDM: shared decision making

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Protocol

Exploring Associations of Housing, Relocation, and Active and Healthy Aging in Sweden: Protocol for a Prospective Longitudinal Mixed Methods Study

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Abstract

Background: While housing and neighborhood features have the potential to impact opportunities for active aging, there is a lack of knowledge related to how older people reason regarding their housing situation and how housing and fulfillment of relocation are associated with active and healthy aging.

Objective: The objectives of Prospective RELOC-AGE are to study housing choices and relocation and explore effects on active and healthy aging among men and women aged 55 years and older in Sweden considering relocation.

Methods: The estimated sample (2800) will include people aged 55 years and older being listed for relocation at either of two housing companies: a local public housing company in Southern Sweden and a national condominium provider. Prospective RELOC-AGE has a 2-level longitudinal mixed methods design and includes quantitative surveys (implemented by a professional survey company) and a telephone interview for baseline data collection in 2021, with follow-ups with the same procedures in 2022 and 2023. The survey and interviews include questions related to present housing and neighborhood, relocation plans and expectations, a range of perspectives on active and healthy aging, and demographics. Linking to national registers will provide additional data on home help and health care use, objective housing, and neighborhood characteristics. To explore what housing attributes older adults considering relocation find important and to what extent when making their decisions on housing, we will develop a discrete choice experiment to be implemented with a subsample of participants. Further, a grounded theory approach will be applied to collect in-depth interview data from participants who have moved to another dwelling, within 6 months of the move. A follow-up interview 12 months later will focus on participants' deepened experience over time in terms of fulfilled expectations and relocation experiences.

Results: As of submission of this protocol (June 2021), recruitment has commenced with approximately 960 respondents to the survey and ongoing telephone interviews. We anticipate recruitment and data collection based on surveys and interviews to continue during 2021.

Conclusions: Prospective RELOC-AGE has the capacity to generate new policy-relevant knowledge on associations of housing, relocation, and active and healthy aging. Such knowledge is relevant for the development of proactive approaches to housing in old age on the individual, group, and societal levels.

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KEYWORDS

accessibility; activity; age-friendly housing; aging-in-place; housing preferences; life-space; mobility; moving expectations; neighborhood; participation

Introduction

Background

Previous research on housing and aging has mainly concerned frail older adults and their needs for residential care toward the end of life. According to the public debate, older people in general are interested in housing options that support active and healthy aging. However, comprehensive studies on housing options in later life incorporating health and social factors as well as factors related to the built environment and housing are lacking [1], and little is known about when and how people start to reflect and act upon housing choices and relocation as they age. Further, there is a lack of knowledge about how housing and relocation are related to active and healthy aging.

The body of recent literature on housing choices and relocation is limited, with interest for moves to special forms of housing at the core [2]. When comparing people remaining in ordinary housing with those moving to supported living in the format of retirement villages, those who did not move were initially better off, but after 3 months the difference decreased due to improvement among the movers, mostly in depression and self-rated health [3]. Somewhat in contrast, a British panel study showed that moving to residential housing was associated with higher mortality in the next 12 months among people aged 65 years and older, especially among men [4]. A study from Australia showed that reasons to move reflect the urge to maintain independence, stay in control, and avoid loneliness, and control over relocation decisions and being proactive contribute to positive adjustment [5].

There is ample evidence that housing is associated with health outcomes as people age, with some support for causal effects between housing and disability-related outcomes [6-9]. As an example, the association between housing accessibility and independence in activities of daily living seems to be mediated by external housing-related control beliefs in younger old [8]. Additional findings point to potentially different role of external housing-related control beliefs in different population groups, such as the very old people [7] or people aging with Parkinson disease [9], calling for further research in this area.

There are also qualitative studies showing that the home environment is important for activity and participation in very old age [10]. Noteworthy, perceived aspects of home are related to health already at age 67 to 70 years [11] with retirement stimulating active reflections regarding housing choices and relocation [12]. There are examples of quantitative cross-national studies of scale targeting neighborhoods and aging [13], but there is no population-level research with detailed data on objective and perceived aspects of housing as related to active and healthy aging.

Relocation has been described as a process negotiated over time [14] until turning points emerge [15]. Residential reasoning (eg, whether to move or not and how to arrange one's housing situation) is a complex and ambivalent matter [16]. Changes in such reasoning relate to the way people strive to build upon or dismiss attachment to place and their attempts to maintain or regain residential normalcy during years of declining health [17]. Relating to such findings, different factors predict relocation to ordinary housing and residential care [17,18]. A study in the United States involving more than 7000 people aged 65 years and older [18] revealed that over a 4-year period, 8% moved within ordinary housing and 4% moved to residential care. Very old people who relocate do move to dwellings with fewer environmental barriers, but because of increasing functional limitations over time, housing accessibility problems persist [19]. Exemplifying complex dynamics of importance for housing choices and relocation in later life, very old people living in housing with more accessibility problems rate perceived meaning of home as worse and are more dependent on external control to manage their situation compared with younger older adults [20].

Active Aging

Active aging is a policy goal referring to "the process of optimizing opportunities for health and participation in the society for all people in line with their needs, goals, and capacities as they age" [21]. Initiatives to promote active aging can be seen from a societal perspective in terms of providing accessible environments including transportation and housing or from a service provider perspective, for example, in terms of health-promoting interventions. In addition to the potential benefits on health, participation, and quality of life, the goal to promote active aging holds the potential to mitigate an expected increase in health and social care expenditures related to the increasingly larger proportion of older adults in the population.

Active aging can also be seen from an individual perspective in terms of strategies and behaviors that the individual can adopt to optimize their opportunities for participation and health. On the individual level, active aging has been described as striving for well-being through activity as per one's goals, opportunities, and abilities [22]. One central, contextual facet of active aging is therefore housing and services that are tailored to address age-friendly housing and relocation and to support independent living [23]. However, in research on housing choices and relocation among older people, active aging has not been used as a core perspective or as an outcome to evaluate the long-term impact of housing and relocation. To inform the design of policies and societal support related to housing, knowledge is needed about how housing and relocation are associated with active aging and health outcomes.

Study Objective and Research Questions

Nurtured by the hypothesis that housing choices and relocation influence opportunities for active and healthy aging, the objectives of Prospective RELOC-AGE are to study housing

choices and relocation and explore effects on active and healthy aging among people aged 55 years and older in Sweden who are considering relocation. The specific research questions are:

- How do housing aspects and relocations affect future activity and health outcomes?
- What aspects of housing and health may explain or predict (1) relocation to different housing options in the ordinary housing stock, (2) relocation to residential care facilities, and (3) remaining in the present dwelling?
- What is the interaction between objective and perceived aspects of housing and social aspects associated with active and healthy aging, and what are the characteristics and trajectories of such dynamics?
- What housing attributes do older adults considering relocation find important and to what extent when making their decisions on housing preferences?
- How do older adults considering relocation decide regarding (1) different housing options and (2) motives for considering and effectuating relocation, and (3) to what extent are their motives fulfilled?
- How are the questions above affected by age, sex, civil status, country of origin, functioning, adverse health events, loss of a partner, and socioeconomic and neighborhood characteristics?

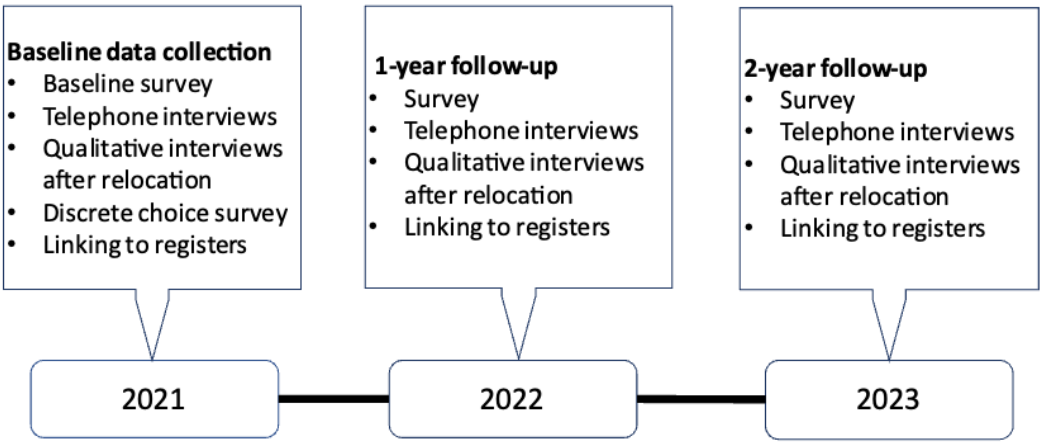
Methods

The overall RELOC-AGE project comprises 3 parts: a population-based register study, a prospective mixed methods longitudinal study, and an intervention study. This paper is the study protocol for the prospective study.

Study Design

Prospective RELOC-AGE has a 2-level longitudinal mixed methods design (Figure 1). Level 1 includes quantitative online surveys and a telephone interview for a baseline data collection in 2021 with follow-ups with the same procedures to be conducted in 2022 and 2023. To decrease participant burden, linking to registers will provide additional data. For level 2, we will retrieve relocation dates from collaborating housing companies or the Swedish Taxation Authority every third month to identify survey participants who have relocated to another dwelling (any type or form). They will be asked to participate in additional quantitative and qualitative data collection at home visits in their new dwelling or by telephone interview no later than 6 months after the move. User involvement is a significant component [24,25] engaging older adults and representatives from housing companies throughout the research process. The study was registered at ClinicalTrials.gov [NCT04765696] [26].

Figure 1. Overview of study design and time plan for data collection in Prospective RELOC-AGE.



Population and Setting

In order to capture dynamics related to housing choices, relocation, and active and healthy aging from an early stage of the aging process, age 55 years or older with a postal address in Sweden serve as inclusion criteria. Targeting people actively considering relocation, additional inclusion criteria are being voluntarily and actively listed based on interest for moving to a dwelling provided by either of 2 housing companies, selected based on established research collaboration. Severe cognitive impairments or insufficient language skills to give informed consent or participate in telephone interviews are exclusion criteria.

The housing companies represent a local public housing company (LPH) in Southern Sweden and a national condominium provider (NCP). In this way, a diversity of types of housing typically attracting people from different socioeconomic groups is represented. More specifically, the LPH provides common apartments as well as apartments designated for senior citizens. In February 2021, 1680 individuals aged 55 years and older were on the LPH waiting list. As condominiums are sold on the open market, NCP has priority and interest lists for new establishments of which some are designated for senior citizens. In February 2021, the NCP had approximately 22,000 individuals aged 55 years and older on their priority list and 33,000 on their interest list.

Based on the explorative overall objective and mixed methods design, the recruitment strives for inclusion of information-rich participants rather than representativity. The annual incidence of moves in the population aged 60 to 84 years is 4% to 5%

[27]. Even if our sample will be younger, as we target a population actively considering relocation, we estimate a 50% higher relocation incidence. Thus, we will be able to study associations hitherto not addressed at scale in a population of older adults actively considering housing choices. Survey participants will fall into 5 categories to be compared with respect to health trajectories in the quasi-experimental design: still queuing for senior housing, moved to a regular dwelling in the ordinary housing stock, moved to needs-assessed residential care, received an offer in senior housing and moved, or deceased. The targeted sample size for the survey is 2800, which will be sufficient for the planned types of analyses. As an example, we have 90% statistical power (5% significance level) to detect if a certain lifestyle exposure, activity, or mobility pattern that is present among 20% of the participants increases the risk with 50% (risk ratio 1.5; 15% vs 10%) for multimorbidity during follow-up.

Recruitment

Following the housing companies' procedures to ensure that data were handled according to General Data Protection Regulations and based on written agreements between them and the research group, contact information for persons on their lists were either delivered to the university or provided directly by interested individuals via an online portal setup by the researchers. The recruitment process will be closely monitored and additional LPH companies will be approached to increase the recruitment base if necessary to reach the targeted sample size.

A stepwise recruitment procedure will include all eligible individuals from the LPH and randomly selected individuals from the NCP. A professional support organization for clinical and epidemiological research (Clinical Studies Sweden Forum South) with longstanding expertise on conducting surveys for research and handling data will implement the data collection.

An invitation letter will be sent by postal mail to the potential participants. The letter includes a description of the project, the methods for data collection, and how data will be handled and stored according to existing regulations. The information stresses that participation is voluntary and participants can decline participation at any time without consequences to their rights and access to be offered a dwelling offer or any societal services. The invitation letter includes information about alternative modes of answering the survey: a web-based survey to be accessed through the project website [28] with a participant-specific username and password provided in the invitation letter or a paper version of the survey to be sent to participants upon request.

Ethics

Following the principles of the Helsinki Declaration and current national legislation and policies on ethics for research involving humans, Prospective RELOC-AGE was approved by the Swedish Ethical Review Authority (No. 2020-03457).

Procedure

Survey Data Collection Procedures and User Involvement

The survey data collection includes a range of established instruments for studies on aging and housing and a study-specific discrete choice questionnaire aimed at exploring stated preferences on housing.

Nonacademic partner representatives and senior citizen representatives were engaged throughout the development of the data collection procedures. All data collection forms were piloted to optimize readability and the logic flow of questions and to minimize respondent burden. Such piloting was implemented in a stepwise manner and typically included 5 to 10 user representatives instructed to use different types of digital devices to respond to the online survey. Comments and suggestions for optimization were considered in the finalization of the data collection formats.

Most of the survey will be administered as a questionnaire, to be completed online or on paper. Due to the complex nature of the questions included, the University of Jyvaskyla Active Aging Scale, Meaning of Home, and External Housing-Related Control Beliefs Questionnaire will be administered during a telephone interview with participants who agree to this additional data collection.

Present Dwelling

Questions about the respondents' present dwelling include type of dwelling (eg, apartment or house); whether the respondent owns their dwelling; if the entrance floor includes bathroom, bedroom, kitchen, place for dining, living room, hall, room for storage, and opportunities to wash and dry clothes (yes/no for each); number of rooms and rooms with opportunities to bath or shower; if there are stairs, ramp, or elevator at the entrance (yes/no); access to garden, balcony, or terrace (yes/no); if the dwelling is situated in an urban or rural area; the number of people living in the dwelling; cohabitants (eg, partner, children); year moved to present dwelling; and time per day spent out of the home.

Perceived Aspects of Housing and Neighborhood

Based on a model of perceived aspects of housing [29], the survey questionnaire includes 4 instruments with acceptable psychometric properties when applied in research on aging and housing.

Usability in the home is evaluated with selected items from the original Usability In My Home instrument [30,31]. The respondent rates to what extent they perceive the current dwelling is designed for managing personal activities of daily living (eg, bathing, toileting); food preparation; washing, cleaning, and flower care; and laundry and grooming (scale ranging from 1 to 5; higher = more usable).

Housing satisfaction [29] is evaluated with the question "Are you satisfied with your dwelling?" (scale ranging from 1 to 5; higher = more satisfied).

Meaning of home is evaluated with the Meaning of Home Questionnaire [29]. The concept is rooted in "What makes the

house a home?" and focuses on the relationship between the sociophysical setting of the home and subjective evaluations, values, emotions, and goals. The questionnaire has a set of statements divided in 4 domains (physical, behavioral, cognitive/emotional, and social) rated on a scale from 0 to 10 how well they fit their own thinking (higher = more agreement). The instrument has adequate psychometric properties for use with adults aged 67 to 70 years in Sweden [32].

External Housing-Related Control Beliefs Questionnaire (HCQ) is evaluated with 16 items from the original HCQ questionnaire [33]. External control in relation to the home means that some other person, luck, chance, or fate are perceived as explanatory factors for what happens. For each item, respondents use a scale from 1 to 5 to rate to what extent they personally agree or disagree with the statements (higher = more external control). The external HCQ scale has adequate psychometric properties for use with adults aged 67 to 70 years in Sweden [32].

Neighborhood and outdoor experiences are evaluated with 2 sets of questions routinely used in regional public health surveys in Sweden [34]. The first set concerns access to societal services (eg, grocery shop, child care), cultural activities (eg, cinema, library), leisure facilities (eg, swimming hall), and public transportation and exposure to disturbing sounds and air pollution (yes/no/no opinion). The second set concerns 8 perceived qualities or characteristics of open green urban areas that can be described as serene, wild, lush, spacious, culture, the common, the pleasure garden/refuge, and festive [35,36] and one additional question about access to blue space (eg, lake, sea, water courses). Participants are asked to score each quality or characteristic within 5 to 10 minutes' walking distance from their dwelling (4-point scale from totally disagree to totally agree). Five of the perceived items have been validated previously against objective landscape data [37].

Neighborhood cohesion is evaluated with a perceived neighborhood social cohesion scale from the National Health and Aging Trends Study [38] with 3 statements to which the respondent is asked to rate their level of agreement (not at all, to some extent, agree). The statements ask if people in their community know each other well, are willing to help each other, and can be trusted.

Relocation

A set of study-specific questions is used to capture reasons for considering relocation, moving expectations, and previous moving experiences. What were the reasons to apply for being on a waiting/interest list for another dwelling (several response alternatives, eg, I do not want or am unable to manage my present dwelling; I want a dwelling that provides better opportunities for me to engage in activities I prefer to do)? When is it likely that you will move (in less than 1 year, 1 to 2 years, 2 years or more)? How likely is it that you have moved within 2 years (on a 5-point scale from 1, completely certain, to 5, not at all likely)? What kind of dwelling would you like to move to (eg, rented or owned apartment, house)? To what extent will a decision to relocate be made by the respondent themself, together with or by others? Are there hindrances to relocate within 2 years (eg, economic reasons, poor health)? How many times have you moved since the age of 18 years? Can housing adaptations be an option rather than moving?

Active and Healthy Aging

Self-rated health is evaluated with the widely used 1-item question from the SF-12 scale [39], "In general, would you say your health is..." (5 response options ranging from poor to excellent).

Illness, disease, and recent health care use is evaluated with study-specific questions on whether the respondent has any type of long-term illness or disease (yes/no), and if so, if that has an impact on work or daily activities (yes/no); if the respondent has ever been diagnosed with depression by a medical doctor (yes, during the previous 12 months, yes, more than 12 months ago, no); whether the person has been admitted to hospital (yes/no) or visited an emergency department (yes/no) during the past 3 months.

Functional limitations are evaluated using 10 items on functional limitations (rated as present, yes, to some extent, or not present) adapted from the person component of the Housing Enabler instrument [40].

Mobility questions related to opportunities for mobility were developed after consultation with a researcher specializing in mobility issues involving older adults. Study-specific questions included whether the respondent has a driver's license (yes/no), access to a car (yes/no), the potential and realized use of (can you... and do you ... respectively): walk, bike, moped/motorcycle, car, train, bus, transportation service, subway/tram, or ferry [41]. Satisfaction with mobility opportunities is rated on a 5-point scale (from very satisfied to very dissatisfied).

Physical activity is evaluated with a question from a well-established public health survey [34] about the total time per week the respondent is physically active (eg, brisk walking, gardening; 6 levels ranging from 0 minutes to 5 hours or more per week). Physical exercise [34] is evaluated with a question from the same survey about the total time per week the respondent is engaged with strenuous activities (5 levels ranging from 0 minutes to 2 hours or more per week).

Use of technical aids is evaluated with 5 study-specific questions about the use of a cane, crutches or similar, rollator, manual wheelchair, electric wheelchair, or scooter (no, yes outdoors, yes indoors).

Life-space mobility is evaluated with the Swedish version [42] of the Life-Space Assessment [43], which includes 5 levels of life-space mobility and whether the respondent, during the previous 4 weeks, has been to any of these locations: indoors to other rooms than the bedroom, immediate outdoor surroundings, neighborhood, town, or beyond town. For each level, the respondent indicates how often (less than once per week, 1 to 3 times per week, 4 to 6 times per week, every day), and if they needed a technical aid or assistance. The composite score ranges from 0 to 120; higher scores indicate greater life-space mobility.

Active aging is evaluated with the University of Jyvaskyla Active Aging Scale [22,44]. This instrument contains 17

self-rated items regarding goals, ability, autonomy, and activity that capture a single construct reflecting individual active aging [22] (total score ranges from 0 to 272). The items include practicing memory, using a computer, advancing matters in one's own life, exercising, enjoying the outdoors, taking care of one's personal appearance, crafting or DIY, making one's home cozy and pleasant, helping others, maintaining friendships, getting to know new people, balancing personal finances, making one's days interesting, practicing artistic hobbies, participating in events, advancing societal/communal matters, and doing things in accord with one's world view [45].

Self-rated health is evaluated with the EQ-5D-5L [46], which includes the items mobility, washing and dressing, and daily activities, which are rated on a 5-point scale with higher scores indicating a worse health status. If the respondent rates at least moderate difficulty on one or more of these 3 items, the respondent is also presented questions about frailty below. Further, the EQ-5D-5L includes items regarding if the respondent experiences pain/discomfort or anxiety/depression; both are rated on a 5-point scale with higher scores indicating a worse health status.

Frailty is evaluated by 4 questions (yes/no) [47]: Have you had any general fatigue or tiredness over the last 3 months? Do you fall often, or are you afraid of falling? Do you need assistance in either getting to the store, managing obstacles to and from the store, or in choosing, paying for, or bringing home groceries? Do you get tired when taking a 15- to 20-minute walk outside?

Life satisfaction is evaluated with the 1-item question, "How satisfied are you with life as a whole?" (6 response options, from very unsatisfying to very satisfying) [48].

Self-efficacy is evaluated with the general self-efficacy scale [49], which includes 10 statements (eg, I always manage to solve problems if I make an effort to do it; In unexpected situations I always know how to act). For each statement, respondents state their agreement on a 4-point scale from 1, completely disagree, to 4, totally agree.

Receiving or providing practical support in daily life is evaluated with a set of study-specific yes/no questions: Do you receive practical support in your daily life from a family member? Do you in your daily life provide practical support for a family member with health or functional limitations in their daily life? Do you have a safety alarm? Do you receive home help? Do you live together with someone who receives home help? Have you received practical support in or outside your house during the last 2 months? If yes, was the support from a family member, neighbor, or friend; municipality handyman; home help; or a private company?

Life events are evaluated with study-specific questions about experiencing major life events during the previous 3 years (yes/no): death of a spouse/partner, own disease, disease/disability of a spouse/partner, disease/disability of other close person, divorce/separation, became grandparent, got married/registered partnership, reduced time working/or retiring, begun to work, or driving cessation.

Demographics

Demographic questions include civil status, Swedish origin (if not, age when coming to Sweden), gender, educational, current occupation, and economic situation.

Stated Preferences on Housing

To explore stated preferences and the importance of various housing attributes when considering relocation, we will conduct a discrete choice experiment (DCE) [50]. A DCE is a quantitative technique for eliciting individual, stated preferences, in this study in relation to housing. Stated preferences have been used to examine housing decisions [51] among tenants in general [52] but not in aging research. A key feature of a DCE is to identify attributes based on existing literature and expert or user consultations. We will develop the DCE using an iterative process including a review of literature, expert consultations, and user involvement. Potential attributes include location, accessibility, costs, distance to bus stops, and services in the local neighborhood [53]. In a DCE, respondents are presented different hypothetical alternatives where the degree to which important attributes are present varies, followed by responses regarding how different alternatives are valued in relation to each other. The DCE included in Prospective RELOC-AGE is under development and will be presented in a forthcoming publication.

Table 1 provides an overview of instruments and study-specific questions.

Table 1. Overview of instruments and study-specific questions used in the survey study.

Question/instrument	Source	Baseline	1 year	2 years
Housing and relocation				
Present dwelling	Study-specific	✓	✓	✓
Usability in the home	[30,31]	✓	✓	✓
Housing satisfaction	[29]	✓	✓	✓
Meaning of home	[29,32]	✓	✓	✓
Housing-related control beliefs	[32,33]	✓	✓	✓
Neighborhood cohesion	[38]	✓	✓	✓
Neighborhood and outdoor experiences	[35,36]	✓	✓	✓
Reasoning around relocation	Study-specific	✓	✓	✓
Moving expectations	Study-specific	✓	✓	✓
Relocation experiences	Study-specific	✓	✓	✓
Active and healthy aging				
Self-rated health	[39]	✓	✓	✓
Illness, disease, recent health care use	Study-specific	✓	✓	✓
Functional limitations	[40]	✓	✓	✓
Physical exercise	[34]	✓	✓	✓
Physical activity	Selected questions from public health survey [34]	✓	✓	✓
Use of technical aids	Study-specific	✓	✓	✓
Life-space mobility	[42,43]	✓	✓	✓
Active aging	[22]	✓	✓	✓
Self-rated health	[46]	✓	✓	✓
Frailty	[47]	✓	✓	✓
Life satisfaction	[48]	✓	✓	✓
Self-efficacy	[49]	✓	✓	✓
Caregiving	Study-specific	✓	✓	✓
Mobility	Study-specific modified from [41]	✓	✓	✓
Life events	Study-specific	✓	✓	✓
Demographics				
Current occupation	Study-specific	✓	✓	✓
Economic situation	[34]	✓	✓	✓
Stated preferences on housing				
Discrete choice experiment	Study-specific	✓	—[a]	—

[a]Not applicable.

Postrelocation In-Depth or Semistructured Interviews

Over time, survey participants who have moved to another dwelling (any type/form) will be asked to participate in an in-depth interview no later than 6 months after the move. Using a grounded theory approach [54,55], we will develop an interview guide focusing on the relocation experience. Performing data collection and analysis in parallel to determine the need for additional sampling, based on the principle of saturation [56] the sample size is not predetermined. Trained research staff will collect data at home visits or online, depending on what is feasible at the time for the data collection. Approximately 12 months after the first in-depth interview, a subsample of typical cases (estimated at 25) will be selected based on the initial in-depth interview. The follow-up interview will deepen the knowledge about the relocation experience fulfillment of expectations over time.

Complementary Data by Linking to National Registers

In order to decrease participant burden and bias related to self-reporting, we will use complementary health and housing data for each time point in the data collection requested for the Register RELOC-AGE Study. These data are made available through Statistics Sweden (eg, the Total Population Register), the National Board of Health and Welfare (eg, National Patient Register), the Municipal Health Care Register, the Real Estate Property Register, and the Apartment Register. Data accessed from registers will concern objective housing data (eg, dwelling unit size), individual- and neighborhood-level demographic and socioeconomic indicators, health care and home help service use as well as causes of death.

Data Analysis Plan

For quantitative data collected by surveys and phone interviews, we will apply exploratory and inferential statistical methods. For longitudinal analyses, we will use regression techniques including generalized linear models or Cox regression with time-dependent covariates. We will investigate how different personal and neighborhood-level characteristics affect the associations of interest by exploring mediation and moderation effects, as well as use different techniques to address confounding.

For analyses of data from the discrete choice experiment, we will use the conditional multinomial logit model as the reference model, but the analysis will be extended to mixed logit and latent class models to take into account preference heterogeneity [57]. The 2 latter models take into account the panel structure of the data and are a standard extension of the analysis [58,59].

In-depth interviews will be audiorecorded and transcribed, followed by analyses guided by principles from grounded theory [55] aided by the NVivo (QSR International) software.

Results

As of submission of this protocol (June 2021), recruitment has commenced with approximately 960 respondents to the survey and telephone interviews ongoing. We anticipate recruitment and data collection based on surveys and interviews to continue during 2021.

Discussion

Summary

Prospective RELOC-AGE will provide new knowledge about whether and how housing choices and relocation have an impact on active and healthy aging among people aged 55 years and older in Sweden who are considering relocation. Following a large sample of information-rich individuals over time including a 2-level data collection in a mixed methods design, the results will add knowledge about associations between housing choices, perceived and objective aspects of housing and neighborhood, a range of socioeconomic factors, health, and active aging. Further, based on the explorative mixed methods approach, the project will contribute to a better understanding of factors that may explain or predict relocation or remaining in the present dwelling.

In housing-related aging research, the concept of aging-in-place is prominent but insufficiently problematized and currently geared toward health care, social services, and residential care needs [60]. The underlying premises are that the vast majority of older adults prefer to age in place [61], and it is less costly to provide care at home than in institutions [62]. Current research has a strong focus on people aging into disability and frailty with increasing needs for special forms of housing, tailored home modifications, or other reactive solutions at the core. The prevailing definition does not relate to proactive public health ambitions and strategies to support active and healthy aging. Results of cross-national research on aging and housing show that aging-in-place is far from applicable to all senior citizens [63]. In the light of such results as well as policies emphasizing the diverse needs of the heterogeneous aging population [64], the static and generalized notion of aging-in-place is facing a dead end. Integrating active and healthy aging with housing and relocation, RELOC-AGE challenges aging-in-place and the prevailing paradigm in this research field and will produce new knowledge for research as well as practice and policy.

As to the association between housing and health, previous research has mainly been focused on very old people (eg, qualitative studies showing that the home environment is important for activity and participation in very old age) [10]. However, as shown by Kylén et al [11], perceived aspects of home are related to health already at ages 67 to 70 years. In line with previous findings showing that processes close to the retirement age seem to stimulate active reflections regarding housing choices and relocation [12], the RELOC-AGE project is designed to capture such processes including a relatively young cohort that will be followed over time. An essential aspect of active aging is the opportunity and ability to engage in prioritized activities [22]. As such, housing and the neighborhood provide a starting point for engagement in such activities. At retirement age, people plan for self-realization, and thus have housing preferences different from those at more advanced ages, where compromised functional capacity and frailty may influence where people wish to live.

In Prospective RELOC-AGE, housing is not limited to the dwelling itself but refers to the location of the dwelling as well, thus including neighborhood features. The research field of natural outdoor environments and health has grown in the past decades [65], contributing to a better understanding about the existing links. In a cross-sectional study, serenity, wilderness, species richness, spaciousness, and cultural history were associated with neighborhood satisfaction, physical activity, and general health [66,67]. Moreover, perceived safety was shown to be a prerequisite for the association between the outdoor qualities and physical activity [68], confirming that the pathways between features in the outdoor environment and health outcomes are complex. While barriers to outdoor mobility located close to the home have been found to be associated with lower physical activity among older adults, barriers further away from home were not [69]. In addition, attractive destinations for outdoor mobility located at least 500 meters away from home were correlated with higher physical activity. While features in the neighborhood as well as in the dwelling provide

opportunities or hindrances for engagement in activities that relate to a person's goals, the association to active aging remains to be explored. Complementing existing research in this field, Prospective RELOC-AGE will shed new light on whether and how housing and relocation impact on active and healthy aging.

The longitudinal approach of Prospective RELOC-AGE in combination with Register RELOC-AGE will provide data that can be used to build causal evidence when it comes to housing and health associations. Self-reported and registry-based data on housing, demographics, and individual facets of active and healthy aging will enable us to explore potential mechanisms of how housing could support active and healthy aging. Such knowledge is essential to develop evidence-based future housing practices and policies in Sweden as well as abroad.

Previous intervention research related to housing issues typically has targeted home modifications, indicating that individual strategies promote participation among people with health conditions [70]. However, to the best of our knowledge, evidence-based interventions with a health promotion approach targeting housing matters before people are frail and need residential care do not exist. Parallel to Prospective RELOC-AGE and drawing on the knowledge gained, a web-based housing counseling intervention will be finalized and piloted (Intervention RELOC-AGE). The Aging in the Right Place was developed by using research circles [24] involving senior citizens, technology experts, and nonacademic partners. The existing prototype includes 3 modules: THINK, LEARN, and ACT, reflecting different stages of the decision-making process related to housing choices and relocation [71]. The knowledge gained from Prospective RELOC-AGE will contribute to further development and the finalization of the Aging in the Right Place intervention, which will subsequently be piloted and evaluated in municipality contexts in Sweden.

Limitations and Strengths

Currently, Prospective RELOC-AGE is limited to a follow-up period of 2 years, which, given the complex associations between housing and relocation and active and healthy aging, could be considered too short. However, the planned follow-up period at this stage is determined based on available funding and will be extended as soon as additional funding has been secured. Thus, the ambition is to establish a solid structure for long-term follow-up, which is required to produce valid results responding to the ambitious research questions.

The 2-level mixed methods design could be seen as a strength as well as a limitation [72]. For example, given the exploratory design, the survey sample will not be representative for the age 55 years and older population in Sweden. The main reason for this is that we want to recruit a sample of information-rich individuals who are actively considering relocation. In Sweden, relocation rates in old age are in general quite low, which implies that in a representative sample of people as young as 55 years, very few could be considering relocation and even fewer actually realizing a move during the period of study. One way to ascertain that the sample includes diversity in terms of socioeconomic characteristics is to recruit participants via an LPH company as well as an NCP. Moreover, the sample will be geographically dispersed across the entire country. Being the first study of its kind, nationally as well as internationally, we consider the 2-level mixed methods design and sampling strategy promising and appropriate to expand the knowledge base on housing, relocation, and active and healthy aging even though results will not be generalizable to the whole population of older people [73]. However, we still anticipate that the longitudinal approach of Prospective RELOC-AGE has potential to yield results regarding housing and health associations that have high internal validity, but it is important that the risk of selection bias jeopardizing validity is assessed for each investigated association separately [74].

The data collection for Prospective RELOC-AGE is being implemented during a period when the COVID-19 pandemic is still affecting people of all ages as well as the society overall. How and to what extent the current situation will influence the data collected will be considered in the analyses and interpretation of results, as well as in the planning of subsequent follow-ups.

Conclusion

Building upon well-established cooperation with nonacademic partners, this large and complex project has the capacity to generate new knowledge and policy-relevant results. The 2-level mixed methods design is novel and challenging, using a combination of quantitative and qualitative data collection methods that will generate data on hitherto understudied associations between housing and active and healthy aging. Such knowledge is relevant for the development of proactive approaches to housing in old age on the individual, group, and societal levels.

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Authors' Contributions

SI generated the project idea, designed the project, and wrote the proposals for funding in collaboration with all coauthors except FN. MZ led the planning of the project and wrote the manuscript assisted by SI and with critical review from all coauthors. FN provided details regarding the recruitment and instruments to be used in the survey. All coauthors approved the final version of the manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Peer-reviewer report from the Swedish Research Council (Vetenskapsrådet).
[PDF File (Adobe PDF File), 91 KB - resprot_v10i9e31137_app1.pdf]

Multimedia Appendix 2
Peer-reviewer report from Forte: the Swedish Research Council for Health, Working Life and Welfare.
[PDF File (Adobe PDF File), 77 KB - resprot_v10i9e31137_app2.pdf]

References

1. Roy N, Dubé R, Després C, Freitas A, Légaré F. Choosing between staying at home or moving: a systematic review of factors influencing housing decisions among frail older adults. PLoS One 2018;13(1):e0189266 [FREE Full text] [doi: 10.1371/journal.pone.0189266] [Medline: 29293511]
2. Lotvonen S, Kyngäs H, Koistinen P, Bloigu R, Elo S. Mental well-being of older people in Finland during the first year in senior housing and its association with physical performance. Int J Environ Res Public Health 2018 Jun 25;15(7):1331 [FREE Full text] [doi: 10.3390/ijerph15071331] [Medline: 29941833]
3. Holland C, Boukouvalas A, Wallis S, Clarkesmith D, Cooke R, Liddell L, et al. Transition from community dwelling to retirement village in older adults: cognitive functioning and psychological health outcomes. Ageing Soc 2016 May 26;37(7):1499-1526. [doi: 10.1017/S0144686X16000477]
4. Robards J, Evandrou M, Falkingham J, Vlachantoni A. Mortality at older ages and moves in residential and sheltered housing: evidence from the UK. J Epidemiol Community Health 2014 Jun;68(6):524-529 [FREE Full text] [doi: 10.1136/jech-2013-203097] [Medline: 24638058]
5. Walker E, McNamara B. Relocating to retirement living: an occupational perspective on successful transitions. Aust Occup Ther J 2013 Dec;60(6):445-453. [doi: 10.1111/1440-1630.12038] [Medline: 24299484]
6. Oswald F, Wahl H, Schilling O, Iwarsson S. Housing-related control beliefs and independence in activities of daily living in very old age. Scand J Occup Ther 2007;14(1):33-43. [doi: 10.1080/11038120601151615] [Medline: 17366076]
7. Wahl H, Schilling O, Oswald F, Iwarsson S. The home environment and quality of life-related outcomes in advanced old age: findings of the ENABLE-AGE project. Eur J Ageing 2009 Jun;6(2):101-111 [FREE Full text] [doi: 10.1007/s10433-009-0114-z] [Medline: 28798597]
8. Gefenaite G, Björk J, Schmidt S, Slaug B, Iwarsson S. Associations among housing accessibility, housing-related control beliefs and independence in activities of daily living: a cross-sectional study among younger old in Sweden. J Hous and the Built Environ 2019 Nov 15;35(3):867-877. [doi: 10.1007/s10901-019-09717-4]
9. Gefenaite G, Björk J, Iwarsson S, Slaug B, Schmidt SM, Nilsson MH. Longitudinal association between housing accessibility and activities of daily living: the role of self-efficacy and control in people ageing with Parkinson's disease. BMC Geriatr 2020 May 25;20(1):181 [FREE Full text] [doi: 10.1186/s12877-020-01574-z] [Medline: 32450800]
10. Haak M, Malmgren Fänge A, Iwarsson S, Dahlin-Ivanoff S. The importance of successful place integration for perceived health in very old age: a qualitative meta-synthesis. Int J Public Health 2011 Dec;56(6):589-595. [doi: 10.1007/s00038-011-0282-4] [Medline: 21818615]
11. Kylén M, Schmidt SM, Iwarsson S, Haak M, Ekström H. Perceived home is associated with psychological well-being in a cohort aged 67–70 years. J Environ Psychol 2017 Aug;51:239-247. [doi: 10.1016/j.jenvp.2017.04.006]
12. Kylén M, Löfqvist C, Haak M, Iwarsson S. Meaning of home and health dynamics among younger older people in Sweden. Eur J Ageing 2019 Sep;16(3):305-315 [FREE Full text] [doi: 10.1007/s10433-019-00501-5] [Medline: 31543725]
13. Vitman Schorr A, Khalaila R. Aging in place and quality of life among the elderly in Europe: a moderated mediation model. Arch Gerontol Geriatr 2018;77:196-204. [doi: 10.1016/j.archger.2018.04.009] [Medline: 29728274]
14. Nygren C, Iwarsson S. Negotiating and effectuating relocation to sheltered housing in old age: a Swedish study over 11 years. Eur J Ageing 2009 Sep;6(3):177-189 [FREE Full text] [doi: 10.1007/s10433-009-0121-0] [Medline: 28798602]
15. Haak M, Fänge A, Iwarsson S, Ivanoff SD. Home as a signification of independence and autonomy: experiences among very old Swedish people. Scand J Occup Ther 2007;14(1):16-24. [doi: 10.1080/11038120601024929] [Medline: 17366074]
16. Löfqvist C, Granbom M, Himmelsbach I, Iwarsson S, Oswald F, Haak M. Voices on relocation and aging in place in very old age—a complex and ambivalent matter. Gerontologist 2013 Dec;53(6):919-927. [doi: 10.1093/geront/gnt034] [Medline: 23626372]
17. Granbom M, Himmelsbach I, Haak M, Löfqvist C, Oswald F, Iwarsson S. Residential normalcy and environmental experiences of very old people: changes in residential reasoning over time. J Aging Stud 2014 Apr;29:9-19. [doi: 10.1016/j.jaging.2013.12.005] [Medline: 24655669]

18. Granbom M, Perrin N, Szanton S, Cudjoe T, Gitlin LN. Household accessibility and residential relocation in older adults. J Gerontol B Psychol Sci Soc Sci 2019 Sep 15;74(7):e72-e83 [FREE Full text] [doi: 10.1093/geronb/gby131] [Medline: 30388250]
19. Granbom M, Slaug B, Löfqvist C, Oswald F, Iwarsson S. Community relocation in very old age: changes in housing accessibility. Am J Occup Ther 2016;70(2):7002270020p1-7002270020p9. [doi: 10.5014/ajot.2016.016147] [Medline: 26943110]
20. Ekström H, Schmidt SM, Iwarsson S. Home and health among different sub-groups of the ageing population: a comparison of two cohorts living in ordinary housing in Sweden. BMC Geriatr 2016 Apr 26;16:90 [FREE Full text] [doi: 10.1186/s12877-016-0265-7] [Medline: 27117314]
21. Active ageing: a policy framework. Geneva: World Health Organization; 2002. URL: http://apps.who.int/iris/bitstream/handle/10665/67215/WHO_NMH_NPH_02.8.pdf [accessed 2021-06-01]
22. Rantanen T, Portegijs E, Kokko K, Rantakokko M, Törmäkangas T, Saajanaho M. Developing an assessment method of active aging: University of Jyvaskyla Active Aging Scale. J Aging Health 2019 Jul;31(6):1002-1024 [FREE Full text] [doi: 10.1177/0898264317750449] [Medline: 29291660]
23. Timonen V. Beyond Successful and Active Ageing. Bristol: Policy Press; 2016.
24. Haak M, Slaug B, Oswald F, Schmidt SM, Rimland JM, Tomsone S, et al. Cross-national user priorities for housing provision and accessibility: findings from the European innovAge Project. Int J Environ Res Public Health 2015 Mar 02;12(3):2670-2686 [FREE Full text] [doi: 10.3390/ijerph120302670] [Medline: 25739003]
25. Iwarsson S, Edberg A, Ivanoff SD, Hanson E, Jönson H, Schmidt S. Understanding user involvement in research in aging and health. Gerontol Geriatr Med 2019;5:2333721419897781 [FREE Full text] [doi: 10.1177/2333721419897781] [Medline: 31909093]
26. Prospective RELOC-AGE: how do housing choices and relocation matter for active ageing? (RELOC-AGE). US National Library of Medicine. 2021. URL: https://clinicaltrials.gov/ct2/show/NCT04765696 [accessed 2021-06-01]
27. Domestic migration by type, age and sex. Year 2000-2020. Statistics Sweden. 2020. URL: https://www.statistikdatabasen.scb.se/pxweb/en/ssd/START__BE__BE0101__BE0101J/FlyttningarInrk/ [accessed 2021-06-01]
28. [Information to participants in RELOC-AGE study]. Center for Ageing and Supportive Environments. URL: https://www.case.lu.se/relocage [accessed 2021-06-01]
29. Oswald F, Schilling O, Wahl H, Fänge A, Sixsmith J, Iwarsson S. Homeward bound: Introducing a four-domain model of perceived housing in very old age. Journal of Environmental Psychology 2006 Sep;26(3):187-201. [doi: 10.1016/j.jenvp.2006.07.002]
30. Fänge A, Iwarsson S. Physical housing environment: development of a self-assessment instrument. Can J Occup Ther 1999 Dec;66(5):250-260. [doi: 10.1177/000841749906600507] [Medline: 10641377]
31. Fänge A, Iwarsson S. Accessibility and usability in housing: construct validity and implications for research and practice. Disabil Rehabil 2003 Dec 02;25(23):1316-1325. [doi: 10.1080/09638280310001616286] [Medline: 14617438]
32. Boonyaratana Y, Hansson EE, Granbom M, Schmidt SM. The psychometric properties of the meaning of home and housing-related control beliefs scales among 67-70 year-olds in Sweden. Int J Environ Res Public Health 2021 Apr 17;18(8):4273 [FREE Full text] [doi: 10.3390/ijerph18084273] [Medline: 33920612]
33. Oswald F, Wahl H, Martin M, Mollenkopf H. Toward measuring proactivity in person-environment transactions in late adulthood. J Housing Elderly 2003 Jan 21;17(1-2):135-152. [doi: 10.1300/j081v17n01_10]
34. Folkhälsorapport Vuxna i Skåne. Utveckling Skåne. 2020. URL: https://utveckling.skane.se/utvecklingsomraden/folkhalsa-och-social-hallbarhet/folkhalsorapporter/folkhalsorapport-vuxna-skane/ [accessed 2021-06-01]
35. Grahn P, Stigsdotter U, Berggren-Bärring AM. Human issues: eight experienced qualities in urban open spaces. In: Werquin AC, Duhem B, Lindholm G, Oppermann B, Paulet S, Tjallingii S, editors. Green Structure and Urban Planning—Final Report of COST Action C11. Brussels: EU Publications Office; 2005:240-248.
36. Grahn P, Stigsdotter UK. The relation between perceived sensory dimensions of urban green space and stress restoration. Landscape Urban Planning 2010 Mar;94(3-4):264-275. [doi: 10.1016/j.landurbplan.2009.10.012]
37. de Jong K, Albin M, Skärbäck E, Grahn P, Wadbro J, Merlo J, et al. Area-aggregated assessments of perceived environmental attributes may overcome single-source bias in studies of green environments and health: results from a cross-sectional survey in southern Sweden. Environ Health 2011 Jan 17;10(1):4 [FREE Full text] [doi: 10.1186/1476-069X-10-4] [Medline: 21235826]
38. Kasper JD, Freedman VA. Findings from the 1st round of the National Health and Aging Trends Study (NHATS): introduction to a special issue. J Gerontol B Psychol Sci Soc Sci 2014 Nov;69 Suppl 1:S1-S7. [doi: 10.1093/geronb/gbu125] [Medline: 25342818]
39. Jenkinson C, Layte R, Jenkinson D, Lawrence K, Petersen S, Paice C, et al. A shorter form health survey: can the SF-12 replicate results from the SF-36 in longitudinal studies? J Public Health Med 1997 Jun;19(2):179-186. [doi: 10.1093/oxfordjournals.pubmed.a024606] [Medline: 9243433]
40. Iwarsson S, Haak M, Slaug B. Current developments of the housing enabler methodology. Br J Occup Ther 2012 Nov 01;75(11):517-521. [doi: 10.4276/030802212x13522194759978]

41. Ryan J. Examining the process of modal choice for everyday travel among older people. Int J Environ Res Public Health 2020 Jan 21;17(3):691 [FREE Full text] [doi: 10.3390/ijerph17030691] [Medline: 31973097]
42. Fristedt S, Kammerlind A, Bravell ME, Fransson EI. Concurrent validity of the Swedish version of the life-space assessment questionnaire. BMC Geriatr 2016 Nov 08;16(1):181 [FREE Full text] [doi: 10.1186/s12877-016-0357-4] [Medline: 27821138]
43. Baker PS, Bodner EV, Allman RM. Measuring life-space mobility in community-dwelling older adults. J Am Geriatr Soc 2003 Nov;51(11):1610-1614. [doi: 10.1046/j.1532-5415.2003.51512.x] [Medline: 14687391]
44. University of Jyvaskyla, Active Ageing Scale UJACAS. Gerontology Research Center. URL: https://www.gerec.fi/en/research/activeageing/active-ageing-agnes-study/active-ageing-scale-ujacas/ [accessed 2021-06-01]
45. Siltanen S, Tourunen A, Saajanaho M, Palmberg L, Portegijs E, Rantanen T. Psychological resilience and active aging among older people with mobility limitations. Eur J Ageing 2021 Mar;18(1):65-74 [FREE Full text] [doi: 10.1007/s10433-020-00569-4] [Medline: 33746682]
46. Herdman M, Gudex C, Lloyd A, Janssen M, Kind P, Parkin D, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). Qual Life Res 2011 Dec;20(10):1727-1736 [FREE Full text] [doi: 10.1007/s11136-011-9903-x] [Medline: 21479777]
47. Eklund K, Wilhelmson K, Landahl S, Ivanoff-Dahlin S. Screening for frailty among older emergency department visitors: validation of the new FRESH-screening instrument. BMC Emerg Med 2016 Jul 22;16(1):27 [FREE Full text] [doi: 10.1186/s12873-016-0087-0] [Medline: 27449526]
48. Fugl-Meyer AR, Melin R, Fugl-Meyer KS. Life satisfaction in 18- to 64-year-old Swedes: in relation to gender, age, partner and immigrant status. J Rehabil Med 2002 Sep;34(5):239-246 [FREE Full text] [doi: 10.1080/165019702760279242] [Medline: 12392240]
49. Luszczynska A, Scholz U, Schwarzer R. The general self-efficacy scale: multicultural validation studies. J Psychol 2005 Sep;139(5):439-457. [doi: 10.3200/JRLP.139.5.439-457] [Medline: 16285214]
50. Mangham LJ, Hanson K, McPake B. How to do (or not to do) ... Designing a discrete choice experiment for application in a low-income country. Health Policy Plan 2009 Mar;24(2):151-158. [doi: 10.1093/heapol/czn047] [Medline: 19112071]
51. Earnhart D. Combining revealed and stated data to examine housing decisions using discrete choice analysi. J Urban Econ 2002 Jan;51(1):143-169. [doi: 10.1006/juec.2001.2241]
52. Walker B, Marsh A, Wardman M, Niner P. Modelling tenants' choices in the public rented sector: a stated preference approach. Urban Studies 2016 Jul 02;39(4):665-688. [doi: 10.1080/00420980220119516]
53. Hensher D, Rose J, Rose J, Greene W. Applied Choice Analysis: A Primer, 2nd Edition. New York: Cambridge University Press; 2015.
54. Charmaz K. Constructing Grounded Theory: A Practical Guide Through Qualitative Analysis. Thousand Oaks: Sage Publications; 2006.
55. Corbin J, Strauss A. Basics of Qualitative Research: Techniques and Procedures for Developing Grounded Theory, 4th Edition. Thousand Oaks: Sage Publications; 2014.
56. Patton M. Qualitative Research & Evaluation Methods, 3rd Edition. Thousand Oaks: Sage Publications; 2002.
57. Hole AR. Modelling heterogeneity in patients' preferences for the attributes of a general practitioner appointment. J Health Econ 2008 Jul;27(4):1078-1094. [doi: 10.1016/j.jhealeco.2007.11.006] [Medline: 18179837]
58. Andersson H, Hole AR, Svensson M. Valuation of small and multiple health risks: a critical analysis of SP data applied to food and water safety. J Environ Econ Manag 2016 Jan;75:41-53. [doi: 10.1016/j.jeem.2015.11.001]
59. Huang D, Andersson H, Zhang S. Willingness to pay to reduce health risks related to air quality: evidence from a choice experiment survey in Beijing. J Environ Planning Manag 2017 Nov 23;61(12):2207-2229. [doi: 10.1080/09640568.2017.1389701]
60. Iecovich E. Aging in place: from theory to practice. Anthropological Notebooks 2014;20(1):21-33 [FREE Full text]
61. Cutchin MP. Using Deweyan philosophy to rename and reframe adaptation-to-environment. Am J Occup Ther 2004;58(3):303-312. [doi: 10.5014/ajot.58.3.303] [Medline: 15202628]
62. Kaye HS, LaPlante MP, Harrington C. Do noninstitutional long-term care services reduce Medicaid spending? Health Aff (Millwood) 2009;28(1):262-272. [doi: 10.1377/hlthaff.28.1.262] [Medline: 19124878]
63. Iwarsson S, Löfqvist C, Oswald F, Slaug B, Schmidt S, Wahl H, et al. Synthesizing ENABLE-AGE research findings to suggest evidence-based home and health interventions. J Housing Elderly 2016 Aug 11;30(3):330-343. [doi: 10.1080/02763893.2016.1198742]
64. World report on ageing and health 2015. Geneva: World Health Organization; 2015. URL: https://www.who.int/ageing/events/world-report-2015-launch/en/ [accessed 2021-06-01]
65. Hartig T, Mitchell R, de Vries S, Frumkin H. Nature and health. Annu Rev Public Health 2014;35:207-228. [doi: 10.1146/annurev-publhealth-032013-182443] [Medline: 24387090]
66. de Jong K, Albin M, Skärbäck E, Grahn P, Björk J. Perceived green qualities were associated with neighborhood satisfaction, physical activity, and general health: results from a cross-sectional study in suburban and rural Scania, southern Sweden. Health Place 2012 Nov;18(6):1374-1380. [doi: 10.1016/j.healthplace.2012.07.001] [Medline: 22889998]

67. Weimann H, Rylander L, Albin M, Skärbäck E, Grahn P, Östergren P, et al. Effects of changing exposure to neighbourhood greenness on general and mental health: a longitudinal study. Health Place 2015 May;33:48-56. [doi: 10.1016/j.healthplace.2015.02.003] [Medline: 25754263]
68. Weimann H, Rylander L, van den Bosch MA, Albin M, Skärbäck E, Grahn P, et al. Perception of safety is a prerequisite for the association between neighbourhood green qualities and physical activity: results from a cross-sectional study in Sweden. Health Place 2017 May;45:124-130. [doi: 10.1016/j.healthplace.2017.03.011] [Medline: 28359908]
69. Portegijs E, Keskinen KE, Eronen J, Saajanaho M, Rantakokko M, Rantanen T. Older adults' physical activity and the relevance of distances to neighborhood destinations and barriers to outdoor mobility. Front Public Health 2020;8:335 [FREE Full text] [doi: 10.3389/fpubh.2020.00335] [Medline: 32850580]
70. Stark S, Keglovits M, Arbesman M, Lieberman D. Effect of home modification interventions on the participation of community-dwelling adults with health conditions: a systematic review. Am J Occup Ther 2017;71(2):7102290010p1-7102290010p11. [doi: 10.5014/ajot.2017.018887] [Medline: 28218595]
71. Granbom M, Szanton S, Gitlin LN, Paulsson U, Zingmark M. Ageing in the right place: a prototype of a web-based housing counselling intervention for later life. Scand J Occup Ther 2020 May;27(4):289-297. [doi: 10.1080/11038128.2019.1634756] [Medline: 31305191]
72. Creswell J, Clark V. Designing and Conducting Mixed Methods Research, 2nd Edition. Thousand Oaks: Sage Publications; 2011.
73. Onwuegbuzie AJ, Collins KMT. The role of sampling in mixed methods research. Köln Z Soziol 2017 Jul 3;69(S2):133-156. [doi: 10.1007/s11577-017-0455-0]
74. Biele G, Gustavson K, Czajkowski NO, Nilsen RM, Reichborn-Kjennerud T, Magnus PM, et al. Bias from self selection and loss to follow-up in prospective cohort studies. Eur J Epidemiol 2019 Oct;34(10):927-938. [doi: 10.1007/s10654-019-00550-1] [Medline: 31451995]

Abbreviations

DCE: discrete choice experiment
HCQ: Housing-Related Control Beliefs Questionnaire
LPH: public housing company in Southern Sweden
NCP: national condominium provider

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Protocol

Understanding Patterns of Healthy Aging Among Men Who Have Sex With Men: Protocol for an Observational Cohort Study

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Abstract

Background: With the graying of sexual and gender minority communities and the growing number of people aged ≥50 years living with HIV, it is increasingly important to understand resilience in the context of the psychosocial aspects of aging and aging well.

Objective: This paper aims to describe the methods and sample for the *Understanding Patterns of Healthy Aging Among Men Who Have Sex With Men* study.

Methods: This observational cohort study was conducted within the Multisite AIDS Cohort Study (MACS) and was designed to explore resiliencies to explain patterns of health and illness among middle-aged and older sexual minority men. To be eligible, a participant had to be an active participant in the MACS, be at least 40 years of age as of April 1, 2016, and report any sex with another man since enrollment in the MACS.

Results: Eligible participants (N=1318) completed six biannual surveys between April 2016 and April 2019. The mean age of the sample was 59.6 years (range 40-91 years). The sample was mostly White, educated, gay-identified, and included both HIV-positive (656/1318, 49.77%) and HIV-negative (662/1318, 50.23%) men.

Conclusions: Understanding resiliencies in aging is a critical springboard for the development of more holistic public health theories and interventions that support healthy aging among older sexual minority men.

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KEYWORDS

HIV; aging; MSM; gay and bisexual men

Introduction

Background

Although difficult to accurately measure, it is estimated that there are currently 1.75 to 2.4 million sexual minorities (eg, lesbian, gay, and bisexual) in the United States who are aged ≥50 years; by 2030, it is estimated that there will be over 5 million sexual minorities [1]. Across the life course, many sexual minority men (SMM; including gay, bisexual, and other men who have sex with men) experience health disparities related to experienced stigma and discrimination, including increased depression or anxiety and substance use [2-7]. These disparities are often compounded by intersecting identities (eg, race or ethnicity and advanced age). The interactions of HIV (including long-term treatment, HIV infection, and HIV-associated non-AIDS conditions), health disparities, and aging—nearly half of persons living with HIV are aged ≥50 years, a majority of whom are SMM [8]—contribute to complex health conditions that create challenges to care and well-being [9,10].

The synergistic interplay of multiple psychosocial conditions that result in disparities in disease burden has been defined as a syndemic (ie, two or more conditions that interact synergistically to create excess disease burden) [11-15]. In a probability sample of urban SMM, Stall et al [15] were the first to show that a syndemic interplay of psychosocial health conditions (ie, depression, substance abuse, childhood sexual abuse, and violence victimization) was associated with HIV behavioral risk-taking and HIV infection among SMM. These initial findings have been replicated with many other independent samples of SMM in the United States and abroad and have been a bedrock in deficit-based theory and practice [16-28].

Resiliencies: A New Approach

Despite these health disparities and exposure to stigma and discrimination, many SMM have managed to survive and thrive in the face of adversity. This study builds on the work of Fredriksen-Goldsen, Emlet, and others who have identified resiliencies in this population [29-32].

Theoretical definitions of resiliency focus on strengths in the face of adversity, suggesting that resilience is an ever-changing interaction of internal and external exposures to risk and protective factors and an individual's adaptation to or recovery from adversity, rather than an innate or static trait [33-37]. Protective factors (ie, assets and resources) in the face of adversity are the foundation for the production of multiple resiliencies that men can draw upon to support health. Two primary resiliency models describing different pathways between protective factors and positive adaptation [33,36,38] have been identified. These are (1) the compensatory (main effects) model, in which the presence of resiliency factors has a direct positive effect on health outcomes, and (2) the protective (interaction) model, in which individual and environmental resiliency factors moderate the relationship between risks and health outcomes.

The development and expression of resiliencies in midlife SMM is still largely unknown. This study is designed to explore multiple factors that may work individually or in combination to act as protective factors that may be associated with better mental and physical health outcomes and moderate effects of syndemic psychosocial conditions on HIV-related health. Our expectation is that this sets the stage for a series of manuscripts that use these data to characterize resiliencies among SMM and may demonstrate protective effects on health.

Current risk-focused theoretical models, such as syndemics, have been unable to fully capture the complexities that underlie health disparities that burden SMM over the life course, including resiliencies that buffer or interact with the stressors that drive these disparities [39]. In creating a theoretical model inclusive of both risk and resilience, we may be able to identify pathways for innovative and practical methods for intervention, complementing the minimization of risk factors while strengthening health-promoting factors.

The study of resiliencies is relatively new to aging SMM health research; therefore, a community-engaged process was used to identify domains of focus [39]. Briefly, in 2011, members of the SMM community, researchers, providers, and other experts in sexual minority health were invited to a symposium to discuss how resiliencies might inform HIV prevention interventions. This group identified more than 200 SMM-specific resiliencies that were qualitatively collapsed and categorized. The symposium organizers then reviewed and amended these resiliencies with other theoretically important factors with a focus on identifying modifiable factors to create a list of factors that might be incorporated into future research efforts. The final list included resiliencies that operate at the level of the individual (eg, managing internalized homophobia and shame, self-monitoring and goal setting, adaptability, and coping), relationship building (eg, ability to form relationships and dyadic support), familial support (eg, building strong relationships with one's family of origin and creating a family of one's own), and structural and community support (eg, connection to community, institutional support, community building, homophobia management, and external monitoring) [39].

Study Objectives

This paper describes the methods for and characterizes the sample of an observational cohort study designed to explore the production of resiliencies and to explain patterns of health and illness in aging among middle-aged and older HIV-positive and HIV-negative SMM. The overarching goals of the National Institutes of Health funded grant were to (1) identify individual interpersonal and structural resiliencies and evaluate their psychometric properties and determine their prevalence among middle-aged and aging SMM with and without HIV over time and (2) to investigate whether these resiliencies impact—separately and jointly—health and wellness outcomes, including virologic and immunologic control, depression, frailty, chronic disease (eg, diabetes and hypertension) management, and physical and cognitive functioning by mitigating the effect of psychosocial and behavioral vulnerabilities (eg, substance and alcohol use, partner violence, internalized homophobia, and social discrimination).

Methods

Study Design and Setting

This study, *Understanding Patterns of Healthy Aging Among Men Who Have Sex With Men* ("Healthy Aging Study," NIMHD, R01M010680, principal investigator: RS, MRF, and MWP), is an observational cohort study conducted within the ongoing Multisite AIDS Cohort Study (MACS).

The Multicenter AIDS Cohort Study

Overview

The MACS started enrollment in 1984 with sites located in Baltimore/Washington DC, Chicago, Pittsburgh, and Los Angeles [40]. In 1987, investigators from the Department of Epidemiology of the Johns Hopkins Bloomberg School of Public Health established the Center for Coordination, Analysis, and Management of the Multicenter AIDS Cohort Study (CAMACS). A total of 7352 men who had sex with men were enrolled in the MACS. In this prospective cohort study, HIV-positive and HIV-negative men were followed up every 6 months with interviews, physical examinations, cognitive testing, and phlebotomy. As one of the longest HIV cohort studies in the United States, the MACS has been able to provide a wealth of longitudinal biological and behavioral data on HIV risk prevention, seroconversion, disease progression or treatment, and quality of life. These factors made the MACS an ideal study to embed this study. More information can be found on the web [41].

Coordinating Center

The Healthy Aging Study Coordinating Center was a collaboration between the University of Pittsburgh School of Public Health and Georgetown University Medical Center. Working closely with CAMACS, the coordinating center was responsible for the oversight of the Healthy Aging Study, including training and working with the local study sites for participant recruitment and follow-up and data collection, data monitoring and safety, assuring communication between local sites, and monitoring the processes of data analysis and manuscript or conference abstract preparation.

Screening, Recruitment, and Enrollment

To be eligible for inclusion, participants had to (1) be an active participant in the MACS (attended at least one semiannual visit in the 2 years before the start of the Heathy Aging Study at MACS visit 65); (2) be at least 40 years of age at visit 65 (April 1, 2016); and (3) report any sex with another man since enrollment in the MACS. The initial eligibility list was updated before each of the subsequent five Healthy Aging Study visits to remove individuals who died, withdrew from the MACS, or requested to be removed from future recruitment. Although the total number of possible participants was set according to the MACS cohort at visit 65 (eg, no one was able to *age into* being eligible), men were able to enroll or choose not to participate in each of the six study visits.

Local site program staff recruited and enrolled all participants using the pre-existing MACS computerized-assisted direct interview (CADI) system. For each potential recruit, CAMACS first conducted an initial screening using historical MACS data. These data were used to program the CADI to alert the local study site staff of an eligible participant during their routine MACS visit. An initial CADI screen prompted the staff to ask eligible participants if they were interested in the study. If yes was entered, the following screen asked if they preferred to fill out a paper or electronic version of the survey. The same procedure was used for both in-person and phone visits. Participants were asked at each study from visit 65 through visit 70.

Data Collection

Healthy Aging Study Surveys

Data collection for this study was completed within the existing structure of the ongoing MACS (ie, visit 65 of the MACS parent study was visit 1 for this substudy). This allowed us to decrease participant burden, as it did not require an additional study visit beyond MACS participation. Eligible participants were asked to complete a web-based or paper survey at each MACS visit between April 2016 and April 2019 for a total of six surveys, yielding a 3-year longitudinal assessment of both vulnerabilities and resiliencies. The periods for each visit were as follows: Healthy Aging Study visit 1-MACS visit 65: April 2, 2016-October 7, 2016; Healthy Aging Study visit 2-MACS visit 66: October 1, 2016-April 8, 2017; Healthy Aging Study visit 3-MACS visit 67: March 31, 2017-October 28, 2017; Healthy Aging Study visit 4-MACS visit 68: September 26, 2017-March 31, 2018; Healthy Aging Study visit 5-MACS visit 69: March 30, 2018-November 8, 2018; and Healthy Aging Study visit 1-MACS visit 70: October 2, 2018-April 8, 2019. Those who preferred an electronic survey were given the opportunity to complete the survey on an electronic tablet during or after their regular MACS visit or on a computer or personal device before or after their MACS visit using a link sent via email. Participants who did not want to complete the survey electronically were given the paper survey to complete after their MACS visit or to take home with an addressed stamped envelope for them to return to the study coordinating center. All surveys were completed within 1 month of the corresponding study visit. Paper surveys were sent to the coordinating center for entry into the study database. The survey was conducted in English and Spanish.

The coordination center provided a weekly tracking report of *Healthy Aging* statistics, including eligibility, enrollment, survey completion, and pending or outstanding survey completions to local MACS sites. Sites used these data to follow up with participants to remind and encourage survey completion using locally established and approved MACS follow-up procedures (eg, phone, email, and mail). The coordinating center worked with individual sites, as necessary, on issues related to follow-up. All surveys had to be completed within 1 month before or after the participant's scheduled MACS visit. Surveys submitted after this window were censored.

Healthy Aging Study Measures

The surveys included a range of questions and scales to assess global resilience (Global Resiliency Scale- Resiliency Scale-14 [42]), theorized resiliencies (eg, social bonding using the Social

Provisions Scale [43] and Relationships structures using the Experiences in Close Relationship-Resiliency Scale [44]), psychosocial and behavioral vulnerabilities (eg, loneliness using the University of California, Los Angeles Loneliness Scale [45] and alcohol use using the Alcohol Use Disorders Identification Test-Concise [46]), and socioeconomic descriptors (eg, sexual or gender identity, income, and employment). We included well-established validated items (eg, Alcohol Use Disorders Identification Test-Concise [46] and Global Resiliency Scale-Resiliency Scale-14 [42]); the study team designed items to assess more novel concepts for which established instruments did not already exist (eg, homophobia management) and some items were developed through community engagement (eg, working with Let's Kick ASS to develop the AIDS survivor syndrome questions [47]).

Theorized resiliencies were chosen based on the domains identified through the community-engaged process described earlier. We intentionally chose measures to assess possible resiliencies at the individual, interpersonal or dyadic, and community levels. We also included several syndemic-informed measures at each level. These measures were primarily selected from previous studies [14,17,39].

To assess the widest range of resilience and syndemic factors while respecting survey length and participant burden, we chose to identify some measures to ask for each survey wave (eg, global resiliency and social bonding), whereas others were asked intermittently, for example, at two of the waves within the 3-year follow-up period (eg, homophobia management and physical activity). This syncopated process also allowed the study team to add additional factors that were not initially included in the first *Healthy Aging* survey (eg, conversion therapy and grit). The final visit 70 survey included nearly every question asked over the course of the study. Table 1 describes each of the study measures, at which visits participants were asked to provide an overview of data points for future longitudinal analyses, and how each measure is connected to the larger MACS.

Table 1. Measures of the Multisite AIDS Cohort Study Healthy Aging Study (2016-2019).

Domain or measure	Study visit[a]					
Aging visit	1	2	3	4	5	6
MACS[b] visit	65	66	67	68	69	70
Individual level resiliencies						
Housing status[c]	✓[d]	✓	✓	✓	✓	✓
Volunteer work: General Social Survey [48]	✓	✓	✓	✓	✓	✓
Global Resiliency Scale (RS-14[e]) [42]	✓	✓	✓	✓	✓	✓
Revised Life Orientation Test [49]	✓	✓	✓	✓	✓	✓
Multidimensional measurement of religiousness or spirituality [50,51]	✓	✓	✓	✓	✓	✓
Self-monitoring and goal setting[c]			✓		✓	✓
Homophobia management[c]		✓	✓		✓	✓
Aging Satisfaction: Attitudes Toward Aging Subscale from Philadelphia Geriatric Center Morale Scale [52]	✓	✓		✓		✓
Grit [53,54]					✓	✓
Medical decision making (adapted from Sudore et al [55])			✓		✓	✓
Mindfulness: MAAS[f] [56]			✓		✓	✓
Sexual health: IIEF[g] [57]				✓		✓
Physical activity: IPAQ-SF[h] [58]	✓	✓	✓			✓
Body image: BIQ[i] [59]		✓	✓			✓
Individual level other						
Internalized homophobia [60]	✓	✓	✓	✓		✓
Employment[c]			✓	✓	✓	✓
Work satisfaction: BIAJS[j] [61]	✓	✓	✓	✓		✓
UCLA[k] loneliness [45]	✓	✓	✓	✓		✓
Sexual orientation[c]	✓	✓	✓	✓	✓	✓
Gender identity[c]	✓	✓	✓			
Sexual behavior with gender minority partners[c]	✓	✓	✓			
Bisexual orientation and stigma[c]			✓			✓
Discrimination experiences[c]	✓	✓	✓	✓	✓	✓
Alcohol use: AUDIT-C[l] [46]	✓	✓	✓	✓	✓	✓
Sex work[c]			✓			✓
Health care satisfaction: PSQ-18[m] [62]	✓	✓	✓	✓	✓	✓
HIV biological prevention techniques[c]			✓		✓	✓
AIDS survivor syndrome[c] [47]	✓	✓	✓	✓	✓	✓
Anxiety: GAD-7[n] [63]	✓	✓	✓	✓	✓	✓
Pain experiences and treatment[c]					✓	✓
Opioid use[c]					✓	✓
Pill burden scale [64]					✓	✓

Domain or measure	Study visit[a]					
Posttraumatic stress disorder: PCL-C[o] [65]				✓	✓	✓
Stigma experiences[c]				✓		✓
Digital communication use[c]				✓		
Technology use[c]				✓		
Conversion therapy experiences[c]		✓	✓			✓
Stress: PSS-10[p] [66]					✓	✓
Interpersonal or dyadic level resiliencies						
Social bonding-Social Provisions Scale [43]	✓	✓	✓	✓	✓	✓
Support[c]	✓	✓	✓	✓	✓	✓
Mentoring: Gay Mentoring Scale [67]	✓	✓	✓	✓	✓	✓
Relationships[c]			✓	✓	✓	✓
Relationship structures-ECR-RS[q] [44]		✓	✓	✓	✓	✓
Interpersonal or dyadic level other						
HIV status and HIV disclosure or stigma[c]	✓	✓	✓	✓		✓
IPV[r] [68,69]					✓	✓
Community or structural level resiliencies						
Emotional connection with gay community [70]	✓	✓	✓	✓	✓	✓
Psychological Sense of Community [70]	✓	✓	✓	✓	✓	✓
Neighborhood contexts[c]		✓	✓		✓	✓

[a]Sample size at each visit: visit 65: n=871; visit 66: n=1118; visit 67: n=1116; visit 68: n=1065; visit 69: n=1071; visit 70: n=1056.
[b]MACS: Multisite AIDS Cohort Study.
[c]Study team–developed measure.
[d]Measure present.
[e]RS-14: 14-item Resilience Scale.
[f]MAAS: Mindful Attention Awareness Scale.
[g]IIEF: International Index of Erectile Function.
[h]IPAQ-SF: International Physical Activity Questionnaire-Short Form.
[i]BIQ: Body Image Questionnaire.
[j]BIAJS: Brief Index of Job Satisfaction Measure.
[k]UCLA: University of California, Los Angeles.
[l]AUDIT-C: Alcohol Use Disorders Identification Test-Concise.
[m]PSQ: Patient Satisfaction Questionnaire.
[n]GAD-7: Generalized Anxiety Disorder-7 item.
[o]PCL-C: Posttraumatic stress disorder checklist.
[p]PSS-10: Perceived Stress Scale-10 item.
[q]ECR-RS: Experiences in Close Relationships-Relationships Structures.
[r]IPV: intimate partner violence.

Childhood, Coming Out, and Early Adulthood Survey

The *Long Term Health Effects of Methamphetamine Use in the MACS* (NIDA, R01DA022936, principal investigator: RS) study between 2008 and 2009 collected information on experiences related to childhood, coming out, and early adulthood [17]. Although some of the *Healthy Aging* Study participants completed this survey at that time, not everyone did. Healthy Aging Study participants who had not completed this survey in 2008-2009 were given the opportunity to do so at each study wave until completion or refusal. The baseline survey provides important additional data on participants' experiences related to childhood, adolescence, and coming out. A total of 195 participants completed the survey.

MACS Core Variables

Overview

Healthy Aging Study participants were matched by unique ID to the longitudinal MACS data, thereby connecting them to many years of psychosocial, behavioral, and biological data collected as part of their regular MACS participation. Data and specimens collected at semiannual visits included prospectively measured HIV status (for HIV-negative participants) demographic and psychosocial characteristics; medications used as pre-exposure prophylaxis or HIV treatment; hematologic variables, including an enumeration of CD3, CD4, and CD8 T-cell subsets; plasma HIV RNA quantification (for HIV-positive participants); a lipid profile; hepatitis serology; liver and renal function assays; evaluation of glucose metabolism and the allocation of samples for repository; HIV-related symptoms; psychomotor functioning; and illnesses and use of health services. Matching participants to these data is essential for completing the *Healthy Aging* Study objectives. This has provided an opportunity for study investigators to develop additional related projects.

Participant Incentives

Participants were reimbursed US $35 for each *Healthy Aging* survey for a possible total of US $210 over the entire study period, in addition to regular MACS participation incentives. For wave 70, to increase participation and adjust for longer lengths, reimbursement was increased to US $45. Participants who completed the *Childhood, Coming Out, and Early Adulthood* Survey during this time (ie, did not complete it in 2008-2009) were reimbursed an additional US $20. MACS staff issued all incentives according to the existing protocols. If not completed onsite, the Healthy Aging Study Coordinating Center notified the local MACS site when a survey was completed, prompting the site to issue the incentive.

Human Subjects and Informed Consent

All study procedures were approved by the coordinating center at the University of Pittsburgh. Subsequently, the approved protocol was submitted for approval by each of the participating MACS sites. Informed consent was obtained from all participants using a click-to-consent procedure at the beginning of each electronic survey at each study wave. Those who completed the hard copy surveys were asked to consent by checking a box. Some local sites also required a hard copy consent to be completed, which was obtained by the local study staff.

To strictly protect participants' confidentiality, all study data were coded by the participant's MACS ID. Any identifying information associated with this ID was kept at the local sites in accordance with the approved protocols. Number-coded information became part of an electronic database, which was password-protected and only accessible to the study staff.

Analyses

Analyses included in this paper were completed in SPSS (version 26) software to characterize the sample at *baseline* (ie, the initial visit for each participant). Frequencies were used to describe the overall sample, with comparisons by HIV status using Pearson chi-square, Fisher exact, and two-tailed *t* tests as appropriate.

Previous publications from this study used several analytical approaches to assess research questions. These approaches include longitudinal latent class analyses to identify associations between social environmental resilience and loneliness [71] and associations between social support typologies and depression symptoms [72]; group-based trajectory approaches to assess predictors of polypharmacy [73]; longitudinal multinomial analyses assessing predictors of romantic partnership structures [74] and predictors of aging satisfaction [75]; multivariable regressions to assess the effects of conversion therapy on depressive symptoms [76]; longitudinal mixed models with lagged variables assessing the effects of employment status on depressive symptomology [77]; and structural equation modeling, using mediation, to assess associations among gay community connection, negative self-appraisal, and fitness engagement [78]. The core investigative team will use Longitudinal Latent Class Analysis and structural equation modeling procedures to assess latent resiliency phenotypes and their direct and indirect effects on biopsychosocial health outcomes in a forthcoming series of manuscripts.

Results

Enrollment and Survey Participation

Figure 1 details the participant enrollment and follow-up for the *Healthy Aging* Study. There were 1497 MACS participants who met the eligibility criteria for the *Healthy Aging* Study at study commencement in April 2016. The target number changed as participants withdrew or passed away. Of the maximum 1497 potentially eligible MACS participants, we enrolled 1318 (88.04%) unique individuals into this study, who contributed a total of 6297 person-visits. Table 2 describes enrollment and participation numbers by visit. A mean of 1185 participants were approached across all waves ranging from 979 at visit 65 to 1199 at visit 70. The sample size was lower in visit 65 because some sites did not begin *Healthy Aging* enrollment until midway through the 6-month study visit period, due to delays in site-based institutional review board approval or logistics delays. Enrollment at visits were as follows: (1) visit 65: 91.6% (897/979); (2) visit 66: 89.93% (1152/1281); (3) visit 67: 86.47% (1120/1295); (4) visit 68: 91.7% (1127/1229); (5) visit 69: 92.16% (1129/1225); and (6) visit 70: 91.74% (1100/1199). The refusal across time was ranged from a high of 13.51% (175/1295) at visit 67 to a low of 7.84% (96/1225) at visit 69. Survey completion at visits were as follows: (1) visit 65: 97.1% (871/897); (2) visit 66: 97.05% (1118/1152); (3) visit 67: 99.64% (1116/1120); (4) visit 68: 94.23% (1062/1127); (5) visit 69: 94.86% (1071/1129); and (6) visit 70: 95.91% (1055/1100). Among Healthy Aging participants, 95.98% (1265/1318) completed two or more study visits, with a median completion of five visits (IQR 4-6).

Overall, just over half (3524/6293, 56%) of the surveys were completed at the clinic; the other 43.86% (2760/6293) were completed at home before or immediately following the study visit. Over time, the number of participants who completed the survey at home increased from 21% (183/871) at visit 65 to

60% (633/1055) at visit 70. When asked about the survey length, from 1=*too short* to 5=*too long*, the mean score across time was 3.7 (3=*just right*). When asked how *interesting* they found the surveys, participants reported an overall score of 3.6 on a scale from 1=very boring, 3=just okay, to 5=very interesting.

Figure 1. Healthy Aging Study participant recruitment and survey completion. IRB: institutional review board; MACS: Multisite AIDS Cohort Study; MSM: men who have sex with men; MSMW: men who have sex with men and women.

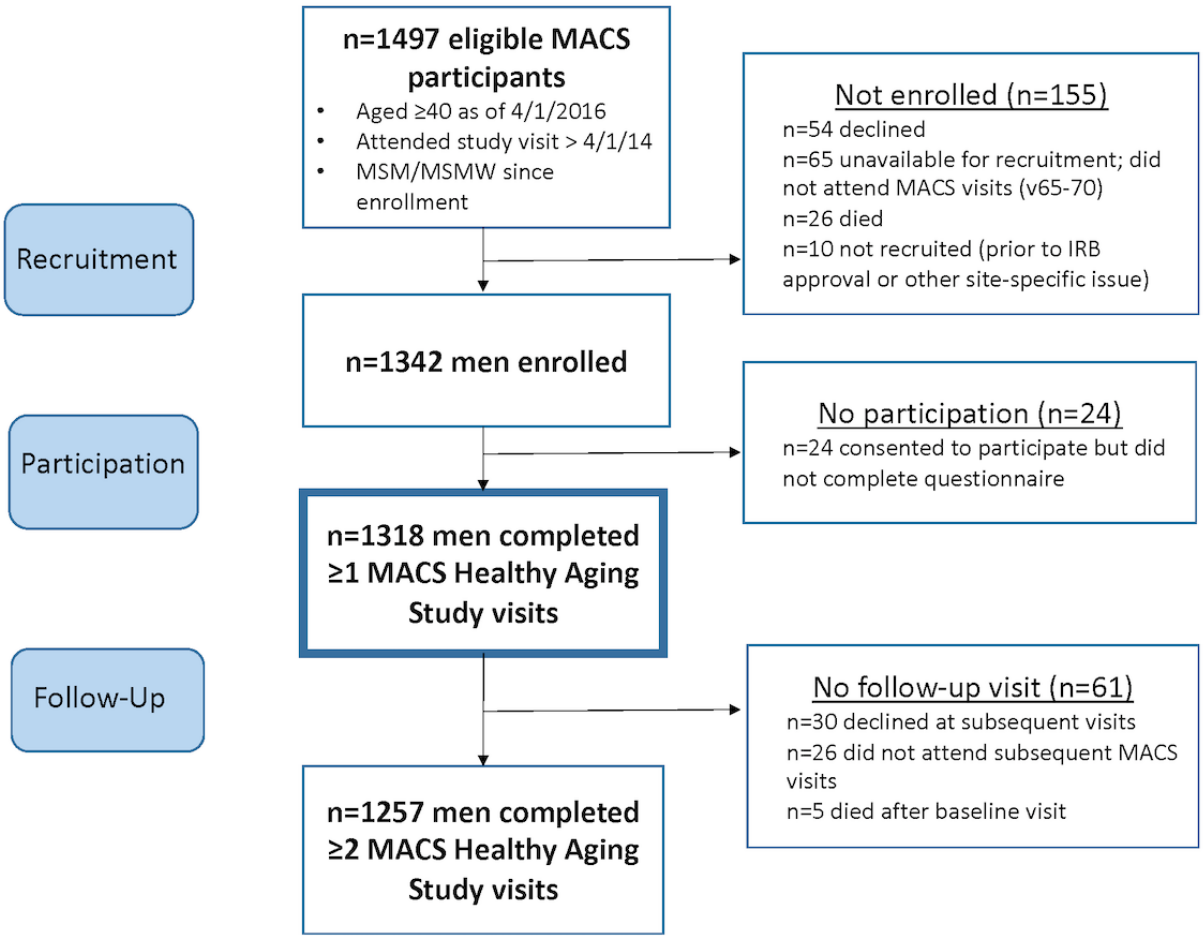

Table 2. Enrollment and participation for the Multisite AIDS Cohort Study Healthy Aging Study (2016-2019).

Visit	Targeted at visit[a], n	Approached, n (%)	Refused, n (%)	Enrolled, n (%)	Complete surveys, n (%)	Incomplete surveys, n (%)
65	1497	979 (65.4)	82 (5.48)	897 (59.92)	871 (58.18)	26 (1.74)
66	1474	1281 (86.91)	129 (8.75)	1152 (78.15)	1118 (75.84)	34 (2.31)
67	1466	1295 (88.34)	175 (11.94)	1120 (76.4)	1116 (76.13)	4 (0.27)
68	1461	1229 (84.12)	102 (6.98)	1127 (77.14)	1062 (72.69)	65 (44.49)
69	1460	1225 (83.9)	96 (6.58)	1129	1071 (77.34)	58 (3.97)
70	1404	1199 (85.4)	99 (7.05)	1100 (78.35)	1055 (75.14)	45 (3.21)

[a]The targeted number changed from visit to visit due to death and withdrawals.

Participant Demographics

Demographic and other descriptions of the sample are presented in Table 3. The mean age of the total sample was 59.6, ranging from 40 to 91. Most of the men were White (962/1318, 72.98%), Black (266/1318, 20.18%), or multiracial (44/1318, 3.34%) and 8.72% (115/1318) identified as Hispanic. Nearly everyone was identified as either gay (1152/1318, 87.41%) or bisexual (60/1318, 4.55%). Overall, the sample was highly educated, with 65.71% (866/1318) reporting a college degree (333/1318, 25.27%) or higher (533/1318, 40.44%); just under a third (41/1318, 3.11%) reported having less than a high school degree or General Educational Development. The sample was virtually equally divided between HIV-positive (656/1318, 49.77%) and HIV-negative (662/1318, 50.23%) participants. There were differences between these subsamples in terms of age, race, ethnicity, education, and sexual orientation. This sample also differs in some regard from those eligible MACS participants who did not enroll in the study (n=179; Multimedia Appendix

1). Overall, the Healthy Aging Study participants were on average younger (59.9 years compared with 62.2 years; *P*=.005) and among those living with HIV, had a higher mean CD4 count (697.9 compared with 623.9; *P*=.03).

Table 3. Participant characteristics of the Multisite AIDS Cohort Study Healthy Aging Study (2016-2019).

Characteristic	Total (N=1318)	HIV negative (n=662)	HIV positive (n=656)
Age (years)[a]			
Value, mean (SD); range	59.8 (8.7); 40-91	62.1 (8.7); 41-91	57.4 (8.1); 40-82
Value, median	60	62	57
Race, n (%)[a]			
White	962 (73)	547 (82.6)	415 (63.3)
Black	266 (20.2)	82 (12.4)	184 (28)
Multiracial	44 (3.3)	13 (2)	31 (2.4)
American Indian or Alaskan Native	14 (1.1)	5 (0.8)	9 (1.4)
Asian	6 (0.5)	5 (0.8)	1 (0.2)
Native Hawaiian or Pacific Islander	2 (0.2)	1 (0.2)	1 (0.2)
Another race	23 (1.7)	9 (1.4)	14 (2.1)
Missing	1 (0.1)	0 (0)	1 (0.2)
Ethnicity, n (%)[a]			
Hispanic	115 (8.7)	628 (94.9)	575 (87.7)
Non-Hispanic	1203 (91.3)	34 (5.1)	81 (12.3)
Education, n (%)[a]			
Less than high school	41 (31.1)	15 (2.3)	26 (4)
High school or GED[b]	126 (9.6)	45 (6.8)	81 (12.3)
Some college	285 (21.6)	106 (16)	179 (27.3)
College degree	333 (25.3)	175 (26.4)	158 (24.1)
Graduate school or higher	533 (40.4)	321 (48.5)	212 (32.3)
Sexual orientation, n (%)[c]			
Gay	1152 (87.4)	598 (90.3)	554 (84.5)
Bisexual	60 (4.6)	21 (3.2)	39 (5.9)
Straight or heterosexual	33 (2.5)	18 (2.7)	15 (2.3)
Something else	24 (1.8)	7 (1.1)	17 (2.6)
Unsure, prefer not to say, or N/A[d]	38 (2.9)	13 (2)	25 (3.8)
Missing	11 (0.8)	5 (0.8)	6 (0.9)

[a]*P*>.001.

[b]GED: General Educational Development.

[c]*P*>.01.

[d]N/A: not applicable.

Discussion

Principal Findings

In this paper, we describe the methods and sample for an observational cohort study to understand the patterns of healthy aging. We successfully recruited, enrolled, and tracked 1318 midlife or SMM (1318/1497, 88.04% of the eligible men within the MACS) over a 3-year period (six total biannual surveys). The mean age of the sample was 59.6, including men aged 40-91 years. Overall, the sample was mostly White, educated, gay-identified, and included both HIV-positive (656/1318, 49.77%) and HIV-negative (662/1318, 50.23%) men.

More than two-thirds of the participants (914/1318, 69.34%) completed at least five of the six surveys. Participation in this new method of data collection for the MACS, including a hybrid

of web-based and hard copy surveys, was high with nearly all men (95.98%, 1265/1318) completing at least two *Healthy Aging* survey across the six visits. Men found that these methods were acceptable with the uptake of web-based home-based surveys, increasing from 21% (183/871) to 60% (633/1055) at the final visit. This suggests the potential utility and importance of using early study visits to acclimate participants to the study and to increase buy-in for home-based data collection. This approach may decrease the cost of longitudinal data collection in similar cohort studies. Participants reported that the survey lengths were *just right* and that their interest level was *just okay*. The high level of survey completion and follow-up over six waves of data collection provide strong evidence to support the feasibility of these methods for data collection in the MACS and similar cohorts.

In this study, we conceived resilience as a myriad of multidimensional processes occurring at multiple levels over the life course. This is informed by and builds upon the important work of others [2,29-32,79]. We used a community-engaged process to develop domains of potential resiliencies specific to SMM at the individual, interpersonal or dyadic, and community levels.

Strengths and Limitations

The methods described here, in particular the use of a staggered survey design, allowed us to collect longitudinal data on a wide range of topics without overburdening participants with exhaustive and overly repetitive surveys at each follow-up. The design also provided opportunities for flexibility and innovation and the possibility of responding to historical or individual-level changes or concerns. As an example, we were able to add a series of questions on how men use different methods of bio-behavioral HIV prevention techniques (eg, pre-exposure prophylaxis), which had greatly expanded during the study period. It also allowed junior investigators to include new constructs of relevance that were highly relevant but not included in the original survey (eg, conversion therapy [76]). This flexibility also resulted in our ability to expand beyond the original syndemic-framed aims, as proposed in the original proposal. In the years since the first and subsequent submissions, being funded, implementation, and now analyses and dissemination of findings, we have begun to place more emphasis on a resiliencies-based frame in this work.

The study was nested within the MACS, the longest running HIV cohort study in the United States, providing a well-established and finely tuned structure within which to implement this work. We were able to capitalize on participants' pre-established MACS visits and the highly trained local study staff with longstanding relationships with the men, which undoubtedly helped with recruitment and follow-up. To some extent, this may limit the generalizability of our findings. These men, many of whom have been enrolled in the MACS for ≥30 years, may be more apt to participate and to continue through follow-up surveys. They may also be unique from men not already engaged in research, for example, with regard to syndemics (eg, substance use) or resiliencies (eg, altruism). Furthermore, while subsequent enrollment periods for the MACS cohorts used a stratified recruitment approach by HIV serostatus that attempted to recruit HIV-positive and HIV-negative SMM with similar baseline characteristics, we recognize that such designs are imperfect and that the stigma and isolation associated with HIV infection is specific to SMM living with HIV. For this reason, we recommend that analyses using these data are stratified by HIV status, so that the effects of protective factors are characterized independently in the context of HIV. Another limitation is that we experienced several unforeseen issues when implementing the first survey (visit 65); therefore, not all sites were able to enroll participants until later in the 6-month cycle, resulting in a smaller sample compared with other periods.

An important strength of this design is the ability to connect the resiliencies captured in this study to the wealth of MACS behavioral and biological data. This provides a unique opportunity to explore resiliencies using longitudinal data on myriad health indicators beyond HIV. For example, our work evaluated the role of psychosocial factors in buffering the development of incident frailty. Another area of research is investigating the roles of perceived health care quality and anticipated discrimination in health settings on the outcomes and equity of diabetes and hypertension control within the *Healthy Aging* cohort.

Conclusions

With the graying of sexual and gender minority communities and the growing population of middle-aged and older adults living with HIV, it is increasingly important to understand the psychosocial aspects of aging and aging well. Currently, there are limited data on aging populations, particularly those that incorporate community-specific questions. Although an assessment of global resilience is important, these communities also have unique stories of survival, traditions, support, and needs (eg, the importance of created or chosen family) in relation to their lives as sexual minority persons and as persons affected by or living with HIV [80]. Opportunities to combine longitudinal psychosocial and biomedical or clinical data are rare. This study provides a foundation to address this gap by connecting innovative measures with decades of biomedical data. More information on the measures and using these data can be found on the web [81]. Understanding resiliencies in aging is a critical springboard for the development of more holistic public health theories and interventions that support healthy aging among older SMM.

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Conflicts of Interest

None declared.

Multimedia Appendix 1
Healthy Aging Study participants compared to all Multisite AIDS Cohort Study participants (data from Healthy Aging Study, 2016-2019).
[DOCX File , 15 KB - resprot_v10i9e25750_app1.docx]

References

1. Choi S, Meyer I. LGBT Aging: A review of research findings, needs, and policy implications. Los Angeles: The Williams Institute. 2016. URL: https://www.lgbtagingcenter.org/resources/pdfs/LGBT-Aging-A-Review.pdf [accessed 2021-08-01]
2. Fredriksen-Goldsen KI, Emlet CA, Kim H, Muraco A, Erosheva EA, Goldsen J, et al. The physical and mental health of lesbian, gay male, and bisexual (LGB) older adults: the role of key health indicators and risk and protective factors. Gerontologist 2013 Aug;53(4):664-675 [FREE Full text] [doi: 10.1093/geront/gns123] [Medline: 23034470]
3. Lesbian, gay, bisexual, and transgender health. Healthy People. 2010. URL: https://www.healthypeople.gov/2020/topics-objectives/topic/lesbian-gay-bisexual-and-transgender-health [accessed 2021-08-01]
4. Wolitski R, Stall R, Valdiserri R. Unequal Opportunity: Health Disparities Affecting Gay and Bisexual Men in the United States. New York, NY: Oxford University Press; 2007.
5. Meyer IH. Minority stress and mental health in gay men. J Health Soc Behav 1995 Mar;36(1):38-56. [Medline: 7738327]
6. Hatzenbuehler ML. How does sexual minority stigma "get under the skin"? A psychological mediation framework. Psychol Bull 2009 Sep;135(5):707-730 [FREE Full text] [doi: 10.1037/a0016441] [Medline: 19702379]
7. Surkan PJ, Wang R, Huang Y, Stall R, Plankey M, Teplin LA, et al. Victimization in early adolescence, stress, and depressive symptoms among aging sexual minority men: findings from the multicenter AIDS cohort study. LGBT Health 2020 Apr;7(3):155-165 [FREE Full text] [doi: 10.1089/lgbt.2019.0036] [Medline: 32186958]
8. HIV and older Americans. Division of HIV/AIDS Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention (CDC). 2019. URL: https://www.cdc.gov/hiv/group/age/olderamericans/index.html [accessed 2021-05-25]
9. Applebaum J. Late adulthood and aging: clinical approaches. In: Makadon HJ, Mayer KH, Potter J, Goldhammer H, editors. Fenway Guide to lesbian, gay, bisexual and transgender health. Philadelphia: American College of Physicians; 2008:135.
10. Emlet CA, Brennan DJ, Brennenstuhl S, Rueda S, Hart TA, Rourke SB. The impact of HIV-related stigma on older and younger adults living with HIV disease: does age matter? AIDS Care 2015;27(4):520-528. [doi: 10.1080/09540121.2014.978734] [Medline: 25397643]
11. Singer M. AIDS and the health crisis of the U.S. urban poor; the perspective of critical medical anthropology. Soc Sci Med 1994 Oct;39(7):931-948. [doi: 10.1016/0277-9536(94)90205-4] [Medline: 7992126]
12. Singer M. A dose of drugs, a touch of violence, a case of AIDS: conceptualizing the SAVA syndemic. Free Inq Creat Sociol 1996;24(2):99-110 [FREE Full text]

13. Singer M. Introduction to syndemics: A critical systems approach to public and community health. San Francisco, CA: Jossey-Bass; 2009:1-304.
14. Stall R, Friedman M, Catania J. Interacting epidemics and gay men's health: A theory of syndemic production among urban gay men. In: Unequal Opportunity: Health Disparities Affecting Gay and Bisexual Men in the United States. New York, NY: Oxford University Press; 2007:251-274.
15. Stall R, Mills TC, Williamson J, Hart T, Greenwood G, Paul J, et al. Association of co-occurring psychosocial health problems and increased vulnerability to HIV/AIDS among urban men who have sex with men. Am J Public Health 2003 Jun;93(6):939-942. [doi: 10.2105/ajph.93.6.939] [Medline: 12773359]
16. Dyer TP, Shoptaw S, Guadamuz TE, Plankey M, Kao U, Ostrow D, et al. Application of syndemic theory to black men who have sex with men in the Multicenter AIDS Cohort Study. J Urban Health 2012 Aug;89(4):697-708 [FREE Full text] [doi: 10.1007/s11524-012-9674-x] [Medline: 22383094]
17. Herrick AL, Lim SH, Plankey MW, Chmiel JS, Guadamuz TE, Guadamuz TT, et al. Adversity and syndemic production among men participating in the multicenter AIDS cohort study: a life-course approach. Am J Public Health 2013 Jan;103(1):79-85 [FREE Full text] [doi: 10.2105/AJPH.2012.300810] [Medline: 23153154]
18. Jie W, Ciyong L, Xueqing D, Hui W, Lingyao H. A syndemic of psychosocial problems places the MSM (men who have sex with men) population at greater risk of HIV infection. PLoS One 2012;7(3):e32312 [FREE Full text] [doi: 10.1371/journal.pone.0032312] [Medline: 22479319]
19. Guadamuz TE, McCarthy K, Wimonsate W, Thienkrua W, Varangrat A, Chaikummao S, et al. Psychosocial health conditions and HIV prevalence and incidence in a cohort of men who have sex with men in Bangkok, Thailand: evidence of a syndemic effect. AIDS Behav 2014 Nov 3;18(11):2089-2096 [FREE Full text] [doi: 10.1007/s10461-014-0826-8] [Medline: 24989128]
20. Mustanski B, Garofalo R, Herrick A, Donenberg G. Psychosocial health problems increase risk for HIV among urban young men who have sex with men: preliminary evidence of a syndemic in need of attention. Ann Behav Med 2007 Aug;34(1):37-45 [FREE Full text] [doi: 10.1080/08836610701495268] [Medline: 17688395]
21. Parsons JT, Grov C, Golub SA. Sexual compulsivity, co-occurring psychosocial health problems, and HIV risk among gay and bisexual men: further evidence of a syndemic. Am J Public Health 2012 Jan;102(1):156-162. [doi: 10.2105/AJPH.2011.300284] [Medline: 22095358]
22. Biello KB, Colby D, Closson E, Mimiaga MJ. The syndemic condition of psychosocial problems and HIV risk among male sex workers in Ho Chi Minh City, Vietnam. AIDS Behav 2014 Jul;18(7):1264-1271 [FREE Full text] [doi: 10.1007/s10461-013-0632-8] [Medline: 24081899]
23. Ferlatte O, Hottes TS, Trussler T, Marchand R. Evidence of a syndemic among young Canadian gay and bisexual men: uncovering the associations between anti-gay experiences, psychosocial issues, and HIV risk. AIDS Behav 2014 Jul;18(7):1256-1263. [doi: 10.1007/s10461-013-0639-1] [Medline: 24129844]
24. Halkitis PN, Moeller RW, Siconolfi DE, Storholm ED, Solomon TM, Bub KL. Measurement model exploring a syndemic in emerging adult gay and bisexual men. AIDS Behav 2013 Feb;17(2):662-673 [FREE Full text] [doi: 10.1007/s10461-012-0273-3] [Medline: 22843250]
25. Kurtz SP, Buttram ME, Surratt HL, Stall RD. Resilience, syndemic factors, and serosorting behaviors among HIV-positive and HIV-negative substance-using MSM. AIDS Educ Prev 2012 Jun;24(3):193-205 [FREE Full text] [doi: 10.1521/aeap.2012.24.3.193] [Medline: 22676460]
26. Yu F, Nehl EJ, Zheng T, He N, Berg CJ, Lemieux AF, et al. A syndemic including cigarette smoking and sexual risk behaviors among a sample of MSM in Shanghai, China. Drug Alcohol Depend 2013 Sep 01;132(1-2):265-270 [FREE Full text] [doi: 10.1016/j.drugalcdep.2013.02.016] [Medline: 23517682]
27. Halkitis PN, Kupprat SA, Hampton MB, Perez-Figueroa R, Kingdon M, Eddy JA, et al. Evidence for a syndemic in aging HIV-positive gay, bisexual, and other MSM: implications for a holistic approach to prevention and healthcare. Nat Resour Model 2012 Nov 01;36(2):365-386 [FREE Full text] [doi: 10.1111/napa.12009] [Medline: 24347817]
28. Wim VB, Christiana N, Marie L. Syndemic and other risk factors for unprotected anal intercourse among an online sample of Belgian HIV negative men who have sex with men. AIDS Behav 2014 Jan;18(1):50-58. [doi: 10.1007/s10461-013-0516-y] [Medline: 23681697]
29. Emlet CA, Fredriksen-Goldsen KI, Kim H. Risk and protective factors associated with health-related quality of life among older gay and bisexual men living with HIV disease. Gerontologist 2013 Dec;53(6):963-972 [FREE Full text] [doi: 10.1093/geront/gns191] [Medline: 23355449]
30. Emlet CA, Shiu C, Kim H, Fredriksen-Goldsen K. Bouncing back: resilience and mastery among HIV-positive older gay and bisexual men. Gerontologist 2017 Feb;57(suppl 1):40-49 [FREE Full text] [doi: 10.1093/geront/gnw171] [Medline: 28087794]
31. Fredriksen-Goldsen KI, Kim H, Bryan AE, Shiu C, Emlet CA. The cascading effects of marginalization and pathways of resilience in attaining good health among LGBT older adults. Gerontologist 2017 Feb 13;57(suppl 1):72-83 [FREE Full text] [doi: 10.1093/geront/gnw170] [Medline: 28087797]
32. Fredriksen-Goldsen KI, Kim H, Shiu C, Goldsen J, Emlet CA. Successful aging among LGBT older adults: physical and mental health-related quality of life by age group. Gerontologist 2015 Feb;55(1):154-168 [FREE Full text] [doi: 10.1093/geront/gnu081] [Medline: 25213483]

33. Garmezy N, Masten AS, Tellegen A. The study of stress and competence in children: a building block for developmental psychopathology. Child Dev 1984 Feb;55(1):97-111. [Medline: 6705637]
34. Luthar SS, Cicchetti D, Becker B. The construct of resilience: a critical evaluation and guidelines for future work. Child Dev 2000;71(3):543-562 [FREE Full text] [doi: 10.1111/1467-8624.00164] [Medline: 10953923]
35. Masten A, Powell J. A resilience framework for research, policy, and practice. In: Luthar SS, editor. Resilience and Vulnerability: Adaptation in the Context of Childhood Adversities. New York: Cambridge University Press; 2003:1-26.
36. Rutter M. Resilience in the face of adversity. Protective factors and resistance to psychiatric disorder. Br J Psychiatry 1985 Dec;147:598-611. [doi: 10.1192/bjp.147.6.598] [Medline: 3830321]
37. Werner EE. The children of Kauai: resiliency and recovery in adolescence and adulthood. J Adolesc Health 1992 Jun;13(4):262-268. [doi: 10.1016/1054-139x(92)90157-7] [Medline: 1610840]
38. Zimmerman MA, Arunkumar R. Resiliency research: implications for schools and policy. Soc Policy Rep 1994 Dec 01;8(4):1-20. [doi: 10.1002/j.2379-3988.1994.tb00032.x]
39. Herrick AL, Stall R, Goldhammer H, Egan JE, Mayer KH. Resilience as a research framework and as a cornerstone of prevention research for gay and bisexual men: theory and evidence. AIDS Behav 2014 Jan;18(1):1-9. [doi: 10.1007/s10461-012-0384-x] [Medline: 23321946]
40. Kaslow RA, Ostrow DG, Detels R, Phair JP, Polk BF, Rinaldo CR. The Multicenter AIDS Cohort Study: rationale, organization, and selected characteristics of the participants. Am J Epidemiol 1987 Aug;126(2):310-318. [doi: 10.1093/aje/126.2.310] [Medline: 3300281]
41. MACS/WIHS Combined Cohort Study (MWCCS). URL: https://statepi.jhsph.edu/mwccs/about-mwccs/ [accessed 2021-08-12]
42. Wagnild GM, Young HM. Development and psychometric evaluation of the Resilience Scale. J Nurs Meas 1993;1(2):165-178. [Medline: 7850498]
43. Cutrona C, Russell D. The provisions of social relationships and adaptation to stress. Adv Pers Relat 1987;1:37-67 [FREE Full text]
44. Fraley RC, Heffernan ME, Vicary AM, Brumbaugh CC. The experiences in close relationships-relationship structures questionnaire: a method for assessing attachment orientations across relationships. Psychol Assess 2011 Sep;23(3):615-625. [doi: 10.1037/a0022898] [Medline: 21443364]
45. Russell DW. UCLA Loneliness Scale (Version 3): reliability, validity, and factor structure. J Pers Assess 1996 Feb;66(1):20-40. [doi: 10.1207/s15327752jpa6601_2] [Medline: 8576833]
46. Bush K, Kivlahan DR, McDonell MB, Fihn SD, Bradley KA. The AUDIT alcohol consumption questions (AUDIT-C): an effective brief screening test for problem drinking. Ambulatory Care Quality Improvement Project (ACQUIP). Alcohol Use Disorders Identification Test. Arch Intern Med 1998 Sep 14;158(16):1789-1795. [doi: 10.1001/archinte.158.16.1789] [Medline: 9738608]
47. Anderson T. HIV Long-Term Survivors Declaration—AIDS at 40: Envisioning a future we never imaged. Let's Kick Ass AIDS. 2015. URL: https://letskickass.hiv/with-courage-and-compassion-long-term-survivors-of-hiv-strive-not-only-to-survive-but-also-to-ee056d372994 [accessed 2021-08-01]
48. Davis JA, Smith TW. General Social Surveys, 1972-1991: Cumulative Codebook. Chicago: National Opinion Research Center (NORC); 1991.
49. Scheier MF, Carver CS, Bridges MW. Distinguishing optimism from neuroticism (and trait anxiety, self-mastery, and self-esteem): a reevaluation of the Life Orientation Test. J Pers Soc Psychol 1994 Dec;67(6):1063-1078. [doi: 10.1037//0022-3514.67.6.1063] [Medline: 7815302]
50. Idler EL, Musick MA, Ellison CG, George LK, Krause N, Ory MG, et al. Measuring multiple dimensions of religion and spirituality for health research. Res Aging 2016 Aug 18;25(4):327-365. [doi: 10.1177/0164027503025004001]
51. Multidimensional Measurement of Religiousness, Spirituality for Use in Health Research. A Report of the Fetzer Institute / National Institute on Aging Working Group. URL: https://fetzer.org/resources/multidimensional-measurement-religiousnessspirituality-use-health-research [accessed 2021-08-03]
52. Lawton MP. The Philadelphia Geriatric Center Morale Scale: a revision. J Gerontol 1975 Jan;30(1):85-89. [doi: 10.1093/geronj/30.1.85] [Medline: 1109399]
53. Duckworth AL, Peterson C, Matthews MD, Kelly DR. Grit: perseverance and passion for long-term goals. J Pers Soc Psychol 2007 Jun;92(6):1087-1101. [doi: 10.1037/0022-3514.92.6.1087] [Medline: 17547490]
54. Duckworth AL, Quinn PD. Development and validation of the short grit scale (grit-s). J Pers Assess 2009 Mar;91(2):166-174. [doi: 10.1080/00223890802634290] [Medline: 19205937]
55. Sudore RL, Stewart AL, Knight SJ, McMahan RD, Feuz M, Miao Y, et al. Development and validation of a questionnaire to detect behavior change in multiple advance care planning behaviors. PLoS One 2013;8(9):e72465 [FREE Full text] [doi: 10.1371/journal.pone.0072465] [Medline: 24039772]
56. Brown KW, Ryan RM. The benefits of being present: mindfulness and its role in psychological well-being. J Pers Soc Psychol 2003 Apr;84(4):822-848. [doi: 10.1037/0022-3514.84.4.822] [Medline: 12703651]

57. Rosen RC, Riley A, Wagner G, Osterloh IH, Kirkpatrick J, Mishra A. The international index of erectile function (IIEF): a multidimensional scale for assessment of erectile dysfunction. Urology 1997 Jun;49(6):822-830. [doi: 10.1016/s0090-4295(97)00238-0] [Medline: 9187685]
58. Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE, et al. International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc 2003 Aug;35(8):1381-1395. [doi: 10.1249/01.MSS.0000078924.61453.FB] [Medline: 12900694]
59. Cash TF, Szymanski ML. The development and validation of the Body-Image Ideals Questionnaire. J Pers Assess 1995 Jun;64(3):466-477. [doi: 10.1207/s15327752jpa6403_6] [Medline: 16367722]
60. Frost DM, Meyer IH. Internalized homophobia and relationship quality among lesbians, gay men, and bisexuals. J Couns Psychol 2009 Jan;56(1):97-109 [FREE Full text] [doi: 10.1037/a0012844] [Medline: 20047016]
61. Thompson ER, Phua FT. A brief index of affective job satisfaction. Group Organ Manag 2012 Mar 15;37(3):275-307. [doi: 10.1177/1059601111434201]
62. Marshall GN, Hays RD. The patient satisfaction questionnaire short form (PSQ-18). RAND Corporation. 1994. URL: https://www.rand.org/content/dam/rand/pubs/papers/2006/P7865.pdf [accessed 2021-08-03]
63. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med 2006 May 22;166(10):1092-1097. [doi: 10.1001/archinte.166.10.1092] [Medline: 16717171]
64. Warren-Jeanpiere L, Dillaway H, Hamilton P, Young M, Goparaju L. Taking it one day at a time: African American women aging with HIV and co-morbidities. AIDS Patient Care STDS 2014 Jul;28(7):372-380 [FREE Full text] [doi: 10.1089/apc.2014.0024] [Medline: 24933093]
65. Lang AJ, Stein MB. An abbreviated PTSD checklist for use as a screening instrument in primary care. Behav Res Ther 2005 May;43(5):585-594. [doi: 10.1016/j.brat.2004.04.005] [Medline: 15865914]
66. Khalili R, Sirati Nir M, Ebadi A, Tavallai A, Habibi M. Validity and reliability of the Cohen 10-item Perceived Stress Scale in patients with chronic headache: Persian version. Asian J Psychiatr 2017 Apr;26:136-140. [doi: 10.1016/j.ajp.2017.01.010] [Medline: 28483077]
67. Hebl MR, Tonidandel S, Ruggs EN. The impact of like-mentors for gay/Lesbian employees. Hum Perform 2012 Jan;25(1):52-71. [doi: 10.1080/08959285.2011.631645]
68. Stephenson R, Finneran C. The IPV-GBM scale: a new scale to measure intimate partner violence among gay and bisexual men. PLoS One 2013;8(6):e62592 [FREE Full text] [doi: 10.1371/journal.pone.0062592] [Medline: 23755098]
69. Strauss MA, Hamby SL, Boney-Mccoy S, Sugarman DB. The Revised Conflict Tactics Scales (CTS2). J Fam Issues 2016 Jun 30;17(3):283-316. [doi: 10.1177/019251396017003001]
70. Proescholdbell RJ, Roosa MW, Nemeroff CJ. Component measures of psychological sense of community among gay men. J Community Psychol 2005 Jan;34(1):9-24. [doi: 10.1002/jcop.20080]
71. De Jesus M, Ware D, Brown AL, Egan JE, Haberlen SA, Palella FJ, et al. Social-environmental resiliencies protect against loneliness among HIV-positive and HIV-negative older men who have sex with men: results from the Multicenter AIDS Cohort Study (MACS). Soc Sci Med 2021 Mar;272:113711. [doi: 10.1016/j.socscimed.2021.113711] [Medline: 33550066]
72. Henderson ER, Egan JE, Haberlen SA, Detels R, Teplin LA, Friedman MR, et al. Does social support predict depressive symptoms? A longitudinal study of midlife and older men who have sex with men from the Multicenter AIDS Cohort Study. Ann LGBTQ Public Popul Health 2021 Jan 05;2(2):142-160. [doi: 10.1891/lgbtq-2020-0042]
73. Ware D, Palella FJ, Chew KW, Friedman MR, D'Souza G, Ho K, et al. Examination of polypharmacy trajectories among HIV-positive and HIC-negative men in an ongoing longitudinal Cohort from 2004 to 2016. AIDS Patient Care STDS 2019 Aug;33(8):354-365 [FREE Full text] [doi: 10.1089/apc.2019.0057] [Medline: 31369298]
74. Statz M, Ware D, Perry N, Huebner D, Cox C, Brown A, et al. Primary and secondary supportive partnerships among HIV-positive and HIV-negative middle-aged and older gay men. PLoS One 2021;16(2):e0245863 [FREE Full text] [doi: 10.1371/journal.pone.0245863] [Medline: 33596240]
75. Tanigawa H, Obori R, Tanaka H, Yoshida J, Kosazuma T. [Reproduction study of 4-ethoxy-2-methyl-5-morpholino-3(2H)-pyridazinone (M73101) in rats (II). Administration of M73101 during the period of major organogenesis (author's transl)]. J Toxicol Sci 1979 May;4(2):175-200 [FREE Full text] [doi: 10.2131/jts.4.175] [Medline: 315476]
76. Meanley S, Haberlen SA, Okafor CN, Brown A, Brennan-Ing M, Ware D, et al. Lifetime exposure to conversion therapy and psychosocial health among midlife and older adult men who have sex with men. Gerontologist 2020 Sep 15;60(7):1291-1302. [doi: 10.1093/geront/gnaa069] [Medline: 32556123]
77. Ware D, Rueda S, Plankey M, Surkan P, Okafor CN, Teplin L, et al. The longitudinal impact of employment, retirement and disability status on depressive symptoms among men living with HIV in the Multicenter AIDS Cohort Study. PLoS One 2020;15(10):e0239291 [FREE Full text] [doi: 10.1371/journal.pone.0239291] [Medline: 33007781]
78. Brennan-Ing M, Haberlen S, Ware D, Egan JE, Brown AL, Meanley S, et al. Psychological connection to the gay community and negative self-appraisals in middle-aged and older men who have sex with men: the mediating effects of fitness engagement. J Gerontol B Psychol Sci Soc Sci 2021 May 04:1-11. [doi: 10.1093/geronb/gbab076] [Medline: 33945614]

79. Emlet CA, Fredriksen-Goldsen KI, Kim H, Hoy-Ellis C. The relationship between sexual minority stigma and sexual health risk behaviors among HIV-positive older gay and bisexual men. J Appl Gerontol 2017 Aug;36(8):931-952 [FREE Full text] [doi: 10.1177/0733464815591210] [Medline: 26100507]
80. Croghan CF, Moone RP, Olson AM. Friends, family, and caregiving among midlife and older lesbian, gay, bisexual, and transgender adults. J Homosex 2014;61(1):79-102. [doi: 10.1080/00918369.2013.835238] [Medline: 24313254]
81. The Healthy Aging Substudy. URL: https://macshealthyaging.library.georgetown.edu [accessed 2021-08-12]

Abbreviations

CADI: computerized-assisted direct interview
CAMACS: Center for Coordination, Analysis, and Management of the Multicenter AIDS Cohort Study
CFAR: Center for AIDS Research
MACS: Multisite AIDS Cohort Study
SMM: sexual minority men

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Protocol

Multiscale Biology of Cardiovascular Risk in Psoriasis: Protocol for a Case-Control Study

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Abstract

Background: Patients with psoriasis have increased risk of cardiovascular disease (CVD) independent of traditional risk factors. The molecular mechanisms underlying the psoriasis-CVD connection are not fully understood. Advances in high-throughput molecular profiling technologies and computational analysis techniques offer new opportunities to improve the understanding of disease connections.

Objective: We aim to characterize the complexity of cardiovascular risk in patients with psoriasis by integrating deep phenotypic data with systems biology techniques to perform comprehensive multiomic analyses and construct network models of the two interacting diseases.

Methods: The study aims to include 120 adult patients with psoriasis (60 with prior atherosclerotic CVD and 60 without CVD). Half of the patients are already receiving systemic antipsoriatic treatment. All patients complete a questionnaire, and a medical interview is conducted to collect medical history and information on, for example, socioeconomics, mental health, diet, and physical exercise. Participants are examined clinically with assessment of the Psoriasis Area and Severity Index and undergo imaging by transthoracic echocardiography, ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG-PET/CT), and carotid artery ultrasonography. Skin swabs are collected for analysis of microbiome metagenomics; skin biopsies and blood samples are collected for transcriptomic profiling by RNA sequencing; skin biopsies are collected for immunohistochemistry; plasma samples are collected for analyses of proteomics, lipidomics, and metabolomics; blood samples are collected for high-dimensional mass cytometry; and feces samples are collected for gut microbiome metagenomics. Bioinformatics and systems biology techniques are utilized to analyze the multiomic data and to integrate data into a network model of CVD in patients with psoriasis.

Results: Recruitment was completed in September 2020. Preliminary results of ^{18}F-FDG-PET/CT data have recently been published, where vascular inflammation was reduced in the ascending aorta (P=.046) and aortic arch (P=.04) in patients treated

with statins and was positively associated with inflammation in the visceral adipose tissue (P<.001), subcutaneous adipose tissue (P=.007), pericardial adipose tissue (P<.001), spleen (P=.001), and bone marrow (P<.001).

Conclusions: This systems biology approach with integration of multiomics and clinical data in patients with psoriasis with or without CVD is likely to provide novel insights into the biological mechanisms underlying these diseases and their interplay that can impact future treatment.

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KEYWORDS

cardiovascular disease; psoriasis; study protocol; cardiovascular imaging; proteomics; lipidomics; microbiome; mass cytometry; bioinformatics; system biology

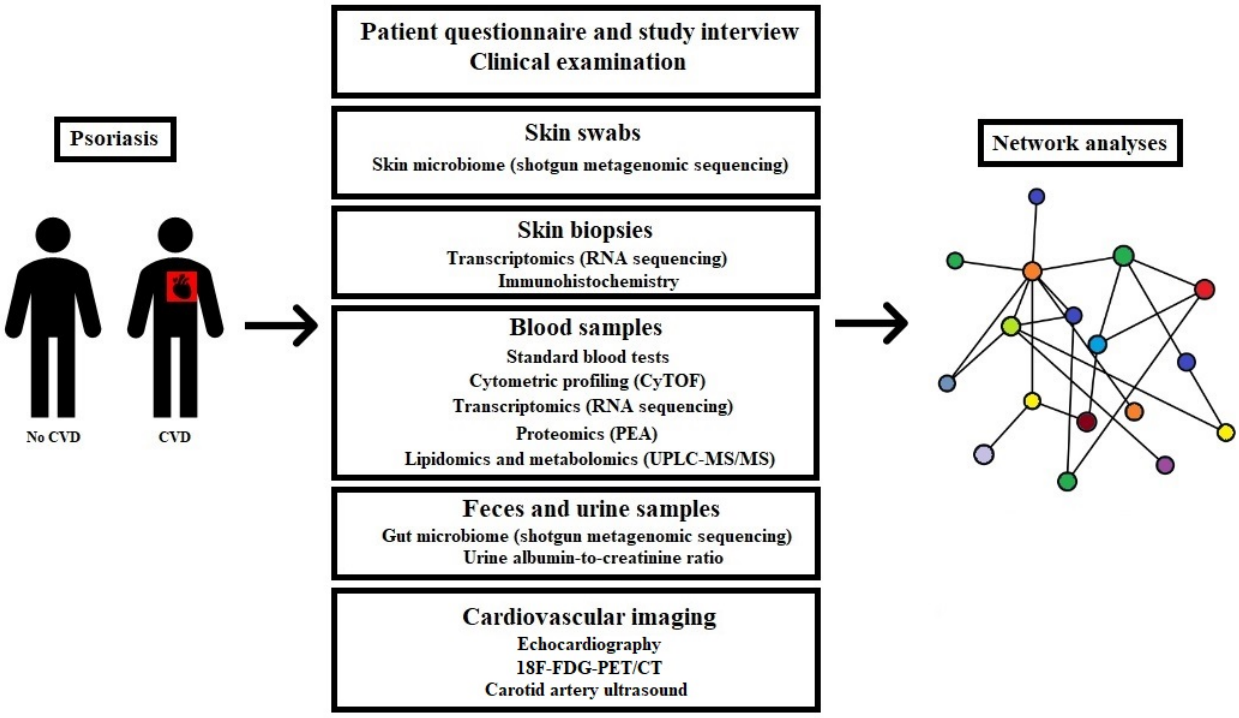
Introduction

Background

Psoriasis is a chronic inflammatory disease affecting 2% to 3% of the adult population and is associated with an increased risk of developing other inflammatory diseases, such as cardiovascular disease (CVD), inflammatory bowel disease, and diabetes [1,2]. Moderate-to-severe psoriasis is associated with increased risks of myocardial infarction and stroke independent of traditional risk factors, such as smoking, BMI, diabetes, hypertension, and dyslipidemia [3,4]. In addition, patients with psoriasis display increased prevalence of subclinical CVD, for example, endothelial dysfunction and increased carotid artery intimamedia thickness (CIMT), compared to controls [5-7]. Although the molecular mechanisms underlying the link between psoriasis and CVD remain to be identified in detail, they may rely, in part, on shared inflammatory pathways [8]. Indeed, psoriasis and atherosclerosis are both immune-driven chronic inflammatory diseases with an overlap of inflammatory mediators, including T-helper 1 (Th1) and Th17 cells [9]. It remains unclear, however, if treatment of psoriasis with systemic antipsoriatic medications can decrease the risk of CVD, but studies have indicated that tumor necrosis factor inhibitors and methotrexate may carry this potential [10,11].

Basic, translational, and clinical research directed separately at psoriasis or CVD has led to the identification of the molecular disease mechanisms and the development of new therapies aimed at psoriasis or CVD. However, this traditional paradigm is built on studies that do not capture deep phenotypes of individual patients, and to identify the central drivers of diseases and enable precision therapy, systems biology–oriented approaches are needed that seek to integrate all relevant available data. Advances in high-throughput molecular profiling and computational analysis techniques offer such novel opportunities to improve the understanding of disease connections and accelerate the discovery of new therapeutic strategies [12-15]. A multiscale biology approach has not, to our knowledge, been applied previously to provide comprehensive insights into the association between psoriasis and CVD. Therefore, we will use these techniques to investigate the pathophysiological links between psoriasis and CVD by integrating deep phenotypic data with multiomic data and use systems biology techniques to interrogate the molecular mechanisms connecting the two diseases (Figure 1). This approach will provide information on the fundamental regulatory circuits that drive psoriasis and CVD, enable the discovery and testing of novel biomarkers and therapeutics, and deliver other insights relevant for future prevention and therapy in these patients.

Figure 1. Overview of study examinations and analyses. ^{18}F-FDG-PET/CT: ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography; CVD: cardiovascular disease; CyTOF: cytometry by time-of-flight; PEA: proximity extension assay; UPLC-MS/MS: ultra-high performance liquid chromatography/tandem mass spectrometry.



Aims and Objectives

This study aims to investigate the complex multiscale interactions that drive cardiovascular risks in individual patients with psoriasis, involving specific gene transcripts, protein and lipid markers, signaling pathways, immune cell types, organ systems, and microbiota. Moreover, the study will examine multiscale differences across patient groups with psoriasis having distinct phenotypic traits, for example, with or without CVD, systemic antipsoriatic treatment or psoriatic arthritis, and early or late onset of psoriasis.

Methods

Study Population

The study will include 120 patients (aged ≥30 years) with moderate-to-severe plaque psoriasis, with 60 having prior (over 6 months before inclusion) atherosclerotic CVD, including myocardial infarction, coronary revascularization, ischemic stroke, and/or peripheral artery disease, and 60 not having this history. Furthermore, half of the patients receive systemic antipsoriatic treatment (unchanged therapy in the preceding 3 months), while the other half of the patients do not receive systemic antipsoriatic treatment. The exclusion criteria are shown in Textbox 1.

Textbox 1. Study exclusion criteria.

Exclusion criteria

- Dementia or other major psychological or physical incapacities
- Other chronic systemic diseases
- History of cancer with throat or thoracic irradiation or history of cancer with <3 years recurrence-free control, and for hematologic cancers, <5 years recurrence-free control
- Major surgery, pregnancy, labor, or breastfeeding ≤6 months before inclusion
- Immobility
- Dysregulated diabetes (glycated hemoglobin >10%)
- Systemic treatment with prednisolone or antibiotics <1 month before inclusion
- Severe claustrophobia
- Severe kidney disease (glomerular filtration rate <30 mL/min)
- Inability to understand the information relating to participation in the study

Patient Recruitment

Patients are recruited at the Department of Dermatology and Allergy, Herlev and Gentofte Hospital, when attending regularly scheduled visits for psoriasis control. Recruitment began in January 2018 and is also at the Department of Dermatology, Bispebjerg Hospital, at selected private dermatology clinics in the Copenhagen area, and through public advertisement of the research project on the home page of Herlev and Gentofte Hospital, social media outlets, and the member magazine of the Danish Psoriasis Association. All patient-related examinations are performed at Herlev and Gentofte Hospital. Because of the extensive examination program, the study visits are extended over 2 days of attendance within a period of 2 weeks.

Patient Questionnaire and Study Interview

Each participant completes a questionnaire containing questions regarding civil status, occupation, educational level, annual household income, psychological stress, depression, self-rated health, diet, and exercise. The questionnaire also contains questions to establish the Dermatology Quality of Life Index. An interview is conducted by study physicians with questions regarding history of psoriasis, current and previous medical treatment of psoriasis, history of CVD, medical treatment of CVD, family history of CVD, comorbidities (diabetes, hypertension, hypercholesterolemia, etc), odontological status, smoking status, alcohol consumption, other medications including use of antibiotics (exclusion if taken within 1 month before consideration for inclusion), and ethnicity.

Clinical Examination

A full skin examination is performed in each patient, and the severity of psoriasis is measured according to the Psoriasis Area and Severity Index and body surface area [16]. In addition, fingernails are examined for signs of psoriasis. Blood pressure is measured on each arm after the patient has rested for 5 minutes in the sitting position and is registered as the mean of these two measurements. BMI and waist-to-hip ratio are registered. The tongue is examined for the presence of a geographical tongue [17].

Skin Swabs: Skin Microbiome

Isohelix DNA/RNA buccal swabs (SK-1S, Cell Projects Ltd) are used to collect samples from the skin. One swab is taken from a psoriasis plaque (if applicable), where the patient has at least 4 to 6 cm^2 of affected skin. A second swab is taken from adjacent clinically healthy skin. The sample is taken by rubbing the skin with the swab for 60 seconds and is stored in DNA/RNA shield (Zymo Research Corp). Site-specific skin microbiomes vary between different body regions [18], and therefore, we attempt to collect samples from the same body site among patients in the following priority: the lumbar area and buttocks, arms, and legs. Sampling controls are collected by holding the swabs freely in the examination room for 3 minutes. The skin microbiome is analyzed by shotgun metagenomics with untargeted sequencing of all microbial genomes [19].

Skin Biopsies: Transcriptomics and Immunohistochemistry

Two 4-mm skin punch biopsies are taken under local anesthesia, including one from active psoriatic skin and one from clinically healthy skin neighboring the psoriatic biopsy area with a minimum distance of 2 cm from the psoriasis biopsy. The biopsy locations have the same priority for body sites as the skin swabs. After collection, biopsies are immediately cut in two parts and processed separately for RNA sequencing and immunohistochemistry.

Biopsies for RNA sequencing are placed directly into RNAprotect Tubes (QIAGEN), which are stored at 4°C overnight and thereafter at −80°C. RNA is isolated from biopsies, and its quality is assessed using the 2100 Bioanalyzer (Agilent). Sequencing libraries are prepared using SureSelect XT RNA Direct (Illumina) for samples with an RNA integrity number (RIN) score >8 and are sequenced at the Genomics Core Facility at Icahn School of Medicine at Mount Sinai.

Biopsies for immunohistochemistry are placed into a cryomold (Tissue Tek, Sakura Finetek) with optimal cutting temperature (OCT) solution (Tissue Tek, Sakura Finetek) that is subsequently snap-frozen with liquid nitrogen and immediately stored at −80°C. OCT samples are cut, mounted, fixed, and stained with hematoxylin and eosin, and with antibodies to selected target antigens using standard immunohistochemical techniques.

Blood Samples: Mass Cytometry, Proteomics, Lipidomics, and Metabolomics

Routine hematological and biochemical parameters, including high-sensitive C-reactive protein and N-terminal pro-brain natriuretic peptide, are analyzed at the Department of Clinical Biochemistry, Herlev and Gentofte Hospital, Denmark.

For mass cytometry profiling, blood is drawn in an ACD-A (acid citrate dextrose, Hettich Lab) tube, and 1 mL of blood is aliquoted into a tube containing 2 µL of Cell Activation Cocktail (phorbol 12-myristate-13-acetate [40.5 µM], ionomycin [669.3 µM], and Brefeldin A [2.5 mg/mL]; Biolegend). A second tube containing 1 mL of blood without the Cell Activation Cocktail is also collected. The tubes are mixed gently and then placed in an incubator at 37°C (5% CO_2). After 6 hours, 1.4 mL of proteomic stabilizer (PROT1, Smart Tube Inc) is added to each tube and mixed. The tubes are incubated for 10 minutes at room temperature and are then immediately placed at −80°C. Immune cell populations and cytokines are analyzed via mass cytometry by time-of-flight (CyTOF) [20] using a panel of 42 antibodies to profile various immune cells, including dendritic cells and T-cell subtypes, such as Th1, Th2, Th9, Th17, Th22, and Treg cells, in addition to relevant cytokines, such as interleukin (IL)-17 and IL-23.

For profiling of plasma proteins, blood is collected in ethylenediaminetetraacetic acid (EDTA) tubes and centrifuged for 10 minutes at 2000 rpm. The plasma is aliquoted into 1-mL tubes and immediately stored at −80°C. Plasma concentrations of proteins are measured using the Olink Proseek multiplex assay (Olink Bioscience), which uses proximity extension assay technology to detect protein biomarkers in liquid samples [21].

In brief, pairs of antibodies linked to oligonucleotides bind to their target protein in close proximity so that the oligonucleotides can hybridize and generate a unique sequence that can be detected and quantified by subsequent quantitative real-time polymerase chain reaction [22,23]. Predesigned Olink multiplex biomarker panels (Inflammation, Cardiovascular II, and Cardiovascular III) are used to determine protein profiles [24].

Lipidomic and metabolomic profiling of plasma are assessed by Metabolon (Morrisville), where approximately 1100 lipids and 5200 metabolites are measured by ultra-high performance liquid chromatography/tandem mass spectrometry [25].

For transcriptomic profiling, blood (2.5 mL) is drawn into PAXgene RNA Tubes (BD Bioscience), placed at −20°C overnight, and then stored at −80°C. RNA is isolated using the PAXgene Blood RNA Kit (QIAGEN), and its quality is assessed using the 2100 Bioanalyzer (Agilent). Sequencing libraries are prepared using TruSeq Stranded Total RNA kits (Illumina) for samples with a RIN score >8 and are sequenced at the Genomics Core Facility at Icahn School of Medicine at Mount Sinai. Owing to the relatively small number of study subjects, genomics are currently not planned to be assessed in this work.

Feces Sample: Gut Microbiome

All patients receive an OMNIgene GUT kit (DNA Genotek) for collection of feces at a maximum of 14 days after the blood samples. The gut microbiome is analyzed by shotgun metagenomics [19].

Urine Sample: Albumin-to-Creatinine Ratio

A urine sample is collected, and the albumin-to-creatinine ratio is determined at the Department of Clinical Biochemistry, Herlev and Gentofte Hospital, Denmark.

Echocardiography

Comprehensive two-dimensional resting transthoracic echocardiography, including tissue Doppler imaging, is performed using a Vivid E-95 ultrasound machine (GE Healthcare) with a M5Sc-D (1.4-4.6 MHz) transducer to determine myocardial structural and functional indices, such as left ventricular mass and systolic and diastolic function, right ventricular function, and left ventricular global longitudinal strain. Epicardial and pericardial adipose tissues are also measured in standard parasternal and short axis views [26,27]. All analyses are performed and stored in EchoPAC version 203.82 (GE Healthcare).

^{18}F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography

At a maximum of 14 days after the blood samples are taken, all patients undergo ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT). In brief, subjects are injected with 3.5 MBq (0.09 mCi) per kilogram FDG after fasting overnight. A whole-body FDG-PET/CT is performed 120 minutes after FDG injection on a GE Discovery 710 scanner (GE Medical Systems) using the proprietary Q.Clear PET reconstruction algorithm. Anatomic localization and attenuation correction are provided by an unenhanced low-dose CT scan. Regions of interest (ROIs) are delineated around the aorta in consecutive 3-mm-thick axial PET and CT slices using MIM 6.9.2 software (MIM Software Inc). FDG uptake in aortic segments is quantified by calculating the mean of the maximum activity in each ROI normalized to the mean activity in the superior vena cava (maximum target-to-background ratio [TBR_{max}]) to determine vascular inflammation according to established methodology [28]. Adipose tissue in brown, pericardial, visceral, and subcutaneous fat is measured by manually locating volumes of interest in the lateral neck, anterior to the pericardium at the level of the aortic root, caudal to the kidneys, and in the loin, respectively. Moreover, FDG uptakes in the bone marrow (lumbar vertebra L1-L5) and spleen are measured to assess activation of hematopoietic tissues. Separate electrocardiogram-gated low-dose CT acquisition is performed for determination of the coronary calcium score using a combined Agatston score for all coronary arteries using Siemens SyngoVia software VB40 (Siemens Healthcare) [29,30].

Carotid Artery Ultrasound Imaging

Ultrasound imaging of CIMT is performed in the right and left common carotid arteries by using an Affiniti 70G ultrasound system with a 5-12 MHz linear array transducer (Philips Ultrasound Inc) with Philips Q-App IMT software (version 3.03). CIMT is measured according to the Mannheim consensus on a 10-mm far wall segment of the distal common carotid artery during diastole, avoiding areas with focal thickening [31]. The presence of atherosclerotic plaques is also assessed in both carotid arteries.

Bioinformatics Analyses

For transcriptomics, RNA sequencing (RNA-seq) FASTQ sequence files are first subject to quality trim followed by alignment to the HG38 human genome and count summarization. Samples are normalized, and differential expression analysis is carried out to detect genes that are expressed at significantly different levels between groups. Gene set enrichment analysis is performed by the CAMERA method using reference data sets that include Hallmark, KEGG, Reactome, and Gene Ontology [32]. Protein-protein interaction network analysis is carried out using Cytoscape with the StringAPP plugin [33-35]. Functional enrichment analysis of the interaction network is performed using STRING enrichment against a collection of gene set databases [34,35].

For metagenomics, FASTQ files are quality trimmed before human genome mapping to filter out human reads. Microbial taxonomy classification is performed by the k-mer–based Kraken2 tool supplied with a microbial database including archaea, bacteria, fungi, protozoa, viruses, and vectors [36]. Relative taxonomy abundance is analyzed by LEfSe, and absolute abundance is analyzed by DESeq2 [37,38]. Alpha diversity is calculated using the phyloseq package in RStudio (R version 3.6) [39].

For high dimensional CyTOF, data are first preprocessed in Cytobank, and then, FCS data files are imported into RStudio [40]. Data are arcsinh-transformed and then scaled for heatmap presentation. Unscaled transformed data are used for FlowSOM hierarchical clustering [41]. The clusters are then manually

annotated and visualized after UMAP dimension reduction [42]. Differential cell lineage markers are further quantified and cytokine levels are stratified by clustered cell populations.

For proteomics, plasma protein levels are measured using the Cardiovascular II, Cardiovascular III, and Inflammation panels (Olink Bioscience), and reported as normalized protein expression levels (NPX) in log2 scale. Proteins are filtered out when 40% of samples are below the limit of detection. Protein changes are analyzed with the *limma*-trend method for comparisons of interest. Functional enrichment analysis is performed as described above for transcriptomic data [43].

The strength of a systems biology approach is the potential to integrate data from multiple platforms. There are several examples of how this approach has been successfully applied in the disease areas of psoriasis and in particular CVD [44,45]. We will use previously described computational methods to integrate multiomics data sets to develop a comprehensive and integrated view of cardiovascular risk in patients with psoriasis [46-48].

Results

The preliminary results of ^{18}F-FDG-PET/CT data have recently been published, where vascular inflammation in patients treated with statins was significantly reduced in the ascending aorta (P=.046) and aortic arch (P=.04) compared to the findings in patients not treated with statins, even though most statin-treated patients were, of course, in the CVD group [49]. Moreover, we very recently reported positive associations between vascular inflammation and inflammation in the visceral adipose tissue (P<.001), subcutaneous adipose tissue (P=.007), pericardial adipose tissue (P<.001), spleen (P=.001), and bone marrow (P<.001) in our study population [50].

The study has been approved by the ethics committee of the Capital Region, Denmark (H-17003458) and the local data protection agency (ID: HGH-2017-103, I-suite: 05977). All participants will be asked to sign an informed consent form before entering the study. The study has been conducted in agreement with the Declaration of Helsinki.

The ethics approval for the study was granted in March 2017. Recruitment for the study began in January 2018 and was completed in September 2020. Analyses of transcriptomics and proteomics have been completed, while analyses involving metagenomics, lipidomics, metabolomics, mass cytometry experiments, and immunohistochemistry are underway. Data processing and statistical analyses began in September 2020, and the first results of the study were published in the beginning of 2021 [49,50].

Discussion

This is an observational study with a case-control design that includes adult patients with psoriasis with or without atherosclerotic cardiovascular disease, and with or without systemic antipsoriatic treatment. The major strength of this study is the extensive number of examinations and samples collected from each patient to achieve deep phenotypic characterization. High-throughput molecular profiling technologies and computational analyses are utilized, and data are integrated by multiscale network analyses. With this approach, results are likely to shed light on new drivers and mechanisms of cardiovascular risk in psoriasis that can impact precision medicine [44,51]. Patients are specifically included with and without prior CVD, and with strict inclusion and exclusion criteria. Moreover, the psoriasis diagnosis is verified by dermatologists.

An important limitation of the study is that a control group without psoriasis is not included, which makes it impossible to compare the results with healthy individuals. Moreover, the computational analyses are data-driven and hypothesis-free, which precludes a priori sample size calculations. Another potential limitation is that patients with CVD are often older than those without CVD, so matching patients with and without CVD can be difficult. Furthermore, due to the extensive number of examinations and the 120 minutes of rest required for patients before the ^{18}F-FDG-PET/CT scan, the scan is not performed on the day of clinical examination and collection of blood and skin samples, potentially leading to temporal changes in the state of systemic inflammation. All skin biopsies and swabs might not be taken from the same body regions in all patients due to variations in the location of psoriasis-affected skin. Moreover, because of the recruitment setup and study hospital localization, most patients will probably be recruited from the Copenhagen area, although patients from other parts of Denmark are eligible and can contact the project through social media or the member magazine of the Danish Psoriasis Association.

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Authors' Contributions

PRH and LS designed the study, and PRH is responsible for the study. HK and AKH are responsible for clinical recruitment, retrieval of biological samples, and overall data collection. MK, PMG, and KMAH performed the ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography scan, carotid artery ultrasound, and echocardiography, respectively. CZ contributed

to study oversight and recruitment. BDM is responsible for sample processing and designing the multiomic profiling protocols. CB and XW contributed toward the design of the multiomic profiling protocols and are responsible for sample processing and analysis of multiomic data. HK, AKH, LS, and PRH drafted the first manuscript. All authors have contributed to this revision of the manuscript, and have read and approved the final manuscript.

Conflicts of Interest

PRH is the recipient of a Borregaard clinical scientist fellowship from the Novo Nordisk Foundation and chairs a clinical academic group supported by the Greater Region of Copenhagen. CB is a consultant for Onegevity Health. LS has been a paid speaker for AbbVie, Eli Lilly, and LEO Pharma, and has been a consultant or has served on advisory boards for AbbVie, Janssen Cilag, Novartis, Eli Lilly, LEO Pharma, UCB, Admirall, and Sanofi. Moreover, she has served as an investigator for AbbVie, Janssen Cilag, Boehringer Ingelheim, AstraZeneca, Eli Lilly, Novartis, Regeneron, and LEO Pharma and has received research and educational grants from Pfizer, AbbVie, Novartis, Sanofi, Janssen Cilag, and LEO Pharma. CZ has been a scientific consultant, advisor, investigator, and speaker for Eli Lilly, Jansen Cilag, Novartis, Abb Vie, Takeda, Amgen, Almirall, CSL Behring, UCB, Regeneron, MSD, and LEO Pharma. HK, AKH, XW, BDM, MK, PMG, and KMAH declare that they have no competing interests.

References

1. Takeshita J, Grewal S, Langan SM, Mehta NN, Ogdie A, Van Voorhees AS, et al. Psoriasis and comorbid diseases: Epidemiology. J Am Acad Dermatol 2017 Mar;76(3):377-390 [FREE Full text] [doi: 10.1016/j.jaad.2016.07.064] [Medline: 28212759]
2. Nestle FO, Kaplan DH, Barker J. Psoriasis. N Engl J Med 2009 Jul 30;361(5):496-509. [doi: 10.1056/NEJMra0804595] [Medline: 19641206]
3. Gelfand JM, Neimann AL, Shin DB, Wang X, Margolis DJ, Troxel AB. Risk of myocardial infarction in patients with psoriasis. JAMA 2006 Oct 11;296(14):1735-1741. [doi: 10.1001/jama.296.14.1735] [Medline: 17032986]
4. Armstrong EJ, Harskamp CT, Armstrong AW. Psoriasis and major adverse cardiovascular events: a systematic review and meta-analysis of observational studies. J Am Heart Assoc 2013 Apr 04;2(2):e000062 [FREE Full text] [doi: 10.1161/JAHA.113.000062] [Medline: 23557749]
5. Evensen K, Slevolden E, Skagen K, Rønning OM, Brunborg C, Krogstad A, et al. Increased subclinical atherosclerosis in patients with chronic plaque psoriasis. Atherosclerosis 2014 Dec;237(2):499-503. [doi: 10.1016/j.atherosclerosis.2014.10.008] [Medline: 25463081]
6. Yeung H, Takeshita J, Mehta NN, Kimmel SE, Ogdie A, Margolis DJ, et al. Psoriasis severity and the prevalence of major medical comorbidity: a population-based study. JAMA Dermatol 2013 Oct;149(10):1173-1179 [FREE Full text] [doi: 10.1001/jamadermatol.2013.5015] [Medline: 23925466]
7. Gonzalez-Juanatey C, Llorca J, Miranda-Filloy JA, Amigo-Diaz E, Testa A, Garcia-Porrua C, et al. Endothelial dysfunction in psoriatic arthritis patients without clinically evident cardiovascular disease or classic atherosclerosis risk factors. Arthritis Rheum 2007 Mar 15;57(2):287-293 [FREE Full text] [doi: 10.1002/art.22530] [Medline: 17330278]
8. Alexandroff AB, Pauriah M, Camp RDR, Lang CC, Struthers AD, Armstrong DJ. More than skin deep: atherosclerosis as a systemic manifestation of psoriasis. Br J Dermatol 2009 Jul;161(1):1-7. [doi: 10.1111/j.1365-2133.2009.09281.x] [Medline: 19500102]
9. Späh F. Inflammation in atherosclerosis and psoriasis: common pathogenic mechanisms and the potential for an integrated treatment approach. Br J Dermatol 2008 Aug;159 Suppl 2:10-17. [doi: 10.1111/j.1365-2133.2008.08780.x] [Medline: 18700910]
10. Ahlehoff O, Skov L, Gislason G, Gniadecki R, Iversen L, Bryld LE, et al. Cardiovascular outcomes and systemic anti-inflammatory drugs in patients with severe psoriasis: 5-year follow-up of a Danish nationwide cohort. J Eur Acad Dermatol Venereol 2015 Jun;29(6):1128-1134. [doi: 10.1111/jdv.12768] [Medline: 25303139]
11. Prodanowich S, Ma F, Taylor JR, Pezon C, Fasihi T, Kirsner RS. Methotrexate reduces incidence of vascular diseases in veterans with psoriasis or rheumatoid arthritis. J Am Acad Dermatol 2005 Feb;52(2):262-267. [doi: 10.1016/j.jaad.2004.06.017] [Medline: 15692471]
12. Kidd BA, Peters LA, Schadt EE, Dudley JT. Unifying immunology with informatics and multiscale biology. Nat Immunol 2014 Feb;15(2):118-127 [FREE Full text] [doi: 10.1038/ni.2787] [Medline: 24448569]
13. Li L, Cheng W, Glicksberg BS, Gottesman O, Tamler R, Chen R, et al. Identification of type 2 diabetes subgroups through topological analysis of patient similarity. Sci Transl Med 2015 Oct 28;7(311):311ra174 [FREE Full text] [doi: 10.1126/scitranslmed.aaa9364] [Medline: 26511511]
14. Hu JX, Thomas CE, Brunak S. Network biology concepts in complex disease comorbidities. Nat Rev Genet 2016 Oct;17(10):615-629. [doi: 10.1038/nrg.2016.87] [Medline: 27498692]
15. Johnson KW, Shameer K, Glicksberg BS, Readhead B, Sengupta PP, Björkegren JLM, et al. Enabling Precision Cardiology Through Multiscale Biology and Systems Medicine. JACC Basic Transl Sci 2017 Jun;2(3):311-327 [FREE Full text] [doi: 10.1016/j.jacbts.2016.11.010] [Medline: 30062151]
16. Schmitt J, Wozel G. The psoriasis area and severity index is the adequate criterion to define severity in chronic plaque-type psoriasis. Dermatology 2005;210(3):194-199. [doi: 10.1159/000083509] [Medline: 15785046]

17. González-Álvarez L, García-Martín JM, García-Pola MJ. Association between geographic tongue and psoriasis: A systematic review and meta-analyses. J Oral Pathol Med 2019 May;48(5):365-372. [doi: 10.1111/jop.12840] [Medline: 30739339]
18. Byrd AL, Belkaid Y, Segre JA. The human skin microbiome. Nat Rev Microbiol 2018 Mar;16(3):143-155. [doi: 10.1038/nrmicro.2017.157] [Medline: 29332945]
19. Quince C, Walker AW, Simpson JT, Loman NJ, Segata N. Shotgun metagenomics, from sampling to analysis. Nat Biotechnol 2017 Sep 12;35(9):833-844. [doi: 10.1038/nbt.3935] [Medline: 28898207]
20. Spitzer MH, Nolan GP. Mass Cytometry: Single Cells, Many Features. Cell 2016 May 05;165(4):780-791 [FREE Full text] [doi: 10.1016/j.cell.2016.04.019] [Medline: 27153492]
21. Lind L, Ärnlöv J, Lindahl B, Siegbahn A, Sundström J, Ingelsson E. Use of a proximity extension assay proteomics chip to discover new biomarkers for human atherosclerosis. Atherosclerosis 2015 Sep;242(1):205-210. [doi: 10.1016/j.atherosclerosis.2015.07.023] [Medline: 26204497]
22. Assarsson E, Lundberg M, Holmquist G, Björkesten J, Thorsen SB, Ekman D, et al. Homogenous 96-plex PEA immunoassay exhibiting high sensitivity, specificity, and excellent scalability. PLoS One 2014;9(4):e95192 [FREE Full text] [doi: 10.1371/journal.pone.0095192] [Medline: 24755770]
23. Lundberg M, Eriksson A, Tran B, Assarsson E, Fredriksson S. Homogeneous antibody-based proximity extension assays provide sensitive and specific detection of low-abundant proteins in human blood. Nucleic Acids Res 2011 Aug;39(15):e102 [FREE Full text] [doi: 10.1093/nar/gkr424] [Medline: 21646338]
24. Brunner PM, Suárez-Fariñas M, He H, Malik K, Wen H, Gonzalez J, et al. The atopic dermatitis blood signature is characterized by increases in inflammatory and cardiovascular risk proteins. Sci Rep 2017 Aug 18;7(1):8707 [FREE Full text] [doi: 10.1038/s41598-017-09207-z] [Medline: 28821884]
25. Evans AM, DeHaven CD, Barrett T, Mitchell M, Milgram E. Integrated, nontargeted ultrahigh performance liquid chromatography/electrospray ionization tandem mass spectrometry platform for the identification and relative quantification of the small-molecule complement of biological systems. Anal Chem 2009 Aug 15;81(16):6656-6667. [doi: 10.1021/ac901536h] [Medline: 19624122]
26. Iacobellis G, Willens HJ. Echocardiographic epicardial fat: a review of research and clinical applications. J Am Soc Echocardiogr 2009 Dec;22(12):1311-1319. [doi: 10.1016/j.echo.2009.10.013] [Medline: 19944955]
27. Davidovich D, Gastaldelli A, Sicari R. Imaging cardiac fat. Eur Heart J Cardiovasc Imaging 2013 Jul;14(7):625-630. [doi: 10.1093/ehjci/jet045] [Medline: 23539476]
28. Bucerius J, Hyafil F, Verberne HJ, Slart RHJA, Lindner O, Sciagra R, Cardiovascular Committee of the European Association of Nuclear Medicine (EANM). Position paper of the Cardiovascular Committee of the European Association of Nuclear Medicine (EANM) on PET imaging of atherosclerosis. Eur J Nucl Med Mol Imaging 2016 Apr;43(4):780-792 [FREE Full text] [doi: 10.1007/s00259-015-3259-3] [Medline: 26678270]
29. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M, Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. Journal of the American College of Cardiology 1990 Mar 15;15(4):827-832 [FREE Full text] [doi: 10.1016/0735-1097(90)90282-t] [Medline: 2407762]
30. Greenland P, Bonow RO, Brundage BH, Budoff MJ, Eisenberg MJ, Grundy SM, American College of Cardiology Foundation Clinical Expert Consensus Task Force (ACCF/AHA Writing Committee to Update the 2000 Expert Consensus Document on Electron Beam Computed Tomography), Society of Atherosclerosis ImagingPrevention, Society of Cardiovascular Computed Tomography. ACCF/AHA 2007 clinical expert consensus document on coronary artery calcium scoring by computed tomography in global cardiovascular risk assessment and in evaluation of patients with chest pain: a report of the American College of Cardiology Foundation Clinical Expert Consensus Task Force (ACCF/AHA Writing Committee to Update the 2000 Expert Consensus Document on Electron Beam Computed Tomography). Circulation 2007 Jan 23;115(3):402-426. [doi: 10.1161/CIRCULATIONAHA..107.181425] [Medline: 17220398]
31. Touboul PJ, Hennerici MG, Meairs S, Adams H, Amarenco P, Bornstein N, et al. Mannheim carotid intima-media thickness and plaque consensus (2004-2006-2011). An update on behalf of the advisory board of the 3rd, 4th and 5th watching the risk symposia, at the 13th, 15th and 20th European Stroke Conferences, Mannheim, Germany, 2004, Brussels, Belgium, 2006, and Hamburg, Germany, 2011. Cerebrovasc Dis 2012;34(4):290-296 [FREE Full text] [doi: 10.1159/000343145] [Medline: 23128470]
32. Wu D, Smyth GK. Camera: a competitive gene set test accounting for inter-gene correlation. Nucleic Acids Res 2012 Sep 01;40(17):e133 [FREE Full text] [doi: 10.1093/nar/gks461] [Medline: 22638577]
33. Shannon P, Markiel A, Ozier O, Baliga NS, Wang JT, Ramage D, et al. Cytoscape: a software environment for integrated models of biomolecular interaction networks. Genome Res 2003 Nov;13(11):2498-2504 [FREE Full text] [doi: 10.1101/gr.1239303] [Medline: 14597658]
34. Doncheva NT, Morris JH, Gorodkin J, Jensen LJ. Cytoscape StringApp: Network Analysis and Visualization of Proteomics Data. J Proteome Res 2019 Feb 01;18(2):623-632 [FREE Full text] [doi: 10.1021/acs.jproteome.8b00702] [Medline: 30450911]
35. Szklarczyk D, Gable AL, Lyon D, Junge A, Wyder S, Huerta-Cepas J, et al. STRING v11: protein-protein association networks with increased coverage, supporting functional discovery in genome-wide experimental datasets. Nucleic Acids Res 2019 Jan 08;47(D1):D607-D613 [FREE Full text] [doi: 10.1093/nar/gky1131] [Medline: 30476243]

36. Wood DE, Lu J, Langmead B. Improved metagenomic analysis with Kraken 2. Genome Biol 2019 Nov 28;20(1):257 [FREE Full text] [doi: 10.1186/s13059-019-1891-0] [Medline: 31779668]
37. Segata N, Izard J, Waldron L, Gevers D, Miropolsky L, Garrett WS, et al. Metagenomic biomarker discovery and explanation. Genome Biol 2011 Jun 24;12(6):R60 [FREE Full text] [doi: 10.1186/gb-2011-12-6-r60] [Medline: 21702898]
38. Love MI, Huber W, Anders S. Moderated estimation of fold change and dispersion for RNA-seq data with DESeq2. Genome Biol 2014;15(12):550 [FREE Full text] [doi: 10.1186/s13059-014-0550-8] [Medline: 25516281]
39. McMurdie PJ, Holmes S. phyloseq: an R package for reproducible interactive analysis and graphics of microbiome census data. PLoS One 2013;8(4):e61217 [FREE Full text] [doi: 10.1371/journal.pone.0061217] [Medline: 23630581]
40. Kotecha N, Krutzik PO, Irish JM. Web-based analysis and publication of flow cytometry experiments. Curr Protoc Cytom 2010 Jul;Chapter 10:Unit10.17 [FREE Full text] [doi: 10.1002/0471142956.cy1017s53] [Medline: 20578106]
41. Van Gassen S, Callebaut B, Van Helden MJ, Lambrecht BN, Demeester P, Dhaene T, et al. FlowSOM: Using self-organizing maps for visualization and interpretation of cytometry data. Cytometry A 2015 Jul;87(7):636-645 [FREE Full text] [doi: 10.1002/cyto.a.22625] [Medline: 25573116]
42. Becht E, McInnes L, Healy J, Dutertre CA, Kwok IWH, Ng LG, et al. Dimensionality reduction for visualizing single-cell data using UMAP. Nat Biotechnol 2018 Dec 03:38-47. [doi: 10.1038/nbt.4314] [Medline: 30531897]
43. Ritchie ME, Phipson B, Wu D, Hu Y, Law CW, Shi W, et al. limma powers differential expression analyses for RNA-sequencing and microarray studies. Nucleic Acids Res 2015 Apr 20;43(7):e47 [FREE Full text] [doi: 10.1093/nar/gkv007] [Medline: 25605792]
44. Zhao Y, Jhamb D, Shu L, Arneson D, Rajpal DK, Yang X. Multi-omics integration reveals molecular networks and regulators of psoriasis. BMC Syst Biol 2019 Jan 14;13(1):8 [FREE Full text] [doi: 10.1186/s12918-018-0671-x] [Medline: 30642337]
45. Joshi A, Rienks M, Theofilatos K, Mayr M. Systems biology in cardiovascular disease: a multiomics approach. Nat Rev Cardiol 2021 May;18(5):313-330. [doi: 10.1038/s41569-020-00477-1] [Medline: 33340009]
46. Hawe JS, Theis FJ, Heinig M. Inferring Interaction Networks From Multi-Omics Data. Front Genet 2019;10:535 [FREE Full text] [doi: 10.3389/fgene.2019.00535] [Medline: 31249591]
47. Yan J, Risacher SL, Shen L, Saykin AJ. Network approaches to systems biology analysis of complex disease: integrative methods for multi-omics data. Brief Bioinform 2018 Nov 27;19(6):1370-1381 [FREE Full text] [doi: 10.1093/bib/bbx066] [Medline: 28679163]
48. Wörheide MA, Krumsiek J, Kastenmüller G, Arnold M. Multi-omics integration in biomedical research - A metabolomics-centric review. Anal Chim Acta 2021 Jan 02;1141:144-162. [doi: 10.1016/j.aca.2020.10.038] [Medline: 33248648]
49. Kaiser H, Kvist-Hansen A, Krakauer M, Gørtz PM, Henningsen KMA, Wang X, et al. Statin Therapy and Vascular Inflammation Detected by Positron Emission Tomography/Computed Tomography in Patients with Psoriasis. Acta Derm Venereol 2021 Feb 24;101(2):adv00406 [FREE Full text] [doi: 10.2340/00015555-3752] [Medline: 33491097]
50. Kaiser H, Kvist-Hansen A, Krakauer M, Gørtz PM, Henningsen KMA, Wang X, et al. Association between Vascular Inflammation and Inflammation in Adipose Tissue, Spleen, and Bone Marrow in Patients with Psoriasis. Life (Basel) 2021 Apr 01;11(4):305 [FREE Full text] [doi: 10.3390/life11040305] [Medline: 33915972]
51. Yang X. Multitissue Multiomics Systems Biology to Dissect Complex Diseases. Trends Mol Med 2020 Aug;26(8):718-728 [FREE Full text] [doi: 10.1016/j.molmed.2020.04.006] [Medline: 32439301]

Abbreviations

CIMT: carotid artery intimamedia thickness
CVD: cardiovascular disease
CyTOF: mass cytometry by time-of-flight
FDG: fluorodeoxyglucose
IL: interleukin
OCT: optimal cutting temperature
PET/CT: positron emission tomography/computed tomography
RIN: RNA integrity number
ROI: region of interest
Th: T-helper

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Protocol

The Good Food for Learning Universal Curriculum-Integrated Healthy School Lunch Intervention: Protocol for a Two-Year Matched Control Pre-Post and Case Study

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Abstract

Background: Good nutrition affects children's health, well-being, and learning, and schools offer an important setting to promote healthy behaviors that can last a lifetime. Once children reach school age, they spend more of their waking hours in school than in any other environment. Children's eating habits may be easier to influence than those of adults. In Canada, households with children are more likely to experience food insecurity, and school food programs that are universally available to all children can support the development of healthy eating patterns across groups of varying socioeconomic status. There is a significant gap in the rigorous community-engaged academic research on the impact of school meal programs, especially universal ones.

Objective: The aim of this population health intervention research is to study the impact of a 2-year universal, curriculum-integrated healthy school lunch program in elementary schools in Saskatoon, Saskatchewan, Canada, on food consumption, dietary quality and food and nutrition-related knowledge, attitudes, and practices.

Methods: This population health intervention study will be conducted in 2 intervention elementary schools matched with 2 control schools. We will collect preintervention data, including objective measurements of food eaten at school and food-related knowledge, attitudes, and behaviors. This will be followed by the intervention itself, along with qualitative case studies of the intervention process in the 2 intervention schools. Then, we will collect postintervention data similar to the preintervention data. Finally, we will finish the data analysis and complete the ongoing sharing of learning from the project.

Results: This study was funded in April 2020 but because of the COVID-19 pandemic, data collection did not begin until May 2021. The intervention will begin in September 2021 and end in June 2023, with end point data collection occurring in May and June 2023. The case study research will begin in September 2021 and will be ongoing for the duration of the intervention.

Conclusions: The opportunity we have to systematically and comprehensively study a curriculum-integrated school lunch program, as well as the promising practices for school food programs across Canada, is without precedent.

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KEYWORDS

school food programs; Canada; nutrition; intervention research; mHealth

Introduction

Background

Two events occurred in 2019 that made rigorous Canadian research on school food programs particularly needed and timely. First, the updated Canadian Food Guide (CFG) was released [1]. Its focus is on reducing the consumption of highly processed foods, encouraging consumption of a variety of healthy foods, shifting to plant proteins, eating as a social and conscious act, and cooking. Second, the March Federal Budget stated the following [2]:

> *Critically important for a child's education is ensuring they have healthy meals before and during school. Currently, Canada has a mix of different school breakfast and lunch programs, but much more could be done. Budget 2019 announces the government's intention to work with the provinces and territories towards the creation of a national school food program.*

Ensuring that Canadians have the capabilities and opportunities to eat in accordance with the new CFG guidelines will be challenging, given that families struggle to consume healthy foods for multiple reasons including affordability, time scarcity, and food availability [3-7]. Debates have focused on how the new CFG recommendations can be achieved, with journalists and researchers stating that a national school food program might be a key approach [8].

Nutrition affects children's health, well-being, and learning, and schools offer an important setting to promote health behaviors that can last a lifetime [9-13]. Households with children are more likely to experience food insecurity; however, recent research shows that the diet quality of Canadian children across the socioeconomic spectrum during school hours is poor [14]. School age children spend more of their waking hours in school than in any other environment, yet Canada is one of the only Organization for Economic Cooperation and Development countries without a national school food policy or program [15]. School food programs can include breakfast, lunch, and snacks, with or without integration into the curricula, and can contribute to child, family, and community health and well-being [16]. School food programs that are available to all children, regardless of a family's ability to pay, can support the development of healthy eating patterns across groups of varying socioeconomic status (SES) [16,17].

The 160 members of the Canadian Coalition for Healthy School Food (CHSF), the largest Canadian organization advocating for school food programs, advocates for a universal school food program that is key to positively evaluated programs [17]. Universality means that all children have access to a school lunch program, and in the case of the intervention discussed here, at no cost, regardless of income. Most school breakfast and lunch programs in Canada are instead targeted to either self-identified or school-identified low-income families [18]. Discussions regarding a school food program for Canada are drawing largely on international evidence because of the limited Canadian data available [19,20]. There is a significant gap in rigorous academic research on the design of and outcomes of school meal programs, especially universal ones [21].

We conducted a scoping review of school food research in Canada to determine what we know from promising practices for school meal programs [20]. A total of 17 peer-reviewed and 19 gray literature articles discussed 24 programs in 10 provinces. There was one randomized control trial, no longitudinal studies, and one study with a control group. The breadth and depth of research on school food programs in Canada is lacking [19]. Upon analysis of the research to date, we concluded that the most promising programs for improved health address social determinants of health and teach about food systems and environmental sustainability.

The purpose of our population health intervention research (PHIR) is to study the process, benefits, and challenges of implementation, as well as impacts of a universal, curriculum-integrated, healthy school lunch program on diet

quality and food and nutrition-related knowledge, attitudes, and practices (KAP) of elementary students. Universal school food programs reduce stigma compared with targeted programs, and Raine et al [22] found that only a minority of the intended target population is actually reached in targeted programs. Previous process evaluation studies have identified universal access and curriculum integration as key factors in the success of snack-based school food programs [23]. Curriculum-integrated means core curriculum (eg, math, science, and social studies) includes teaching aspects of food, nutrition, and food systems at the same time as providing the school lunch. Children also gain hands-on experience by growing some of the vegetables and preparing food for consumption.

This study is funded by the Canadian Institutes for Health Research and has undergone peer review (see Multimedia Appendices 1-4).

Literature Review

Evolution of School Food Programs

The development of school food programs in high-income countries has followed three phases, the third of which is just taking hold today [16]. Globally, school food programs were often established primarily to reduce hunger [16]. In the 1970s, in some parts of Europe and in the 1990s and the 2000s in the United States of America and the United Kingdom, a shift toward improving food quality began, creating the second phase of school food programs. This second phase shifted the focus toward dietary guidelines for school food programs to improve the nutritional quality of food served. The third phase, in its infancy in most countries (Canada included), is a response to increased rates of childhood obesity and nutrition-related chronic diseases, a larger societal context of challenges in the food system, climate change, and environmental degradation. This phase incorporates food systems and societal issues into food programs and policies and generally integrates them more closely with curricula and the school environment as a whole [16,24]. Various researchers argue that this approach is the future of school food programs around the world and is consistent with the principles outlined in the CFG [25,26]. We recently examined international literature on school food programs in high-income countries and outlined key characteristics needed in a national school food program for Canada, including universality, curriculum integration, adaptation to local contexts, and sustainable funding [21].

School Food Programs, Nutrition, and Health

International research on the health and dietary behavior impacts of school food programs in high-income countries has found modest positive effects overall, including higher vitamin intake and increased vegetable and fruit consumption, especially in younger children [27-30]. Studies from various countries that compare the nutritional quality of food consumed at school that was brought from home versus food acquired through school food programs has found that school food programs provide healthier food overall (regardless of the SES of child participants) [31-38].

Only a small proportion of Canadian children meet the Canadian eating recommendations, with low vegetable and fruit consumption of particular concern [39,40]. Research on overall dietary patterns in Canada highlights the very large proportions of ultraprocessed foods high in salt, sugar, and some fats being consumed [41,42]. Families struggle to introduce minimally processed healthy foods for a variety of reasons [3-5].

Provision of healthy school lunches is challenging in the context of parents working long hours [43,44], and families are struggling to adopt healthy food behaviors [44]. Parents may rely on highly processed foods, low in key nutrients but high in salt, sugar, and fat, to cope with demands on time [45,46]. The diets of Canadian children across the socioeconomic spectrum are poor [47]. There is some evidence from the United States that school food programs can reduce disparities in vegetable and fruit consumption between children from higher versus lower SES households and limit the intake of minimally nutritious foods among higher SES households [48]. Introduction of healthy foods in a universal school food program could provide all children with greater opportunities to learn about and eat healthy foods in a way that is not stigmatizing [49].

Our team's previous observational research on school food in and around Saskatoon, Saskatchewan, Canada, characterized lunches using a school food checklist and digital photography in randomly selected urban schools with a meal program (n=3), urban schools without a meal program (n=3), and rural schools without a meal program (n=3) [50]. The number of servings of each CFG food group was determined and compared with one-third of the recommended daily intake. The Healthy Eating Index (HEI) scores were calculated. In results similar to Tugault-Lafleur et al [14] using the national Canadian Community Health Survey data for the school day, just over half of the students who brought lunches from home met the recommendations for grain products and meat and alternatives, less than one-third met recommendations for vegetables and fruits, under one-fourth met the recommendations for whole grains, and even fewer met the recommendations for milk and alternatives. The HEI scores of students in meal programs were greater than those of students who brought lunches from home because they included more whole grains, met meat and alternatives recommendations, and contained fewer calories from minimally nutritious foods (high-fat and high-sugar foods such as candies, chocolate, and sauces). Children not participating in meal programs brought about one-third of calories as minimally nutritious food, about double that of meal program student lunches.

There are numerous reports of school staff and other stakeholders expressing a desire to offer universal lunch programs rather than the more common targeted programs and expressing concern about the quality of food currently consumed by Canadian children at school outside of lunch programs [51,52]. Drawing on international evidence, an evaluation was conducted of a 2-year pilot of free school meals in 3 local authorities in the United Kingdom [53]. Two local authorities made free school meals universal to all primary school children, whereas the third extended free school meal entitlements to a larger number of students but was not universally free. In the extended entitlement (not universal) authority, there were no impacts found on children's eating habits, whereas in the

universal entitlement authorities, there were reductions in the consumption of potato chips and soft drinks and an increase in vegetables consumed. In the universal pilot areas, parents' perceptions of school meals for health were more positive and they thought that their children were more willing to try new foods.

Learning Outcomes and School Food Programs

Educational achievement is associated with health across life span [54]. Studies on school food programs and academic achievement, attendance, tardiness, and dropout rates point to important impacts of school food programs. Attendance and tardiness appear to be the educational outcomes with the most available evidence, but some studies have found improvements in academic achievement with the introduction of school food programs [55-65]. School food programs can also contribute to teaching culinary heritage, social norms around food, and environmental sustainability [26,66,67]. We are conducting a separate study in partnership with educational research colleagues on educational outcome changes as a result of this intervention.

Food Literacy, Environmental Education, and School Food Programs

Various countries, including Canada most recently, have adopted nutritional recommendations that recognize the connections between nutrition and environmental sustainability [1,68]. According to Cullen et al [69], food literacy is "the ability to make decisions to support the achievement of personal health and a sustainable food system considering environmental, social, economic, cultural, and political components." School food programs focused on the provision of healthy, sustainable foods (including vegetables and fruit, plant proteins, and locally produced foods) along with the promotion of sustainable food behaviors such as school gardening and learning how to reduce food waste, may work together to change food behaviors [26], which may spill into life away from school [70]. Stone [71] and Weaver-Hightower [72] explain how children can be involved in age-appropriate ways to grow and prepare food, along with learning how the food system works and its environmental and social challenges, to integrate learning with a meal program. This integration enables appreciation for food and a greater willingness to try new foods [73,74].

The evidence for school food interventions that include both meals and curriculum is getting stronger internationally, but not much Canadian evidence is available [19,20,62,75]. These interventions include introducing healthy foods, integrated with the curriculum, and with parent involvement [28,76]. They take an education-integrated approach that involves children in growing and preparing food, teaching about food system sustainability, and healthy behaviors [26]. Internationally, Oostindjer et al [26] juxtapose the Swedish and British school food programs and the Japanese, French, Italian, and Finnish school food programs on this front. The Finnish universal lunch program, which is a key aspect of their education system, is integrated with the curriculum, including learning objectives related to social relationships and eating norms that are lacking in Sweden and the United Kingdom [77-79]. According to a review of international literature, this emerging integration of school meals with classroom curricula aligned with food cultural learning and establishing an optimal food and social environment may facilitate learning of healthy and sustainable food behaviors [26].

Methods

Overview

This multimethod PHIR is informed by the theory of change, where the ways in which a program brings about specific outcomes are explicitly described, as is commonly done with complex population health program evaluations [80]. We have also developed a program logic model for population health intervention as part of our theory of change. The overall research design is a case study with an embedded matched control pre and post study of a universal, curriculum-integrated school lunch program in elementary schools consistent with promising practices in school food programs for Canada [19,26,75]. The case study will fill an important research gap in rigorous PHIR that is critical to inform policy change, given that it examines both implementation and health-related outcomes [81-83]. Our design includes the following:

1. A comprehensive case study of the process of implementation, benefits, challenges, and perceptions of a universal, curriculum-integrated school lunch program including key informant and caregiver interviews and structured and unstructured observations of the intervention school food environment.
2. An embedded, nonblinded, experimental study with a control group including an assessment of plate-waste of lunches to examine contribution to overall diet quality (based on a third of daily food consumption [14]) and surveys of food-related KAP.

Research Objective and Research Questions

The objective of our study is to examine the process of implementation and the impacts of a universal, curriculum-integrated school lunch program in 2 schools by responding to the following research questions (RQs):

- What are the benefits of and challenges faced in establishing and administering a universal curriculum-integrated healthy school lunch program?
- What is the difference in diet quality, food group, and key nutrient consumption among children in intervention schools after the implementation of a comprehensive, curriculum-integrated universal school lunch program as compared with children in control schools?
- What is the difference in food-related KAP among child participants in intervention schools after the implementation of a comprehensive, curriculum-integrated universal school lunch program as compared with children in control schools?
- What aspects of curriculum integration show promise in enhancing food-related learning?

Hypotheses

Owing to the qualitative nature of the case study RQs, we do not have hypotheses for them. For the embedded experimental

study, we hypothesize that there will be significant differences in food consumption and dietary quality between intervention and control schools at the end point, with children in intervention schools having higher consumption of vegetables and fruits, whole grains, and dairy products and lower consumption of minimally nutritious foods. We expect differences in food-related KAP of children in intervention versus control schools, with intervention school participants having greater knowledge and more positive attitudes and practices with regard to nutritious and sustainable food.

Sample

We conducted a sample size calculation that indicated that we needed a minimum sample of 148 children from 2 intervention schools matched with 148 children from 2 control schools to detect changes in eating behavior, accounting for attrition from the baseline (pretest) to the end point (posttest). Furthermore, 2 intervention and 2 control elementary schools were selected by the Saskatoon Public Schools Division (SPSD) from the 8 schools that currently have small lunch programs and the infrastructure to scale up to serve the whole school. Saskatoon is a midsized Canadian Prairie city with a population of approximately 325,000 residents. The 4 schools were selected from among the 8 schools because the school staff in these schools are willing to participate in this initial intervention study which is critical at this stage. The schools are located in lower SES neighborhoods with more ethnic diversity including relatively large numbers of newcomers and Indigenous children compared with other neighborhoods in Saskatoon [84].

Our sample of students in the intervention schools is a 1:1 matched sample of children from 2 control schools based on self-identified gender, age, school grade, and school neighborhood median income, who will be followed from the baseline to the end point (2 full school years with a summer break in between). All children in grades 1-6 in each school will be invited to participate (approximately 170 students in each school in these grades). Our total sample from which participants will be drawn is about 340 (170 in each school), much more than the minimum 148 needed in our sample size calculation. They will be matched with an equivalent number in control schools.

Intervention Details

The intervention comprises (1) the universal school lunch program and (2) the associated curriculum. The intervention will last 2 full school years (plus a summer between) to allow time for the schools to adapt to new food and curricular practices. Case study research will be ongoing over 20 months of school.

The school lunch will be offered every day at no cost to all students in the intervention schools and will focus on nutritious foods, including a variety of vegetables and fruits, whole grains, dairy products, plant proteins, and some meat. With SPSD staff and CHSF input, we developed a 6-week menu for the school food program with considerations for cultural appropriateness and the new CFG recommendations, including more plant-based proteins and whole grains. We are working with a community-based organization that works with local producers to incorporate local foods where possible into school food menus. The menu includes a variety of vegetables and fruits because they are particularly low in the diets of Canadian children [14,46], and it has been reviewed by a dietitian.

For curriculum integration, we adapted 6 lesson plans each from kindergarten up to grade 6 (ages 5-12 years) to teach food safety, food preparation, nutrition, gardening, and food waste reduction tied to the Saskatchewan curriculum and informed by our scoping review. The curriculum was developed with the CHSF and several Saskatchewan teachers and is ready to use in the classroom with little additional preparation by teachers. In addition to the lesson plans, all classrooms in each grade will also have two experiences involved in cooking: one indoor and one outdoor food-growing experience. Consistent with best education practices, our focus is on a hands-on curriculum.

Data Collection and Analysis

Phase 1: Intervention Planning

We have ethical approval in place (University of Saskatchewan BEH-509) and a memorandum of understanding prepared between principal investigator RES and the SPSD. In 2018, we collected baseline data on school food environments in the 2 intervention schools to inform study preparation. Intervention planning was supposed to be conducted from March to May 2020; however, because of the COVID-19 pandemic, it was put off and conducted between January and May 2021. The COVID-19 pandemic-related prohibitions on field data collection also affected this study, and permission to enter schools was granted in mid-May 2021.

Phase 2 and Phase 4: Baseline and End Point Measurement

RQ2: What is the difference in diet quality, food group, and key nutrient consumption among children in intervention schools after the implementation of a comprehensive, curriculum-integrated universal school lunch program as compared with children in control schools?

A digital photography–enhanced plate-waste study will assess food eaten for lunch by students in intervention and control schools (n=148 minimum each for a total of 296; 4 schools) on 2 days at baseline (preintervention) and then on 2 days at the end point (in the last 2 months of the intervention). Each participating child will have four measurements of plate-waste data (two baseline and two end point data). We will follow the protocol developed by coinvestigator HV, which has been extensively used in studies of school-aged children [85-87]. The procedures for data collection involve weighing the served food and leftovers, using digital photography and a food scale during the lunchtime with an app installed on tablets. This method is considered the most precise measurement of dietary intake compared with other dietary assessment methods that are typically used, such as food records [88,89]. The literature indicates no significant impact of the method on eating behaviors in children [88,89]. Digital photography of plate-waste will be conducted by 2 research assistants in half the school classrooms on each data collection day, for a total of 4 data collection days at both baseline and at end point in each school. The practice of collecting data from half the classrooms in a single school

on each data collection day will ensure minimal disruption of regular school days.

Our plate-waste approach allows us to infer the amount of food consumed by calculating the difference between the amount served and the amount left over [88,90]. At the end point, the information about the menus (recipe level data) on the days of data collection will be entered in the app on tablets before lunch. A label with the identification number of the child is placed on the tableware to correctly identify each child's meal and leftovers and scanned at the time of data collection for each child. A photograph (62 cm away from the food, at a 45° angle [91]) is taken of student's tableware (ie, each container in a lunch box, plates, or other) to visually capture the size and general appearance of items to subtract them from the food consumed. Each entry contains the child's identification number, the photo forms to record the weight of the food, and whether the photo was taken before or after the child's meal. Leftover food is weighed and photographed again at the end of the meal. By subtracting the weighed leftovers from the weighed food served, the food consumed will be obtained. The information pertaining to energy, macronutrients, and micronutrients consumed will be derived using Food Processor nutrition analysis software (The Food Processor, Esha Research version 11.3.285). The final report will be exported to Microsoft Excel where food groups based on the new CFG will be calculated (new recommendations on the amount and type of food taken by age group are not available as of June 2021 but will be used once released by Health Canada).

The collated baseline and end point data will go through data cleaning, processing, and quality control using protocols developed in the Vatanparast Nutritional Epidemiology laboratory. After creating the master data file including original and derived variables of interest, such as the Nutrient Rich Food index (9.3) [92], HEI [14] based on the new CFG, sex assigned at birth, self-identified gender, age, grade, and neighborhood of residence as a proxy for SES, the descriptive analyses will provide the initial information on these variables. Categorical variables (ie, HEI categories) will be summarized in frequency tables. Regression models will examine changes from baseline to the end point across key outcome variables including the Nutrient Rich Food index scores, HEI scores, CFG servings, and key nutrients (calcium, sodium, vitamin D, folate, and calories from minimally nutritious food) and whether changes differ between the control and intervention schools. Final models will adjust for potentially confounding factors including sex assigned at birth, self-identified gender, age, grade, neighborhood of residence, and baseline dietary intake (for more detail on identifying a priori potential confounders and controlling for them, see *Phase 5: Final Analysis and Dissemination* section below). We will also examine potential interaction effects between the intervention and control groups and age, sex, and gender (as detailed above in the sample description) to assess whether the effect of the intervention on dietary outcomes was modified by key student-level characteristics. Clustering of students within the classroom and schools (nonindependence) will be taken into account by applying random-effects multilevel modeling approaches to data.

RQ3: What is the difference in food-related KAP among child participants in intervention schools after the implementation of a comprehensive, curriculum-integrated universal school lunch program as compared with children in control schools?

At baseline and at the end point in both intervention and control schools, we will administer a survey of food-related KAP adapted from the Individual Eating Assessment Tool (I-EAT) to all participating students in grades 4-6 in the intervention and control schools. According to the KAP model, knowledge (K) accumulates and attitudes (A) change and these changes promote changes in practices (P) over time. We cannot administer the survey to children younger than grade 4 because of inconsistent literacy levels before that age and older than grade 6 because they will no longer be at the school at the end point. Given our expected 80% response rate, we will have a sufficiently large sample in these three grades only to carry out these analyses. This survey was originally developed by Black et al [47,93-95] and we have adapted and piloted it with 100 children. We conducted a factor analysis of the pilot results for validation and then made some additional minor changes following the analysis, specifically removing four questions that did not add relevant data. We included I-EAT questions on food, cooking and nutrition knowledge and beliefs, confidence in participating in various food-related activities, attitudes toward whole grains, vegetable and fruit consumption, participation in learning about food, nutrition and cooking, confidence in engaging in food-related activities, engagement in food-related sustainability practices, and demographics.[47,93,94] We will analyze I-EAT derived outcome data and compare the differences at end point between the intervention and control student data.

Further Quantitative Analyses

Analyses of plate-waste data and survey data will be conducted using the intention-to-treat principle [96]. To assess the effect of the intervention, we will use mixed-effect models using time of measurement (baseline or end point), group (intervention or control), and an interaction between time and group as fixed effects (base model). The neighborhood of residence (proxy for SES) will be used to determine whether SES influences the response to the intervention. To account for clustering related to repeated measures and because of sampling of students within classes and schools, variables representing participants and schools will be included as random effects in all models. Additional models will account for potentially confounding variables identified using directed acyclic graphs for each outcome [97,98]. Directed acyclic graphs are used to identify potential confounders using prespecified conceptual diagrams and testing these using the data to increase the precision of estimates and causal paths based on regression models. Analyses will be conducted using the MIXED procedure in SAS version 9.4 (SAS Institute, Inc).

Phase 3: Qualitative Data Collection and Analysis

RQ1: What are the benefits and challenges faced in establishing and administering a universal, curriculum-integrated healthy school lunch program?

RQ4: What aspects of curriculum integration show promise in enhancing food-related learning?

We will collect qualitative data from the 2 intervention schools. In the case study research, the investigator explores a bounded system or case (a school) over time through detailed data collection, drawing on multiple sources of information [99,100]. We have already conducted preintervention research in the intervention schools examining the school food environment using a tool called the School Food Environment Assessment Tool (SF-EAT) [101]. SF-EAT assesses the integration of healthy and sustainable food strategies in the school food environment, including food availability, food preparation facilities, gardening, composting, integration of food issues into the curriculum, and availability of healthy and environmentally sustainable food [101]. The administration of the SF-EAT tool was complemented with key informant interviews on barriers and facilitators for adopting the curriculum-integrated lunch program.

We will use semiparticipant observation and key informant interviews with school staff to evaluate the process of implementing the curriculum-integrated school lunch programs in the 2 intervention schools. We will study 3-5 individual classrooms in different grades to detail the aspects of each case. Observation will occur during (1) meetings when school staff are planning for the establishment of the school lunch program; (2) meetings when school staff are discussing curricular integration; (3) during lunch preparation, service, and clean-up; (4) when children are involved in preparation; and (5) during other curriculum integration activities such as during lessons involving growing vegetables. Observations will occur at minimum for 1 school day each month in each school and at school staff meetings as needed during the intervention period, with key informant interviews occurring throughout. Observations will be recorded using voice memos and field notebooks, which will be transcribed or detailed upon leaving the school at the end of the day. We will focus our data collection on how the intervention is being carried out, including challenges experienced and its fidelity to the original intervention design. We will interview caregivers on their perceptions of the program and behavioral changes they identify, including caregivers of children who have never participated in a school food program and those who have, across grades.

The qualitative data will document how schools establish a universal lunch and parent perceptions of the program. Our observations and interview questions will focus on the perceived benefits and challenges of establishing and administering a universal, curriculum-integrated healthy school lunch program and on the aspects of curriculum integration that appear to show promise in terms of enhancing food-related learning. The cases will inform the establishment of programs on a larger scale and in other contexts.

Interviews will be audio-recorded, transcribed verbatim, and analyzed using NVivo software (QSR International) for coding and theme development. Semiparticipant observation data will be recorded as field notes during observation as well as immediately after. Qualitative data will be analyzed initially in an open coding process to allow for emerging themes, followed by analysis using a priori generated code lists derived from the literature and our RQs. Our analytical approach will build concepts and themes inductively, testing and refining them with participants [102]. This hybrid inductive and deductive thematic analysis has been described by Fereday and Muir-Cochrane [103]. A regular debriefing with the research team and key school informants will assist in the refinement of concepts and themes. These steps will strengthen the credibility and dependability of the results [104,105]. Our contextualized interpretation and meaning making with stakeholders is consistent with Moss and Dahlberg [106] for research in educational contexts.

Phase 5: Final Analysis and Dissemination

We will enter, clean, and analyze postintervention data. This phase will include end-of-study knowledge translation (KT), although because of the existing collaborative relationship between the academic and nonacademic partners, KT will be ongoing throughout the entire study. Although this study is about filling gaps in the academic literature, it is also about ensuring practice relevance. Everything from conceiving the study to the development of RQs and practices has been and will be conducted closely with the school division, the CHSF, and other partners.

We have experience with integrated community-university KT strategies, which have generated practice and policy change [107-110], and we will apply what we have learned [111,112]. The inclusion of knowledge users or decision makers as members of the research team will facilitate evidence-informed decision-making and integrated knowledge transfer and exchange. This collaborative approach informs and directs our research and sharing of results and other outputs and is consistent with the Canadian Institutes of Health Research Guidelines for Research with Aboriginal People [113]. Although the focus of this research is not Indigenous people, we believe that these guidelines are relevant for all community-based research. We will work closely with our partners to conduct KT as needed and requested. Materials will be developed and designed with the goal of their use in future programming.

Results

This study was funded in April 2020, but because of the COVID-19 pandemic, data collection did not begin until May 2021. The intervention will begin in September 2021 and end in June 2023, with end point data collection occurring in May and June 2023. The case study research will begin in September 2021 and will be ongoing for the duration of the intervention.

Discussion

Principal Findings

In real-world settings, there are a number of potential challenges to this research, some we can anticipate now and some we will have to address as they come up. Fortunately, our team has a wealth of experience conducting research with children and school staff in the school environment. First, the research team is also an intervention team. As we are piloting a type of universal, curriculum-integrated intervention that is quite innovative, we do not think that operating separately would be either feasible or appropriate. Part of the strength of this research is the collaboration, and we will draw on this with the intention

that future research, once the intervention has benefited from this intensive study, will be conducted separately from the intervention.

We have already encountered the challenge of the COVID-19 pandemic. This project was funded in April 2020; however, because of school closures between March and June 2020, and the uncertainty of opening schools during a pandemic, the project was delayed by a year. Baseline data were collected in May and June of 2021. The intervention will begin in September 2021 with the new school year, but as of July 2021, we do not know what new challenges will exist with case study data collection because of the pandemic. We will need to adapt our protocols to whatever public health measures are in place over the 2 intervention school years.

We may encounter challenges with curriculum integration with teachers and other school staff. To minimize this, we have developed an intervention and research with the school division and have already been collecting baseline data in the intervention schools on current practices and needs. We have practiced limited family and teacher engagement (due to the COVID-19 pandemic) within the schools and will adapt as needed to ensure that both families and teachers continue to participate.

Next, although plate-waste studies are considered to be the best approach available for collecting nutrition data, there are limitations to conducting them in school settings. At baseline, weighing and photographing the foods brought from home before anything has been eaten at lunchtime and then again after is relatively straightforward in our considerable experience, but that would not capture any food shared between child participants nor food eaten before and after. It is also difficult to capture anything eaten outside of the lunch program as plate-waste data collection must occur before and after eating lunch only. This may mean that we slightly underrepresent what is eaten at school. We will test our method by comparing observations conducted during the case study with the plate-waste data at both the baseline and at the end point.

There are limitations to what we can infer from the measurement of KAP, but this is the most appropriate approach for a study at this stage. We are not measuring aspects of health status beyond nutritional outcomes. We are also collecting only interview data on the perceptions of the program from parents. We have limited our study in this way to keep it feasible but are working on efforts to examine additional aspects of health.

Conclusions

Numerous national organizations are calling for a Canadian school food program [52,114]. Up until now, hundreds of ad hoc programs have been operating across the country. Although they contribute to the health of participating children, a national program has the potential to support the health and learning of all Canadian children. The opportunity we have is to systematically and comprehensively study a curriculum-integrated school lunch program without precedent. We have assembled a very strong team and a supportive research environment to address complex issues, apply innovative approaches, and translate our research findings into action.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Scientific officer notes.
[PDF File (Adobe PDF File), 6 KB - resprot_v10i9e30899_app1.pdf]

Multimedia Appendix 2
Notice of decision.
[PDF File (Adobe PDF File), 451 KB - resprot_v10i9e30899_app2.pdf]

Multimedia Appendix 3
Ranking and funding decision.
[PDF File (Adobe PDF File), 6 KB - resprot_v10i9e30899_app3.pdf]

Multimedia Appendix 4
Complete reviews.
[PDF File (Adobe PDF File), 34 KB - resprot_v10i9e30899_app4.pdf]

References

1. Canada's Food Guide. Health Canada. 2019. URL: https://food-guide.canada.ca/en/ [accessed 2019-02-06]
2. Budget 2019. Government of Canada, Ottawa. URL: https://www.budget.gc.ca/2019/docs/plan/chap-04-en.html#Introducing-a-Food-Policy-for-Canada [accessed 2019-08-21]
3. Engler-Stringer R. The domestic foodscapes of young low-income women in Montreal: cooking practices in the context of an increasingly processed food supply. Health Educ Behav 2010 Apr;37(2):211-226. [doi: 10.1177/1090198109339453] [Medline: 19690290]

4. Daniel C. Economic constraints on taste formation and the true cost of healthy eating. Soc Sci Med 2016 Jan;148:34-41 [FREE Full text] [doi: 10.1016/j.socscimed.2015.11.025] [Medline: 26650928]
5. Slater J, Sevenhuysen G, Edginton B, O'neil J. 'Trying to make it all come together': structuration and employed mothers' experience of family food provisioning in Canada. Health Promot Int 2012 Sep;27(3):405-415. [doi: 10.1093/heapro/dar037] [Medline: 21693474]
6. Bowen S, Elliott S, Brenton J. The joy of cooking? Contexts 2014 Aug 22;13(3):20-25. [doi: 10.1177/1536504214545755]
7. Bowen S, Brenton J, Elliott S. Pressure Cooker: Why Home Cooking Won't Solve Our Problems and What We Can Do About It. New York: Oxford University Press; 2019.
8. Solyen C. New Canada's Food Guide is a giant step forward, dietitians say. Montreal Gazette. 2019 Jan 22. URL: https://montrealgazette.com/health/new-canadas-food-guide-is-a-giant-step-forward-dietitians-say [accessed 2021-08-05]
9. No authors listed. Guidelines for school health programs to promote lifelong healthy eating. Centers for Disease Control and Prevention. MMWR Recomm Rep 1996 Jun 14;45(RR-9):1-41 [FREE Full text] [Medline: 8637498]
10. Abood DA, Black DR, Coster DC. Evaluation of a school-based teen obesity prevention minimal intervention. J Nutr Educ Behav 2008;40(3):168-174. [doi: 10.1016/j.jneb.2007.02.009] [Medline: 18457785]
11. Adamo KB, Goldfield GS, Colapinto CK, Grattan KP, Harvey A, Barrowman N. Evaluating a fruit and vegetable program: in eastern Ontario schools. Can J Diet Pract Res 2013;74(4):167-174. [doi: 10.3148/74.4.2013.167] [Medline: 24472164]
12. Adams MA, Pelletier RL, Zive MM, Sallis JF. Salad bars and fruit and vegetable consumption in elementary schools: a plate waste study. J Am Diet Assoc 2005 Nov;105(11):1789-1792. [doi: 10.1016/j.jada.2005.08.013] [Medline: 16256765]
13. Bartrina J, Pérez-Rodrigo C. Resources for a healthy diet: school meals. Br J Nutr 2006 Aug;96 Suppl 1:78-81. [doi: 10.1079/bjn20061705] [Medline: 16923256]
14. Tugault-Lafleur CN, Black JL, Barr SI. Examining school-day dietary intakes among Canadian children. Appl Physiol Nutr Metab 2017 Oct;42(10):1064-1072 [FREE Full text] [doi: 10.1139/apnm-2017-0125] [Medline: 28831845]
15. Koç M, Bas J. Canada's action plan for food security: the interactions between civil society and the state to advance food security in Canada. In: Health and Sustainability in the Canadian Food System: Advocacy and Opportunity for Civil Society. Vancouver: UBC Press; 2012:173-203.
16. Oostindjer M, Aschemann-Witzel J, Wang Q, Skuland SE, Egelandsdal B, Amdam GV, et al. Are school meals a viable and sustainable tool to improve the healthiness and sustainability of children´s diet and food consumption? A cross-national comparative perspective. Crit Rev Food Sci Nutr 2017 Dec 12;57(18):3942-3958. [doi: 10.1080/10408398.2016.1197180] [Medline: 27712088]
17. Ismail MR, Seabrook JA, Gilliland JA. Outcome evaluation of fruits and vegetables distribution interventions in schools: a systematic review and meta-analysis. Public Health Nutr 2021 Apr 19:1-13. [doi: 10.1017/S1368980021001683] [Medline: 33866997]
18. Mcisaac JD, Read K, Williams PL, Raine KD, Veugelers PJ, Kirk SF. Reproducing or reducing inequity? Considerations for school food programs. Can J Diet Pract Res 2018 Mar 01;79(1):18-22. [doi: 10.3148/cjdpr-2017-029] [Medline: 28971692]
19. Colley P, Myer B, Seabrook J, Gilliland J. The impact of Canadian school food programs on children's nutrition and health: a systematic review. Can J Diet Pract Res 2019 Jun 01;80(2):79-86. [doi: 10.3148/cjdpr-2018-037] [Medline: 30430855]
20. Everitt T, Engler-Stringer R, Martin W. Determining promising practices for Canadian school food programs: a scoping review. J Hunger Environ Nutr 2020 Sep 18:1-20. [doi: 10.1080/19320248.2020.1823925]
21. Hernandez K, Engler-Stringer R, Kirk S, Wittman H, McNicholl S. The case for a Canadian national school food program. Can Food Stud 2018 Sep 30;5(3):208-229. [doi: 10.15353/cfs-rcea.v5i3.260]
22. Raine K, McIntyre L, Dayle JB. The failure of charitable school- and community-based nutrition programmes to feed hungry children. Crit Public Health 2003 Jun;13(2):155-169. [doi: 10.1080/0958159031000097634]
23. Ismail MR, Seabrook JA, Gilliland JA. Process evaluation of fruit and vegetables distribution interventions in school-based settings: a systematic review. Prev Med Rep 2020 Dec 7;21:101281-10128- [FREE Full text] [doi: 10.1016/j.pmedr.2020.101281] [Medline: 33364152]
24. Rojas A, Black J, Orrego E, Chapman G, Valley W. Can Food Studies 2017 Dec 22;4(2):25-46 [FREE Full text] [doi: 10.15353/cfs-rcea.v4i2.225]
25. Powell LJ, Wittman H. Farm to school in British Columbia: mobilizing food literacy for food sovereignty. Agric Human Values 2017 Jul 18;35:193-206. [doi: 10.1007/s10460-017-9815-7]
26. Oostindjer M, Aschemann-Witzel J, Wang Q, Skuland SE, Egelandsdal B, Amdam GV, et al. Are school meals a viable and sustainable tool to improve the healthiness and sustainability of children´s diet and food consumption? A cross-national comparative perspective. Crit Rev Food Sci Nutr 2017 Dec 12;57(18):3942-3958. [doi: 10.1080/10408398.2016.1197180] [Medline: 27712088]
27. Kristjansson EA, Robinson V, Petticrew M, MacDonald B, Krasevec J, Janzen L, et al. School feeding for improving the physical and psychosocial health of disadvantaged elementary school children. Cochrane Database Syst Rev 2007 Jan 24(1):CD004676-CD00467-. [doi: 10.1002/14651858.CD004676.pub2] [Medline: 17253518]

28. Van Cauwenberghe E, Maes L, Spittaels H, van Lenthe FJ, Brug J, Oppert J, et al. Effectiveness of school-based interventions in Europe to promote healthy nutrition in children and adolescents: systematic review of published and 'grey' literature. Br J Nutr 2010 Mar;103(6):781-797. [doi: 10.1017/S0007114509993370] [Medline: 20070915]
29. Joshi A, Azuma AM, Feenstra G. Do farm-to-school programs make a difference? Findings and future research needs. J Hunger Environ Nutr 2008 Oct 11;3(2-3):229-246. [doi: 10.1080/19320240802244025]
30. Yoder AB, Liebhart JL, McCarty DJ, Meinen A, Schoeller D, Vargas C, et al. Farm to elementary school programming increases access to fruits and vegetables and increases their consumption among those with low intake. J Nutr Educ Behav 2014;46(5):341-349. [doi: 10.1016/j.jneb.2014.04.297] [Medline: 24953435]
31. Evans C, Cleghorn C, Greenwood D, Cade J. A comparison of British school meals and packed lunches from 1990 to 2007: meta-analysis by lunch type. Br J Nutr 2010 Aug;104(4):474-487. [doi: 10.1017/S0007114510001601] [Medline: 20500928]
32. Caruso ML, Cullen KW. Quality and cost of student lunches brought from home. JAMA Pediatr 2015 Jan;169(1):86-90. [doi: 10.1001/jamapediatrics.2014.2220] [Medline: 25419622]
33. Neilson LJ, Macaskill LA, Luk JM, Sharma N, Killip SM, Salvadori MI, et al. Students' food intake from home-packed lunches in the traditional versus balanced school day. Can J Diet Pract Res 2017 Mar;78(1):3-10 [FREE Full text] [doi: 10.3148/cjdpr-2016-024] [Medline: 27779893]
34. Hur I, Burgess-Champoux T, Reicks M. Higher quality intake from school lunch meals compared with bagged lunches. Infant Child Adolesc Nutr 2011 Mar 29;3(2):70-75. [doi: 10.1177/1941406411399124]
35. Taylor JP, Hernandez KJ, Caiger JM, Giberson D, MacLellan D, Sweeney-Nixon M, et al. Nutritional quality of children's school lunches: differences according to food source. Public Health Nutr 2012 Dec;15(12):2259-2264. [doi: 10.1017/S1368980012000699] [Medline: 22463765]
36. Hubbard KL, Must A, Eliasziw M, Folta SC, Goldberg J. What's in children's backpacks: foods brought from home. J Acad Nutr Diet 2014 Sep;114(9):1424-1431 [FREE Full text] [doi: 10.1016/j.jand.2014.05.010] [Medline: 25037557]
37. Johnston CA, Moreno JP, El-Mubasher A, Woehler D. School lunches and lunches brought from home: a comparative analysis. Child Obes 2012 Aug;8(4):364-368. [doi: 10.1089/chi.2012.0012] [Medline: 22867076]
38. Stevens L, Nelson M. The contribution of school meals and packed lunch to food consumption and nutrient intakes in UK primary school children from a low income population. J Hum Nutr Diet 2011 Jun;24(3):223-232. [doi: 10.1111/j.1365-277X.2010.01148.x] [Medline: 21332839]
39. Black JL, Billette J. Do Canadians meet Canada's Food Guide's recommendations for fruits and vegetables? Appl Physiol Nutr Metab 2013 Mar;38(3):234-242 [FREE Full text] [doi: 10.1139/apnm-2012-0166] [Medline: 23537013]
40. Do Canadian children meet their nutrient requirements through food intake alone? In: Health Canada. Ottawa: Government of Canada; 2012.
41. Moubarac J, Batal M, Louzada ML, Steele EM, Monteiro CA. Consumption of ultra-processed foods predicts diet quality in Canada. Appetite 2017 Jan 01;108:512-520. [doi: 10.1016/j.appet.2016.11.006] [Medline: 27825941]
42. Moubarac J, Batal M, Martins AP, Claro R, Levy RB, Cannon G, et al. Processed and ultra-processed food products: consumption trends in Canada from 1938 to 2011. Can J Diet Pract Res 2014;75(1):15-21. [doi: 10.3148/75.1.2014.15] [Medline: 24606955]
43. Griggs TL, Casper WJ, Eby LT. Work, family and community support as predictors of work–family conflict: a study of low-income workers. J Vocat Behav 2013 Feb;82(1):59-68. [doi: 10.1016/j.jvb.2012.11.006]
44. Bauer KW, Hearst MO, Escoto K, Berge JM, Neumark-Sztainer D. Parental employment and work-family stress: associations with family food environments. Soc Sci Med 2012 Aug;75(3):496-504 [FREE Full text] [doi: 10.1016/j.socscimed.2012.03.026] [Medline: 22591825]
45. Slater J, Sevenhuysen G, Edginton B, O'neil J. 'Trying to make it all come together': structuration and employed mothers' experience of family food provisioning in Canada. Health Promotion International 2011 Jun 21;27(3):405-415. [doi: 10.1093/heapro/dar037]
46. Tugault-Lafleur CN, Black JL. Lunch on school days in Canada: examining contributions to nutrient and food group intake and differences across eating locations. J Acad Nutr Diet 2020 Sep;120(9):1484-1497 [FREE Full text] [doi: 10.1016/j.jand.2020.01.011] [Medline: 32507319]
47. Ahmadi N, Black JL, Velazquez CE, Chapman GE, Veenstra G. Associations between socio-economic status and school-day dietary intake in a sample of grade 5-8 students in Vancouver, Canada. Public Health Nutr 2015 Apr;18(5):764-773. [doi: 10.1017/S1368980014001499] [Medline: 25098190]
48. Longacre MR, Drake KM, Titus LJ, Peterson KE, Beach ML, Langeloh G, et al. School food reduces household income disparities in adolescents' frequency of fruit and vegetable intake. Prev Med 2014 Dec;69:202-207 [FREE Full text] [doi: 10.1016/j.ypmed.2014.10.008] [Medline: 25456807]
49. Mcisaac JD, Read K, Williams PL, Raine KD, Veugelers PJ, Kirk SF. Reproducing or Reducing Inequity? Considerations for School Food Programs. Canadian Journal of Dietetic Practice and Research 2018 Mar;79(1):18-22. [doi: 10.3148/cjdpr-2017-029]
50. Everitt T, Engler-Stringer R, Martin W, Vatanparast H. Comparing diet quality of school meals versus food brought from home. Can J Diet Pract Res 2020 Dec 01;81(4):179-185. [doi: 10.3148/cjdpr-2020-013] [Medline: 32495636]

51. Biloski G. Why teachers are telling parents what to feed their children, even when it isn't their responsibility. National Post. 2016 Nov 10. URL: https://nationalpost.com/life/food/why-teachers-are-telling-parents-what-to-feed-their-children-even-when-it-isnt-their-responsibility [accessed 2021-08-05]
52. School-based meal programs need to be available to all Canadian children. Conference Board of Canada. 2013. URL: https://www.prnewswire.com/news-releases/school-based-meal-programs-need-to-be-available-to-all-canadian-children-512843191.html [accessed 2021-08-18]
53. Greaves E, Crawford C, Dearden L, Kitchen S, Tanner E, Brown V, et al. Evaluation of the free school meals pilot: impact report. Department for Education. 2012. URL: https://research-information.bris.ac.uk/en/publications/evaluation-of-the-free-school-meals-pilot-impact-report [accessed 2021-08-18]
54. Sasson I. Trends in life expectancy and lifespan variation by educational attainment: United States, 1990-2010. Demography 2016 Apr;53(2):269-293 [FREE Full text] [doi: 10.1007/s13524-015-0453-7] [Medline: 26813781]
55. Meyers AF, Sampson AE, Weitzman M, Rogers BL, Kayne H. School breakfast program and school performance. Am J Dis Child 1989 Oct;143(10):1234-1239. [doi: 10.1001/archpedi.1989.02150220142035] [Medline: 2801668]
56. Alaimo K, Olson CM, Frongillo EA. Food insufficiency and American school-aged children's cognitive, academic, and psychosocial development. Pediatrics 2001 Jul;108(1):44-53. [Medline: 11433053]
57. Symons C, Cinelli B, James T, Groff P. Bridging student health risks and academic achievement through comprehensive school health programs. J Sch Health 1997 Aug;67(6):220-227. [doi: 10.1111/j.1746-1561.1997.tb06309.x] [Medline: 9285867]
58. Weitzman M, Klerman LV, Lamb G, Menary J, Alpert JJ. School absence: a problem for the pediatrician. Pediatrics 1982 Jun;69(6):739-746. [Medline: 7200604]
59. Pollitt E, Gersovitz M, Gargiulo M. Educational benefits of the United States school feeding program: a critical review of the literature. Am J Public Health 1978 May;68(5):477-481. [doi: 10.2105/ajph.68.5.477] [Medline: 347957]
60. Florence MD, Asbridge M, Veugelers PJ. Diet quality and academic performance. J Sch Health 2008 Apr;78(4):209-215. [doi: 10.1111/j.1746-1561.2008.00288.x] [Medline: 18336680]
61. Murphy JM, Pagano ME, Nachmani J, Sperling P, Kane S, Kleinman RE. The relationship of school breakfast to psychosocial and academic functioning: cross-sectional and longitudinal observations in an inner-city school sample. Arch Pediatr Adolesc Med 1998 Sep;152(9):899-907. [doi: 10.1001/archpedi.152.9.899] [Medline: 9743037]
62. Hollar D, Lombardo M, Lopez-Mitnik G, Hollar TL, Almon M, Agatston AS, et al. Effective multi-level, multi-sector, school-based obesity prevention programming improves weight, blood pressure, and academic performance, especially among low-income, minority children. J Health Care Poor Underserved 2010 May;21(2 Suppl):93-108. [doi: 10.1353/hpu.0.0304] [Medline: 20453379]
63. Kleinman R, Hall S, Green H, Korzec-Ramirez D, Patton K, Pagano M, et al. Diet, breakfast, and academic performance in children. Ann Nutr Metab 2002;46 Suppl 1(0 1):24-30 [FREE Full text] [doi: 10.1159/000066399] [Medline: 12428078]
64. Turner L, Chaloupka FJ. Continued promise of school breakfast programs for improving academic outcomes : breakfast is still the most important meal of the day. JAMA Pediatr 2015 Jan;169(1):13-14. [doi: 10.1001/jamapediatrics.2014.2409] [Medline: 25419963]
65. Anderson M, Gallagher J, Ritchie E. School lunch quality and academic performance. Natl Bur Econ Res Working Paper Series 2017 Mar:w23218. [doi: 10.3386/w23218]
66. Larson N, Story M. A review of environmental influences on food choices. Ann Behav Med 2009 Dec;38 Suppl 1:56-73. [doi: 10.1007/s12160-009-9120-9] [Medline: 19802648]
67. Moffat T, Thrasher D. School meal programs and their potential to operate as school-based obesity prevention and nutrition interventions: case studies from France and Japan. Crit Public Health 2014 Sep 12;26(2):133-146. [doi: 10.1080/09581596.2014.957654]
68. Lee A, McLeod-Kilmurray H, Chalifour N. Canada's Food Guide update needs to address sustainability. Policy Options. 2017 Jan 24. URL: https://policyoptions.irpp.org/magazines/january-2017/canadas-food-guide-update-needs-to-address-sustainability/ [accessed 2021-08-05]
69. Cullen T, Hatch J, Martin W, Higgins JW, Sheppard R. Food literacy: definition and framework for action. Can J Diet Pract Res 2015 Sep;76(3):140-145. [doi: 10.3148/cjdpr-2015-010] [Medline: 26280794]
70. Suarez-Balcazar Y, Kouba J, Jones LM, Lukyanova VV. A university--school collaboration to enhance healthy choices among children. J Prev Interv Community 2014;42(2):140-151. [doi: 10.1080/10852352.2014.881193] [Medline: 24702664]
71. Stone MK. Rethinking school lunch: education for sustainability in practice. Can J Environ Educ 2007;12(1):19-32 [FREE Full text] [doi: 10.4324/9781351171601-3]
72. Weaver-Hightower MB. Why education researchers should take school food seriously. Educ Res 2011 Jan 01;40(1):15-21. [doi: 10.3102/0013189x10397043]
73. Morris JL, Neustadter A, Zidenberg-Cherr S. First-grade gardeners more likely to taste vegetables. Cal Ag 2001;55(1):43-46. [doi: 10.3733/ca.v055n01p43]
74. Dohle S, Rall S, Siegrist M. I cooked it myself: preparing food increases liking and consumption. Food Qual Prefer 2014 Apr;33:14-16. [doi: 10.1016/j.foodqual.2013.11.001]

75. Greenhalgh T, Kristjansson E, Robinson V. Realist review to understand the efficacy of school feeding programmes. Br Med J 2007 Oct 27;335(7625):858-861 [FREE Full text] [doi: 10.1136/bmj.39359.525174.AD] [Medline: 17954518]
76. Jones M, Dailami N, Weitkamp E, Salmon D, Kimberlee R, Morley A, et al. Food sustainability education as a route to healthier eating: evaluation of a multi-component school programme in English primary schools. Health Educ Res 2012 Jun;27(3):448-458. [doi: 10.1093/her/cys016] [Medline: 22355199]
77. Benn J, Carlsson M. Learning through school meals? Appetite 2014 Jul;78:23-31. [doi: 10.1016/j.appet.2014.03.008] [Medline: 24656948]
78. Tanaka N, Miyoshi M. School lunch program for health promotion among children in Japan. Asia Pac J Clin Nutr 2012;21(1):155-158 [FREE Full text] [Medline: 22374573]
79. Kubik MY, Lytle LA, Hannan PJ, Perry CL, Story M. The association of the school food environment with dietary behaviors of young adolescents. Am J Public Health 2003 Jul;93(7):1168-1173. [doi: 10.2105/ajph.93.7.1168] [Medline: 12835204]
80. Breuer E, Lee L, De Silva M, Lund C. Using theory of change to design and evaluate public health interventions: a systematic review. Implement Sci 2016 May 06;11:63-6- [FREE Full text] [doi: 10.1186/s13012-016-0422-6] [Medline: 27153985]
81. Corter C, Pelletier J. Schools as integrated service hubs for young children and families: policy implications of the Toronto First duty project. Int Child Care Educ Policy 2015 Feb 20;4(2):45-54. [doi: 10.1007/2288-6729-4-2-45]
82. Woolf SH, Purnell JQ, Simon SM, Zimmerman EB, Camberos GJ, Haley A, et al. Translating evidence into population health improvement: strategies and barriers. Annu Rev Public Health 2015 Mar 18;36:463-482. [doi: 10.1146/annurev-publhealth-082214-110901] [Medline: 25581146]
83. Crammond B, Carey G. Policy change for the social determinants of health: the strange irrelevance of social epidemiology. Evid Policy 2017 May 19;13(2):365-374. [doi: 10.1332/174426416x14538920677201]
84. City of Saskatoon neighbourhood profiles. City of Saskatoon Planning and Development. 2019 Dec. URL: https://www.saskatoon.ca/sites/default/files/documents/community-services/planning-development/research/neighbourhood-profiles/neighbourhood_profiles_2019.pdf [accessed 2021-08-05]
85. Blakeway SF, Knickrehm ME. Nutrition education in the Little Rock school lunch program. J Am Diet Assoc 1978 Apr;72(4):389-391. [Medline: 565371]
86. Lee HS, Lee KE, Shanklin CW. Elementary students' food consumption at lunch does not meet recommended dietary allowance for energy, iron, and vitamin A. J Am Diet Assoc 2001 Sep;101(9):1060-1063. [doi: 10.1016/S0002-8223(01)00261-9] [Medline: 11573762]
87. Whatley JE, Donnelly JE, Jacobsen DJ, Hill JO, Carlson MK. Energy and macronutrient consumption of elementary school children served modified lower fat and sodium lunches or standard higher fat and sodium lunches. J Am Coll Nutr 1996 Dec;15(6):602-607. [doi: 10.1080/07315724.1996.10718636] [Medline: 8951738]
88. Jacko C, Dellava J, Ensle K, Hoffman DJ. Use of the plate-waste method to measure food intake in children. J Ext 2007 Dec;45(6) [FREE Full text]
89. Dhingra P, Sazawa S, Menon V, Dhingra U, Black R. Validation of visual estimation of portion size consumed as a method for estimating food intake by young Indian children. J Health Popul Nutr 2007 Mar;25(1):112-115 [FREE Full text] [Medline: 17615912]
90. Measuring food intake: an overview. In: Handbook of Assessment Methods for Eating Behaviors and Weight-Related Problems. Thousand Oaks: Sage Publication; 1995:215-240.
91. Williamson DA, Allen HR, Martin PD, Alfonso AJ, Gerald B, Hunt A. Comparison of digital photography to weighed and visual estimation of portion sizes. J Am Diet Assoc 2003 Sep;103(9):1139-1145. [doi: 10.1016/s0002-8223(03)00974-x] [Medline: 12963941]
92. Barr SI, Vatanparast H, Smith J. Breakfast in Canada: prevalence of consumption, contribution to nutrient and food group intakes, and variability across tertiles of daily diet quality. A study from the international breakfast research initiative. Nutrients 2018 Jul 27;10(8):985-98- [FREE Full text] [doi: 10.3390/nu10080985] [Medline: 30060534]
93. Velazquez CE, Black JL, Billette J, Ahmadi N, Chapman GE. A comparison of dietary practices at or en route to school between elementary and secondary school students in Vancouver, Canada. J Acad Nutr Diet 2015 Aug;115(8):1308-1317. [doi: 10.1016/j.jand.2015.02.030] [Medline: 25935568]
94. Stephens TA, Black JL, Chapman GE, Velazquez CE, Rojas A. Participation in school food and nutrition activities among grade 6-8 students in Vancouver. Can J Diet Pract Res 2016 Sep;77(3):148-153. [doi: 10.3148/cjdpr-2016-003] [Medline: 27182726]
95. Ahmadi N. Examining the Associations Between Socioeconomic Status and School Day Dietary Intake Among Vancouver Children and Adolescents. Vancouver: University of British Columbia; 2013.
96. Gupta SK. Intention-to-treat concept: a review. Perspect Clin Res 2011 Jul;2(3):109-112 [FREE Full text] [doi: 10.4103/2229-3485.83221] [Medline: 21897887]
97. Fleischer NL, Diez Roux AV. Using directed acyclic graphs to guide analyses of neighbourhood health effects: an introduction. J Epidemiol Community Health 2008 Sep;62(9):842-846. [doi: 10.1136/jech.2007.067371] [Medline: 18701738]
98. Mitchell-Box K, Braun KL. Fathers' thoughts on breastfeeding and implications for a theory-based intervention. J Obstet Gynecol Neonatal Nurs 2012;41(6):41-50. [doi: 10.1111/j.1552-6909.2012.01399.x] [Medline: 22861175]
99. Yin R. Case Study Research: Design and Methods. 5th edition. Thousand Oaks, CA: Sage Publications; 2014.

100. Creswell JW. Qualitative Inquiry and Research Design: Choosing Among Five Approaches. Thousand Oaks, CA: Sage Publications; 2007.
101. Black JL, Velazquez CE, Ahmadi N, Chapman GE, Carten S, Edward J, et al. Sustainability and public health nutrition at school: assessing the integration of healthy and environmentally sustainable food initiatives in Vancouver schools. Public Health Nutr 2015 Sep;18(13):2379-2391. [doi: 10.1017/S1368980015000531] [Medline: 25771940]
102. Rubin H, Rubin I. Qualitative Interviewing: The Art of Hearing Data. 2nd Edition. Thousand Oaks, CA: Sage Publications; 2005.
103. Fereday J, Muir-Cochrane E. Demonstrating rigor using thematic analysis: a hybrid approach of inductive and deductive coding and theme development. Int J Qual Methods 2006 Mar 1;5(1):80-92. [doi: 10.1177/160940690600500107]
104. Lincoln Y, Guba E. Naturalistic Inquiry. Thousand Oaks, CA: Sage Publications; Apr 1985.
105. Baxter J, Eyles J. Evaluating qualitative research in social geography: establishing 'rigour' in interview analysis. Trans Inst Br Geog 1997 Dec;22(4):505-525. [doi: 10.1111/j.0020-2754.1997.00505.x]
106. Moss P, Dahlberg G, Pence A. Beyond Quality in Early Childhood Education and Care? Languages of Evaluation. London: Routledge; 2013.
107. Muhajarine N, Ng J, Bowen A, Cushon J, Johnson S. Understanding the impact of the Canada Prenatal Nutrition Program: a quantitative evaluation. Can J Public Health 2012 Mar 29;103(7 Suppl 1):26-31 [FREE Full text] [Medline: 23618045]
108. Muhajarine N, Labonte R, Winquist BD. The Canadian Index of Wellbeing: key findings from the healthy populations domain. Can J Public Health 2012 Jul 18;103(5):342-347 [FREE Full text] [doi: 10.1007/BF03404438] [Medline: 23617985]
109. Muhajarine N, Fortin P, Smith F, Majnemer A. Practices and plans for knowledge translation at NeuroDevNet. Semin Pediatr Neurol 2011 Mar;18(1):26-30. [doi: 10.1016/j.spen.2011.02.005] [Medline: 21575838]
110. McIsaac JD, Penney TL, Storey KE, Sigfridson L, Cunningham J, Kuhle S, et al. Integrated knowledge translation in population health intervention research: a case study of implementation and outcomes from a school-based project. Health Res Policy Syst 2018 Aug 02;16(1):72-7- [FREE Full text] [doi: 10.1186/s12961-018-0351-8] [Medline: 30068359]
111. Macqueen SF. Strengthening ties between researchers and decision-makers in person and online: The Saskatchewan Knowledge to Action Network for Early Childhood Development. Saskatchewan Population Health and Evaluation Research Unit Knowledge Translation Casebook(peer-reviewed) 2021 Aug 05:2011.
112. Muhajarine N, Fortin P, Macqueen Smith F, Majnemer A. Practices and Plans for Knowledge Translation at NeuroDevNet. Seminars in Pediatric Neurology 2011 Mar;18(1):26-30. [doi: 10.1016/j.spen.2011.02.005]
113. CIHR Guidelines for Health Research Involving Aboriginal People. Ottawa, ON: Canadian Institutes of Health Research; 2007.
114. The coalition for healthy school food. Food Secure Canada. 2017. URL: https://www.healthyschoolfood.ca/ [accessed 2021-07-03]

Abbreviations

CFG: Canadian Food Guide
CHSF: Coalition for Healthy School Food
HEI: Healthy Eating Index
I-EAT: Individual Eating Assessment Tool
KAP: knowledge, attitudes, and practices
KT: knowledge translation
PHIR: population health intervention research
RQ: research question
SES: socioeconomic status
SF-EAT: School Food Environment Assessment Tool
SPSD: Saskatoon Public Schools Division

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Protocol

Longitudinal, Interdisciplinary Home Visits Versus Usual Care for Homebound People With Advanced Parkinson Disease: Protocol for a Controlled Trial

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Abstract

Background: The current understanding of advanced Parkinson disease (PD) and its treatment is largely based on data from outpatient visits. The most advanced and disabled individuals with PD are disconnected from both care and research. A previous pilot study among older, multimorbid patients with advanced PD demonstrated the feasibility of interdisciplinary home visits to reach the target population, improve care quality, and potentially avoid institutionalization.

Objective: The aim of this study protocol is to investigate whether interdisciplinary home visits can prevent a decline in quality of life of patients with PD and prevent worsening of caregiver strain. The protocol also explores whether program costs are offset by savings in health care utilization and institutionalization compared with usual care.

Methods: In this single-center, controlled trial, 65 patient-caregiver dyads affected by advanced PD (Hoehn and Yahr stages 3-5 and homebound) are recruited to receive quarterly interdisciplinary home visits over 1 year. The 1-year intervention is delivered by a nurse and a research coordinator, who travel to the home, and it is supported by a movement disorder specialist and social worker (both present by video). Each dyad is compared with age-, sex-, and Hoehn and Yahr stage–matched control dyads drawn from US participants in the longitudinal Parkinson's Outcome Project registry. The primary outcome measure is the change in patient quality of life between baseline and 1 year. Secondary outcome measures include changes in Hoehn and Yahr stage, caregiver strain, self-reported fall frequency, emergency room visits, hospital admissions, and time to institutionalization or death.

Intervention costs and changes in health care utilization will be analyzed in a budget impact analysis to explore the potential for model adaptation and dissemination.

Results: The protocol was funded in September 2017 and approved by the Rush Institutional Review Board in October 2017. Recruitment began in May 2018 and closed in November 2019 with 65 patient-caregiver dyads enrolled. All study visits have been completed, and analysis is underway.

Conclusions: To our knowledge, this is the first controlled trial to investigate the effects of interdisciplinary home visits among homebound individuals with advanced PD and their caregivers. This study also establishes a unique cohort of patients from whom we can study the natural course of advanced PD, its treatments, and unmet needs.

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KEYWORDS

home visits; telehealth, Parkinson disease; homebound; palliative care; quality of life; interdisciplinary care; caregiver; caregiver strain

Introduction

Background

Parkinson disease (PD) is the second most common neurodegenerative condition; however, a substantial proportion of patients with advanced PD are disconnected from clinicians and researchers [1,2]. Many individuals with PD become homebound because of the progressive motor and functional disabilities that their disease imposes. Other comorbidities, limitations, absence of a caregiver, distance from care, or a combination thereof also contribute to a growing number of homebound individuals with PD. Consequently, care becomes fragmented or absent, increasing the likelihood of poor outcomes, including medication errors and other complications [3-6]. Caregivers bear the burden of meeting the needs of these complex and often severely disabled patients. The resulting caregiver strain often leads to institutionalization, excess morbidity, and mortality [7-12].

Little is known about the natural progression of homebound individuals with PD or their caregivers. PD can be staged using the Hoehn and Yahr (HY) scale: HY 1 and 2 comprise mild unilateral and bilateral motor symptoms, respectively; HY 3 signifies moderate symptoms with balance impairment; advanced disease is indicated by HY 4, severe symptoms necessitating an assistive device to walk; or HY 5, which indicates a wheelchair or bedbound status. Our knowledge of advanced PD, treatment strategies, quality of life (QoL), and caregiver outcomes are based primarily on cohorts derived from outpatient clinics. The most advanced and disabled individuals, whose very disease creates tangible barriers to care, are often unable to leave their homes for any variety of necessary clinical visits or research opportunities [13]. An ongoing international observational study is investigating the course of advanced or late-stage parkinsonism [14]; however, this remains limited to individuals accessing outpatient care.

The substantial economic burden of PD has been well described, including a 2017 analysis reporting direct medical costs of US $25.4 billion and an additional US $26.5 billion in indirect costs, including unpaid caregiving time, time spent by the patient and caregivers in contact with services, and lost productivity [15]. However, few economic analyses have been sufficiently powered to examine the costs of care in advanced PD patients, who comprise at most 6%-10% of the largest population-based studies [16]. In a community-based UK PD cohort, direct costs were 184% higher for HY 4-5 patients than HY 1, and indirect costs were 31% higher [17]. In the multinational European Care of Late-Stage Parkinsonism study, in which 93.9% (214/228) of participants were stage HY 4-5, the mean annualized direct care costs were €35,980 (US $42,697.43), which were 166% to 384% higher than previously reported cohorts [16].

In response to other chronic, complex, and disabling conditions of older adults, home visits have re-emerged as a way to maintain continuity of care, avoid institutionalization, and improve QoL [18-21], with equivocal findings on cost-effectiveness depending on the health care system [22-24]. Although the travel, time, and labor costs of home visits exceed traditional outpatient visits, the opportunity to proactively identify previously undetected symptoms, signs, and safety risks may avert crises and acute health care utilization, offsetting or potentially saving costs. The majority of home visit models are interdisciplinary, incorporating primary care, nursing, and social work [19,25-30]. Two specialized home visit programs for PD have been described [31,32]; however, neither used interdisciplinary care, addressed caregiver burden, or defined the population served, the outcomes achieved, or programmatic costs.

In a pilot study, we demonstrated the feasibility of delivering comprehensive, expert, interdisciplinary care via home visits for homebound patients with advanced PD and related disorders [33]. In the initial cohort, 85 individuals with PD or related disorders received 272 home visits over 2 years throughout New York City by a traveling team of a movement disorder specialist, a nurse, and a social worker. Nearly 70% of enrolled patients were rated HY stage 4 or 5 at their first visit (severe symptoms requiring an assistive device to ambulate, or being wheelchair or bedbound, respectively), demonstrating the ability to reach and recruit the target population. Both the program satisfaction and retention exceeded 95%.

To better understand longitudinal changes in homebound individuals, we enrolled a subset of those 85 individuals

receiving clinical home visits in a 1-year prospective cohort study. Among the 85, we excluded 58 (68%) individuals for the following reasons: 11 (13%) had atypical parkinsonism, 7 (8%) were non–English-speaking, and 4 (19%) each who died, moved out of the catchment area, expressed no further need for home visits, or declined participation before the enrollment visit, respectively. Finally, we excluded 24 (28%) individuals because of either impaired decisional capacity (Mini-Mental State Examination [MMSE] <10 or nonverbal; 15/85, 18%), or potentially impaired decisional capacity with MMSE <20 and no caregiver to consent (5/85, 6%) or MMSE <20 and caregiver with significant health issues or at risk for caregiver loss (4/85, 5%). However, in the 27 eligible individuals with advanced PD consenting to four visits over 1 year, we found a marked worsening of the Unified Parkinson's Disease Rating Scale (UPDRS) total score after 1 year, without an accompanying decline in QoL [34]. Although our pilot results suggest that the presumed parallel decline and inextricable connection between PD severity and QoL may be disentangled, the study was limited by size, had restricted geographic diversity, and lacked a control group. To address sustainability and costs, we developed a hybrid approach with the in-home nurse connecting to the physician by video, and the social worker attending initial visits in-home and subsequent visits by video alongside the physician, creating a telehealth-enhanced home visit [35].

Objective

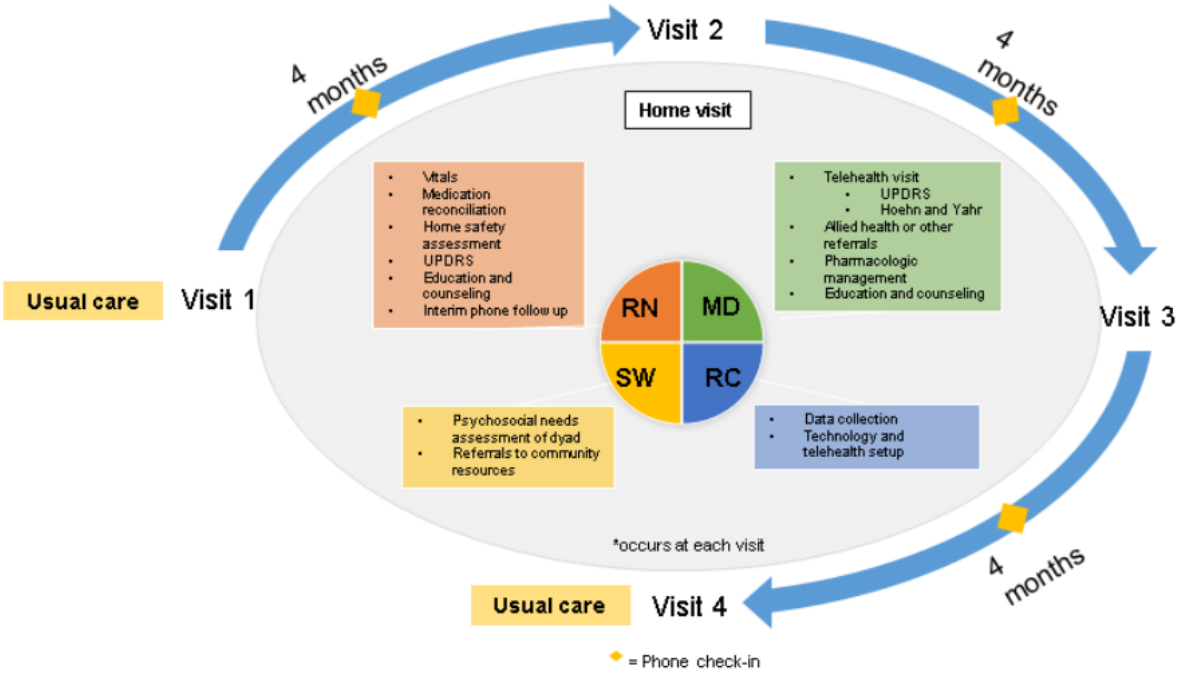
On the basis of this experience and subsequent modifications as described, we present this protocol for a prospective study of telehealth-enhanced home visits by a movement disorder specialist, a nurse, and a social worker, compared with age-, sex-, and HY stage-matched controls from a national, longitudinal PD registry [36,37]. We hypothesize that providing comprehensive, longitudinal, interdisciplinary, and in-home consultation to individuals with advanced PD and their caregivers might inform and transform care for this growing population. By strategically adding telehealth, many opportunities develop in terms of shared specialty care resources across broader geographical regions [38-40]. We aim to determine the impact of these quarterly home visits on (1) patient QoL, (2) caregiver strain, and (3) caregiver depression and anxiety. As an exploratory aim, we will conduct a budget impact analysis to evaluate the feasibility and cost-effectiveness of this model.

Methods

Study Setting and Design

The Interdisciplinary Home Visits for Parkinson's Disease (IN-HOME-PD) study is a single-center cohort study of quarterly, interdisciplinary home visits enhanced by telehealth for homebound individuals with advanced PD and their caregivers. Enrolled patient-caregiver dyads are compared with matched controls drawn from the Parkinson's Foundation (PF) Parkinson's Outcome Project (POP). Recruitment began on May 7, 2018. IN-HOME-PD participants are recruited from the Rush University Medical Center PF Center of Excellence in Chicago, Illinois. We are enrolling 65 pairs of patients and caregivers. Screenings take place via electronic medical record (EMR) chart review and phone call, whereas visit 1 assessments take place in patients' homes (Figure 1). Visits 2-4 are performed where the patient resides at the time of the visit (eg, home, skilled nursing facility, or nursing home).

Figure 1. Interdisciplinary home visits for Parkinson disease study structure, visit flow, and discipline-specific responsibilities at each visit. MD: movement disorders specialist; RC: research co-ordinator; RN: nurse; SW: social worker; UPDRS: Unified Parkinson's Disease Rating Scale.



Patient Inclusion Criteria

The patients must be aged ≥40 years, be seen within the past 2 years at the Rush Movement Disorders Clinic with a diagnosis of PD according to the UK PD Brain Bank criteria [41] from their treating neurologist and HY stage 3-5 at the most recent visit, have one or more criteria for advanced PD as delineated in Textbox 1, and live within 30 miles of the Rush Movement Disorders Clinic. The patients must have a caregiver willing to serve as their study partner, with the respective inclusion and exclusion criteria listed below. Finally, these patients must be considered homebound [42], be community-dwelling (an independent dwelling such as an apartment, condominium, or house owned or rented by, or provided to or shared with the patient), and either demonstrate the capacity to consent, or have a consenting study partner and capacity to assent to participation [43].

Textbox 1. Inclusion and exclusion criteria for Interdisciplinary Home Visits for Parkinson's Disease patients and caregivers.

Interdisciplinary Home Visits for Parkinson's Disease Patient

- Inclusion criteria
  - Aged ≥40 years
  - Diagnosis of idiopathic Parkinson disease by a neurologist
  - ≥1 visit in the past 2 years at Rush Outpatient Movement Disorders Clinic
  - Hoehn and Yahr stage 3-5 at the most recent clinical visit
  - Reside within 30-mile radius of Rush University
  - Community-dwelling and homebound
  - ≥1 of the following criteria, as determined by the referring neurologist: Motor or cognitive fluctuations Multi-morbidity Medication mismanagement Cognitive impairment Symptoms of depression and/or anxiety High risk for hospitalization or hospital readmission High risk for nursing facility admission Suspected elder abuse Recent history of increased falls at home Suspected caregiver burnout ≥2 canceled or no-show appointments with neurologist in past 12 months
  - Caregiver willing to serve as study partner
  - Capacity to consent or caregiver consent and assent or caregiver consent without dissent
- Exclusion criteria
  - Severe psychiatric disorder interfering with ability to participate in the study, as determined by the referring neurologist or principal investigator
  - Non–English-speaking
  - Atypical, vascular, or drug-induced parkinsonism
  - Subjects without an informal caregiver

Interdisciplinary Home Visits for Parkinson's Disease Caregiver

- Inclusion criteria
  - Aged >30 years
  - Unpaid individual spending an average of >20 hours weekly engaged in care-related tasks related to the patient-subject
  - Capacity to consent
  - Agree to participate in nested trial of caregiver peer mentoring
  - Working telephone number at which participant can be contacted by study team
- Exclusion criteria
  - Non–English-speaking
  - Active psychosis or other severe psychiatric disease, as reported by participant or determined by study team member during screening
  - Terminal illness (life expectancy <12 months)

Patient Exclusion Criteria

Patients are excluded from participation if they have a severe unstable psychiatric disorder (exclusive of PD psychosis), are non–English-speaking, or have an atypical form of parkinsonism according to the most recent visit with their treating neurologist.

Caregiver Inclusion Criteria

Caregivers must be aged ≥30 years; demonstrate the capacity to consent; serve as a caregiver to the patient, defined as either cohabitating with the patient or spending an average of >20 hours weekly engaged in unpaid care-related tasks; have a working telephone; and agree to participate in a nested trial of caregiver peer mentoring.

Caregiver Exclusion Criteria

Caregivers are excluded if they are diagnosed with a severe psychiatric disorder, non–English-speaking, terminally ill (have been told by a medical professional that they have <12 months to live, by self-report), and hired and paid as a formal caregiver in a part-time or full-time capacity.

Control Participants

The matched control participants are drawn from the POP longitudinal registry [36]. Once all first visits are completed, the team provides the PF with a deidentified data set containing the age, sex, and HY stage of all patients at visit 1. The PF then provides a subset of POP participants with at least two consecutive annual visits and a caregiver study partner, matched to patients by exact HY, sex, and age ±5 years). The pilot feasibility data from the initial New York–based cohort (with similar eligibility requirements to this study) indicated that we could match 93% of those participants on sex, age, and HY stage, to at least two POP controls. Sex, age, and HY stage were selected as matching variables because of their association with PD duration, severity, caregiver strain, and institutionalization [37,44,45]. In the event of insufficient POP matches, the study team will use propensity score matching rather than direct 1:1 matches.

Recruitment and Screening Strategies

The potential participants are identified and recruited by direct referral from the Rush Movement Disorder Clinic neurologists or via chart review. The study team presents the structure and logistics, eligibility criteria, and referral process to referring neurologists at regular intervals throughout the recruitment period. Referring neurologists contact the coordinator directly with the names of potential participants. The coordinator also prospectively screens clinic schedules and retrospectively queries the EMR for potential participants seen in the past 2 years. If a potential participant is identified in the EMR, the coordinator confirms eligibility with the neurologist before contacting the patient. Once potential participants are provided with additional information about study requirements and confirm interest in the study, visit 1 is scheduled. As of July 2021, recruitment is complete.

Clinical Assessment

As shown in Table 1, all assessments occur at quarterly visits over a 365-day timeframe (with a 60-day window of flexibility). Visits, interim follow-up calls, and documentation have all been designed to incorporate principles of geriatrics, palliative care, and best practices in the management of PD and to be integrated into the EMR. At visit 1, the nurse, social worker, and coordinator travel to the home and complete the capacity assessment and informed consent process. The coordinator sets up an internet hotspot and tests the tablet connectivity via a Health Insurance Portability and Accountability Act (HIPAA)–secure videoconferencing app. While the coordinator arranges telehealth technology, the nurse assesses the patient for the following: demographics, orthostatic vitals (or supine vitals if bedbound), disease history, and comorbidities.

Table 1. Study assessments.

Domains	Instruments	Study visit			
		1[a]	2[b]	3[b]	4[b]
Patient					
Medical history	Standardized initial and interim medical history	✓[c]	✓	✓	✓
Orthostatic vital signs	Manual sphygmomanometer	✓	✓	✓	✓
Demographics and PD[d] history	Standardized questionnaire	✓			
Comorbidities	Self-administered comorbidity questionnaire	✓			
Medication reconciliation	Standardized questionnaire	✓	✓	✓	✓
Nonmotor activities of daily living	UPDRS[e] I	✓	✓	✓	✓
Motor activities of daily living	UPDRS II	✓	✓	✓	✓
Physical examination	UPDRS III	✓	✓	✓	✓
Motor complications	UPDRS IV	✓	✓	✓	✓
PD stage	Hoehn and Yahr	✓	✓	✓	✓
Cognitive assessment	Abbreviated MoCA[f]	✓			✓
Home safety assessment	Standardized questionnaire	✓			
Resource utilization questionnaire	Standardized questionnaire	✓	✓	✓	✓
Quality of life					
Quality of life assessment, long form	PDQ-39[g]	✓			✓
Quality of life assessment, short form	PDQ-8[h]		✓	✓	
Program satisfaction	CSI-SF[i]	✓			✓
Satisfaction with telehealth visits	Telehealth satisfaction survey				✓
Caregiver					
Demographics	Standardized questionnaire	✓			
Comorbidities	Self-administered comorbidity questionnaire	✓			
Caregiver strain	MCSI[j]	✓	✓	✓	✓
Anxiety and depression	HADS[k]	✓	✓	✓	✓
Self-efficacy	Self-efficacy questionnaire	✓	✓	✓	✓
Cognition	Abbreviated MoCA	✓			✓
Program satisfaction	CSI-SF	✓		✓	✓
Postvisit follow-up					
Approximately 4 week follow-up phone call	Semistructured template in electronic medical record	✓	✓	✓	✓

[a]Visit 1: coordinator, nurse, social worker present at home; movement disorder specialist present by video.

[b]Visits 2-4: coordinator and nurse present at home; social worker and movement disorder specialist present in real time via telehealth. Visit 4: 365 (SD 60) days after visit 1.

[c]Domain examined.

[d]PD: Parkinson disease.

[e]UPDRS: Unified Parkinson's Disease Rating Scale.

[f]MoCA: Montreal Cognitive Assessment (four-item shortened version of MoCA used in the Parkinson's Outcome Project, including immediate and delayed five-item recall, oral trails, and category fluency).

[g]PDQ-39: Parkinson's Disease Questionnaire.

[h]PDQ-8: Parkinson's Disease Questionnaire-Short Form.

[i]CSI-SF: Client Satisfaction Inventory-Short Form.

[j]MCSI: Multidimensional Caregiver Strain Index.

[k]HADS: Hospital Anxiety and Depression Scale.

At each visit, the nurse and dyad complete a medication reconciliation and ensure that the EMR-documented medication list and schedule align with actual administration at home. Specifically, the nurse identifies medication strength and frequency errors, expired medications, and duplicate medications. The nurse also documents errors in omission (ie, not taking prescribed medication) or commission (ie, actively taking a discontinued or deprescribed medication). Any errors detected are relayed to the movement disorder specialist and addressed in the shared assessment and plan.

The nurse performs a standardized checklist-based home safety assessment including the following: safe entrance and exit from the home; fall risks within the home such as unstable throw rugs, poorly lit hallways, or lack of handrails for indoor steps; bathroom and bedroom safety, including bath or shower grab bars, seats, and toilet aids; and presence of working fire alarms, fire extinguishers, and an emergency escape plan.

The team measures both patient and caregiver cognition with a shortened version of the Montreal Cognitive Assessment (MoCA), mirroring the assessment used for POP participants for comparability [36]. Items include immediate and delayed five-item recall, oral trails, and category fluency. To minimize priming or interference with the MoCA, the team engages the caregiver in other assessments while the patient completes the MoCA and vice versa.

The social worker assesses the caregiver's demographics, comorbidities, strain (Multidimensional Caregiver Strain Index [MCSI]) [46], and mood (Hospital Anxiety and Depression Scale) [47]. The caregiver completes surveys on self-efficacy [48] and satisfaction with preintervention PD care using the Client Satisfaction Inventory-Short Form (CSI-SF) [49]. Finally, the social worker initiates a discussion of goals of care and advance directives with the dyad.

After the nurse and social worker perform their assessments, they call the movement disorder specialist to present their respective data and develop a preliminary plan. While the team members are conferring, the coordinator completes the Parkinson's Disease Questionnaire (PDQ-39) [50] and the CSI-SF with the patient. For these two assessments, the remaining team members are blinded, and both data collection and entry are completed by the coordinator alone.

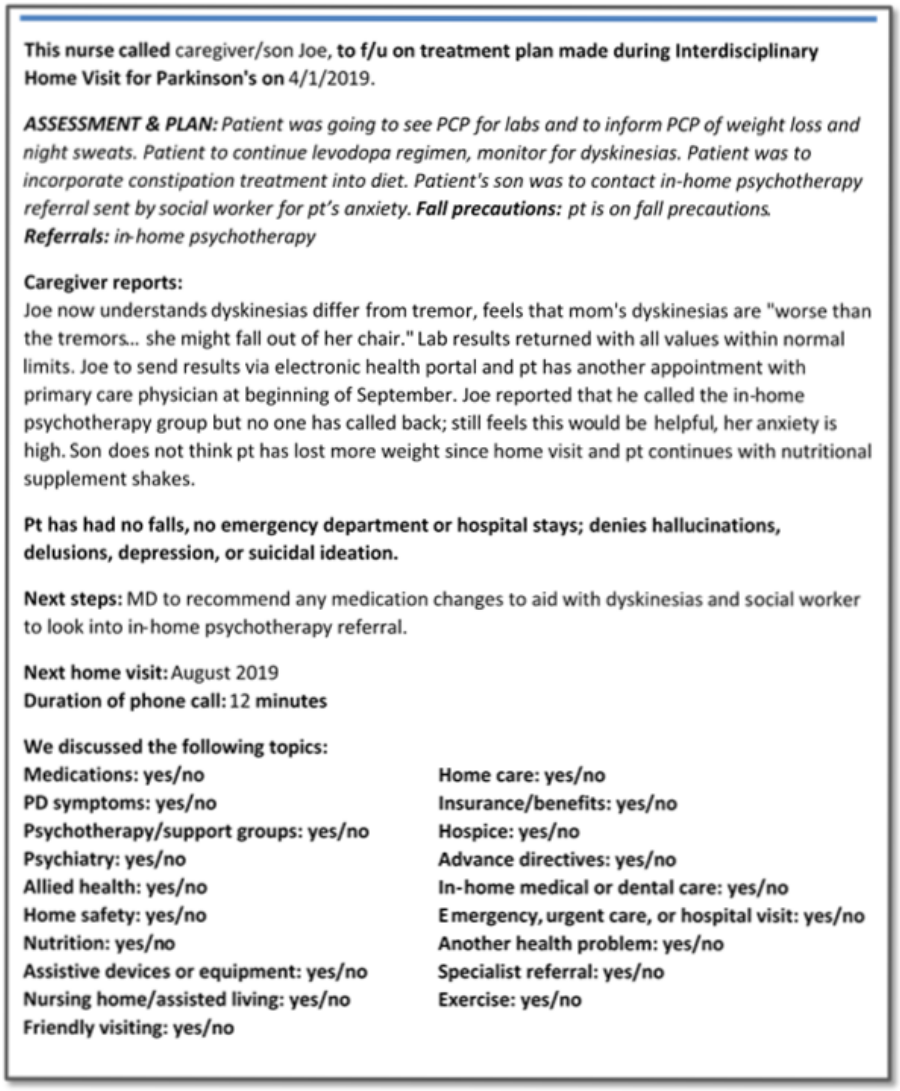
Once the nurse, social worker, and movement disorder specialist have conferred, the telehealth component of the visit begins. The movement disorder specialist joins the visit by video (VidyoConnect, Vidyo Inc) and explores and addresses symptoms and concerns. The movement disorder specialist completes a physical examination using observation and prompted actions supported by the nurse, including the Unified Parkinson's Disease Rating Scale (UPDRS) [51,52]. For rigidity and postural instability items, the registered nurse assesses these items in person with the movement disorder specialist's supervision. The movement disorder specialist determines the HY score [53]. On the basis of all of the visit assessments, the movement disorder specialist revises and presents a unified plan to address symptoms and unmet needs. Before departure, the team provides an after-visit summary, including an accurate health-literacy–friendly medication schedule and relevant educational material. Each team member completes a templated note in the EMR and later collates it into a comprehensive document shared with all health care providers involved in the patient's care. Patients are permitted to continue seeing any of their existing health care providers during the course of the study, including primary care providers.

Visits 2-4 (and their corresponding follow-up phone calls) are identical to visit 1, with the following exceptions: the social worker joins via telehealth, and the home safety assessment and static measures, such as demographics, are omitted. At visits 2 and 3, the Parkinson's Disease Questionnaire-Short Form (PDQ-8) [54], a validated, shortened version of the PDQ-39, is used. At visit 4, the full PDQ-39 is used, and the dyad completes a telehealth satisfaction survey [55]. The duration of the visits, including all clinical and study assessments, is approximately 90-180 minutes.

Follow-Up Calls

Approximately 4 weeks after each home visit, the team calls the dyad to follow up on the care plan, any updates, and further recommendations from the team or referring neurologist. Again, this is documented in a templated telephone encounter (example in Figure 2) and shared with the relevant team members. Interim calls afford additional opportunities for the detection of clinical deterioration and interdisciplinary case management and intervention.

Figure 2. Example of a follow-up phone call note for an interdisciplinary home visit for Parkinson disease in the electronic medical record using a standardized template. MD: movement disorders specialist; PCP: primary care provider; PD: Parkinson disease.



This nurse called caregiver/son Joe, **to f/u on treatment plan made during Interdisciplinary Home Visit for Parkinson's on** 4/1/2019.

ASSESSMENT & PLAN: *Patient was going to see PCP for labs and to inform PCP of weight loss and night sweats. Patient to continue levodopa regimen, monitor for dyskinesias. Patient was to incorporate constipation treatment into diet. Patient's son was to contact in-home psychotherapy referral sent by social worker for pt's anxiety.* ***Fall precautions:*** *pt is on fall precautions.*
Referrals: *in-home psychotherapy*

Caregiver reports:
Joe now understands dyskinesias differ from tremor, feels that mom's dyskinesias are "worse than the tremors... she might fall out of her chair." Lab results returned with all values within normal limits. Joe to send results via electronic health portal and pt has another appointment with primary care physician at beginning of September. Joe reported that he called the in-home psychotherapy group but no one has called back; still feels this would be helpful, her anxiety is high. Son does not think pt has lost more weight since home visit and pt continues with nutritional supplement shakes.

Pt has had no falls, no emergency department or hospital stays; denies hallucinations, delusions, depression, or suicidal ideation.

Next steps: MD to recommend any medication changes to aid with dyskinesias and social worker to look into in-home psychotherapy referral.

Next home visit: August 2019
Duration of phone call: 12 minutes

We discussed the following topics:

Medications: yes/no	**Home care: yes/no**
PD symptoms: yes/no	**Insurance/benefits: yes/no**
Psychotherapy/support groups: yes/no	**Hospice: yes/no**
Psychiatry: yes/no	**Advance directives: yes/no**
Allied health: yes/no	**In-home medical or dental care: yes/no**
Home safety: yes/no	**Emergency, urgent care, or hospital visit: yes/no**
Nutrition: yes/no	**Another health problem: yes/no**
Assistive devices or equipment: yes/no	**Specialist referral: yes/no**
Nursing home/assisted living: yes/no	**Exercise: yes/no**
Friendly visiting: yes/no	

Outcome Measures

The instruments illustrated in Table 1 are used to collect data from the patients and their caregivers throughout the study.

IN-HOME-PD Patients Only

QoL is assessed using the PDQ-39 (visits 1 and 4) and PDQ-8 (visits 2 and 3). The former is a 39-item, eight-domain tool, with each item scored 0 (never) to 4 (always). The latter is an 8-item version, with each item representing one PDQ-39 domain [50]. Domain scores as well as a summary index score (0-100), can be calculated, with higher scores signifying worse QoL. PDQ-8 is administered at visits 2 and 3 to minimize assessment time and avoid missing data if dyads are lost to follow-up before visit 4. If the patient is unable to complete the PDQ-39 or PDQ-8 because of cognitive impairment, the caregiver may answer on the patient's behalf.

IN-HOME-PD Patients and Caregivers

Both patients and caregivers complete the CSI-SF to measure participants' satisfaction with the program. The CSI-SF is a nine-item instrument used to assess client satisfaction with multidisciplinary programs. Subjects indicate their satisfaction on a 7-point Likert scale at baseline and at visit 4 [49]. At the end of visit 4, dyads complete the telehealth satisfaction survey, a 17-item instrument designed specifically for telemedicine visits in patients with PD [56].

Caregivers Only

The MCSI is an 18-item tool measuring six dimensions of subjective responses to stressors in caregivers [46]. Subscales include physical strain, social constraints, financial strain, time constraints, interpersonal strain, and demanding or manipulative stress. Respondents are asked about the frequency with which items apply, ranging from *never* to *all of the time* on a 5-point scale. The 14-item validated Hospital Anxiety and Depression Scale (HADS) measures anxiety and depression [47]. Scores >8 for either anxiety or depression subscores indicate probable symptoms. A nine-item scale measures symptom management self-efficacy [48].

Budget Impact Analysis

The exploratory budget impact analysis takes a health care system perspective based on provider time and health care utilization [57]. Budget-related data include prospectively captured research- and intervention-specific costs,

telehealth-associated difficulties and delay, item purchases for study use, health care utilization by the patient, and provider time dedicated to their care. We capture health care utilization via a standardized questionnaire from the POP, which includes falls, emergency department visits, hospitalizations, institutionalization, allied health referrals, outpatient care, and binary data on the use of various PD medication categories. The average health care utilization and cost per patient per year will be compared with the use data available through the POP.

The total yearly costs will be divided into intervention and health care utilization costs. The intervention costs are recorded by the study team, who track their program-related activities, costs, and time. Each team member is prompted on a monthly basis to record 1 week's worth of effort, indicating time spent on study-specific tasks (ie, screening, visit scheduling and preparation, travel, EMR charting, and both scheduled and unscheduled interim calls). All entries are categorized as intervention-related or research-related, and research-related costs will be excluded from the analysis. Health care utilization information will be described for the 12 months before and following baseline for IN-HOME-PD and POP subjects, with descriptive statistics for each category of health care utilization, including emergency department visits, hospitalizations, outpatient services, and use of various PD-related medication categories. In addition, the proportion of subjects institutionalized over the course of 1 year will be included. The total yearly costs (intervention and health care utilization) per IN-HOME-PD patient-year will be calculated and compared with those of POP controls.

Primary End Point

The primary end point is the change in PDQ-39 over 1 year between IN-HOME-PD patients and controls (visit 1 to visit 4 in IN-HOME-PD patients; annual POP assessments in controls).

Secondary End Points

Secondary end points include changes in caregiver strain within IN-HOME-PD caregivers over 1 year and between IN-HOME-PD caregivers and matched control caregivers, using the MCSI. Additional secondary patient end points compared between IN-HOME-PD patients and matched controls include self-reported fall frequency, count and presenting complaint for any emergency department visits and hospitalizations, institutionalization, and death. Among the IN-HOME-PD dyads only, we are assessing the change in caregiver anxiety, depression, and self-efficacy, as these variables are not present in the POP database. We are assessing telehealth satisfaction and dyad satisfaction with IN-HOME-PD care, using the change in CSI-SF from visit 1 to visit 4. Finally, exploratory end points include the cost per visit and annualized cost per dyad based on team member time and labor and modeled costs of health care utilization (emergency department visits and hospitalizations) among both IN-HOME-PD patients and controls. Indirect costs, including time spent caregiving or lost wages because of PD or caregiving, are beyond the scope of this study and absent from the POP; thus, we did not include them in this analysis.

Ethics Approval and Consent to Participate

The Rush University Medical Center Institutional Review Board initially approved this study on October 25, 2017 (current protocol version 8, dated March 19, 2020), and the trial is posted in a national database (registration number NCT03189459). All participants in this study (patients and their caregivers) provided written informed consent. In the event that the patient lacks the capacity to consent because of cognitive impairment, the caregiver may consent on their behalf with the patient giving assent. Participants may withdraw from the study and return to their prior care provider at any time. If a caregiver wants to withdraw but the patient wants to continue participation, a suitable alternative caregiver, approved by the patient's legally authorized representative, must be willing and able to participate to allow for the patient's continued participation. If a suitable caregiver is not willing and able to participate, the patient will be withdrawn from the study, and the study team will reconnect the patient with their prior care provider.

Sample Size

Our preliminary data and recruitment support our ability to enroll 65 dyads in 16 months. On the basis of a 12% attrition rate in our pilot New York–based cohort, we conservatively planned for a 20% drop out rate in this larger study, yielding 52 dyads. This affords 79% power to detect a minimal clinically important between-group difference of 6 in the PDQ-39 summary index [58-60] with a sample size of 50 pairs using an estimated baseline mean of 52.0 (SD 15.0) and α=.05, using a two-sided paired *t* test [61]. This is a conservative estimate given our anticipated higher ratio of matched controls (3-4:1). A sample size of 50 dyads yields 99% power to detect a 10-point difference in change in MCSI (from a mean of 24 to 34, SD 8) over 12 months compared with controls, as measured using a two-sample paired-means test with a significance level of 0.05, based on pilot data. The budget impact analysis is exploratory in nature.

Data Collection and Monitoring

The team meets weekly, outside of study visits, to identify potential issues with consent or assessment procedures, manage any reported adverse events or unintended effects of home visits, and monitor progress. A REDCap (Research Electronic Data Capture) database was created to house the data, with quarterly audits to ensure fidelity [62]. Data will be exported in deidentified form to Stata 15 (StataCorp LLC) for analysis.

Statistical Analysis

IN-HOME-PD Patients

Demographics and confounders include race, ethnicity, insurance, socioeconomic status (average household income for zip code) [63,64], living situation (home or nursing facility), PD duration (from the year of PD onset or diagnosis, if onset unknown), cognition as measured in the POP using items from the MoCA, and comorbidities (self-reported presence and severity of heart and respiratory problems, diabetes, cancer, arthritis, and other neurological disorders) The following items not in the POP are used in analyses of program dyads only: education, caregiver demographics (age, race, ethnicity, and education), depression, hallucinations, motor severity (UPDRS),

satisfaction with the program (CSI-SF), and telehealth satisfaction [56].

Baseline demographics, PD characteristics, and QoL in program and POP subjects, with categorical variables summarized by frequencies and percentages, will be described. Continuous variables will be assessed for normality and summarized as mean and SD or median and IQR, as appropriate. Using chi-square and two-tailed *t* tests, as appropriate, we will evaluate the adequacy of matching [65,66]. We will compare the change in Parkinson's Disease Questionnaire-Summary Index (PDQ-SI) over 1 year for each matched pair using a paired *t* test or nonparametric Wilcoxon signed-rank test. If a subject dies or is lost to follow-up, the last value of the PDQ-8 SI will be carried forward [54]. We will analyze the association with change in PDQ-SI for each demographic, confounder, and covariate via multivariable analysis of variance to account for matching. We will correct for multiple comparisons as appropriate. We will construct a linear regression model with change in PDQ-SI as the dependent variable and home visits as the primary independent variable. We will use stratified linear regression, accounting for matching variables, to assess the contributions of each as potential confounders. Model building will include manual stepwise backward elimination testing for multicollinearity, confounding, and effect modification. Finally, we will describe patient and caregiver satisfaction with the home visit intervention and telehealth, respectively, analyzing patient and caregiver predictors of change in satisfaction, or predictors of dyadic discordance in satisfaction, if appropriate.

Caregivers

We will describe demographics and baseline caregiver strain, anxiety, depression, and satisfaction with their loved one's preintervention PD care. We will compare within-subject changes in MCSI over 12 months and between-subject changes across IN-HOME-PD and POP caregivers. The last MCSI value will be carried forward in the event of loss to follow-up. We will evaluate the proportion of caregivers in each group with a categorical change in strain (eg, from moderate to severe). We will construct a linear regression model with change in MCSI as the dependent variable, home visits as the primary independent variable, and we will adjust for potential confounders, such as caregiver and patient demographics and cognitive impairment.

Budget Impact

We will describe health care utilization in the 12 months before and following baseline, respectively, for program and POP subjects. Health care utilization includes the limited data set assessed in the POP, namely, self-reported frequency of emergency department visits and hospitalizations, along with their admitting diagnoses. In addition, at each home visit, we gather the frequency of primary care, neurologist, and other specialist visits, respectively, and the frequency of phone calls or health portal electronic messages reported by the dyad in the interim since the prior home visit. To calculate the costs of the program (ie, intervention), we will include the study team's time spent on phone calls, emails, and other intervention-related communication. We will exclude research-related program costs (eg, coordinator time spent on questionnaires not directly pertaining to clinical care) from the budget impact analysis. All program component costs will be summed to calculate total program costs, and program and health care costs will be summed to calculate total costs. We will present descriptive statistics for each category of health care utilization and the proportion of subjects institutionalized over 1 year, defined as a change in living situation from *home* to a *skilled nursing facility or nursing home*. We will compare IN-HOME-PD with POP subjects on hospitalizations, emergency department visits, institutionalization, and total costs during the 1-year observation period using chi-square and *t* tests, as appropriate. We will determine the effect size of the intervention on each use category and analyze the association between each category and each demographic, confounder, and variable of interest via *t* test or analysis of variance.

In the budget impact analysis, multivariable analyses will consist of constructing two model types: (1) multivariable logistic regression models for any hospitalization, emergency department visit, or institutionalization within 1 year (three separate, dichotomous outcomes), and (2) multivariable Poisson regression models for counts of hospitalizations and counts of emergency department visits (two separate count outcomes). More complex models will be built as above, focusing on PD duration, cognitive impairment, QoL, caregiver strain, and prior use as confounders or effect modifiers in the relationship between intervention and use. Using a dependent variable of total costs, we will construct a generalized linear model with log link and gamma distribution, testing for significant differences in total costs by treatment status [67,68]. The achievable savings estimate of implementing this program nationwide will be calculated by extrapolating our results to 5% of the PD population (a conservative estimate of those seen at PF Centers of Excellence) [36]. In sensitivity analyses of the home visit intervention, we will vary the costs of team composition, duration and cost of travel, and geographic region.

Results

This protocol was funded in September 2017 and approved by the Rush Institutional Review Board in October 2017. Recruitment began in May 2018 and closed in November 2019, with 65 patient-caregiver dyads enrolled and having completed visit 1. When the SARS-CoV-2 pandemic reached the United States and lockdowns went into place in mid-March 2020, all in-person portions of the home visits were converted to video or phone visits on the participants' own devices, if available, and marked as pandemic-modified visits in the database for subsequent analyses. All dyads enrolled at that time had already completed at least visits 1 and 2. For these pandemic-modified visits, the nurse obtains vital signs gathered on the dyad's home blood pressure monitoring cuffs, if available, and coaches the caregiver through obtaining orthostatic vital signs. Medication reconciliation is conducted by video or phone with the caregiver, and the movement disorder neurologist conducts a remote UPDRS examination by video whenever possible [52]. Given the advanced stage of many IN-HOME-PD patients and the risk of attrition, the study team determined that it would be preferable to conduct modified quarterly visits on the predetermined schedule rather than defer visits until after the pandemic. In

exploratory analyses, we will identify differences in primary and secondary outcomes, overall satisfaction, and telehealth satisfaction among participants completing all visits per protocol and those with pandemic-modified visits.

As of June 2021, all study visits have been completed. Matching is underway, followed by data analysis, with results expected to be published in fall 2021.

Discussion

Rationale for This Model

Our prior work in New York City identified an understudied population of advanced homebound PD patients with high symptom and caregiver burden and poor QoL who were amenable to interdisciplinary home visits [33,34]. In pilot studies of home visits, QoL did not significantly decline during the yearlong follow-up, suggesting that expert care delivered directly to the patient-caregiver dyad may mitigate some of the decline previously deemed inevitable. Given the ethical considerations of withholding care from those unable to access it [69,70] and the high dropout rates seen in PD interventions with waitlist controls [70,71], a randomized controlled trial of interdisciplinary home visits is neither appropriate nor feasible. However, matched controls can provide a reasonable comparison group in this understudied population [69].

During the development of the model in 2014-2017, the availability and use of video telehealth increased, with growing interest and evidence to support telehealth as an effective care model in PD [55,72,73]. Particularly in the pre-COVID era, several limitations affected its implementation in the homebound population, including possession of both relevant technology and connectivity, digital literacy [74,75], and neuropsychiatric and sensory impairments that would render unsupported telehealth difficult or impossible, and therefore, reliance on a care partner with the equipment and skills to facilitate telehealth [76,77]. Cognitive interviews with pilot participants revealed a significant amount of paranoia and apprehension regarding new cameras, computers, wires, and other devices being brought into the home. With these concerns in mind, we piloted several telehealth models and determined that the use of a mobile hotspot and tablet brought and operated by the study team, rather than relying on the participants' own devices or connectivity, was the most efficient and acceptable. Telehealth connectivity and overcoming the digital divide created by users, technology, and internet and cellular barriers will remain an important variable in studying any intervention reliant upon them.

Recruitment is an additional and anticipated challenge inherent to a population that has eluded care and clinical research until recently [14,78-80]. Identifying potentially eligible patients through the EMR offers certain advantages; however, documentation may not reflect the correct diagnosis, stage, or presence of a caregiver. In some instances, the record may not be updated in a timely manner following the patient's demise; thus, screening phone calls must be handled with sensitivity. In addition, the labor and time intensity of the model required us to determine a catchment area large and geographically diverse enough to meet recruitment goals, however, circumscribed enough to prevent extensive travel time and remain within state boundaries because of licensure limitations.

Despite the challenges of reaching advanced homebound individuals with PD and their caregivers before and during the SARS-CoV-2 pandemic, the potential impact of this and subsequent studies to aid in defining and ultimately addressing QoL and caregiver strain in this population is significant. This is among the first of several studies to longitudinally follow such advanced, underserved patients and caregivers and report on the trajectories of QoL, caregiver strain, and health care utilization. This is also the first study to compare interdisciplinary home visits to usual care for this population and longitudinally investigates both patient, caregiver, and cost outcomes. By standardizing the roles and responsibilities of each team member, including video telehealth, and incorporating templated documentation, this model may be leveraged to foster continuity of care, effective interdisciplinary case management, and improve QoL and caregiver strain for countless homebound individuals with PD and other neurodegenerative diseases.

Availability of Data and Materials

The deidentified data sets generated and analyzed during this trial will be available from the corresponding author upon reasonable request. Data from all control subjects were retrospective and available to the investigators by request to the PF.

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Authors' Contributions

JEF, TJJ, DAH, and JC conceived the program and wrote the protocol; JRW, JB, SH, EKW, JL, MS, and EM provided ongoing critical reviews. BO aided the sample size calculation and analyses. JEF, SH, BJS, EKW, and KW drafted the manuscript, and all authors reviewed and approved the final version of the manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Peer-reviewer report from National Institute of Neurological Disorders and Stroke (National Institutes of Health).
[PDF File (Adobe PDF File), 177 KB - resprot_v10i9e31690_app1.pdf]

References

1. Dorsey ER, Constantinescu R, Thompson JP, Biglan KM, Holloway RG, Kieburtz K, et al. Projected number of people with Parkinson disease in the most populous nations, 2005 through 2030. Neurology 2007 Jan 30;68(5):384-386. [doi: 10.1212/01.wnl.0000247740.47667.03] [Medline: 17082464]
2. Savica R, Grossardt BR, Rocca WA, Bower JH. Parkinson disease with and without dementia: a prevalence study and future projections. Mov Disord 2018 Apr;33(4):537-543 [FREE Full text] [doi: 10.1002/mds.27277] [Medline: 29356127]
3. Ornstein KA, Leff B, Covinsky KE, Ritchie CS, Federman AD, Roberts L, et al. Epidemiology of the homebound population in the United States. JAMA Intern Med 2015 Jul 01;175(7):1180-1186 [FREE Full text] [doi: 10.1001/jamainternmed.2015.1849] [Medline: 26010119]
4. Tulner LR, Kuper IM, Frankfort SV, van Campen JP, Koks CH, Brandjes DP, et al. Discrepancies in reported drug use in geriatric outpatients: relevance to adverse events and drug-drug interactions. Am J Geriatr Pharmacother 2009 Apr;7(2):93-104. [doi: 10.1016/j.amjopharm.2009.04.006] [Medline: 19447362]
5. Stromski C, Popavetsky G, Defranco B, Reed J. The prevalence and accuracy of medication lists in an elderly ED population. Am J Emerg Med 2004 Oct;22(6):497-498. [doi: 10.1016/j.ajem.2004.07.006] [Medline: 15520952]
6. Mira JJ, Lorenzo S, Guilabert M, Navarro I, Pérez-Jover V. A systematic review of patient medication error on self-administering medication at home. Expert Opin Drug Saf 2015 Jun;14(6):815-838. [doi: 10.1517/14740338.2015.1026326] [Medline: 25774444]
7. Hassan A, Wu SS, Schmidt P, Dai Y, Simuni T, Giladi N, NPF-QII Investigators. High rates and the risk factors for emergency room visits and hospitalization in Parkinson's disease. Parkinsonism Relat Disord 2013 Nov;19(11):949-954. [doi: 10.1016/j.parkreldis.2013.06.006] [Medline: 23835430]
8. Shahgholi L, De Jesus S, Wu SS, Pei Q, Hassan A, Armstrong MJ, et al. Hospitalization and rehospitalization in Parkinson disease patients: data from the National Parkinson Foundation Centers of Excellence. PLoS One 2017 Jul 6;12(7):e0180425 [FREE Full text] [doi: 10.1371/journal.pone.0180425] [Medline: 28683150]
9. Svendsboe E, Terum T, Testad I, Aarsland D, Ulstein I, Corbett A, et al. Caregiver burden in family carers of people with dementia with Lewy bodies and Alzheimer's disease. Int J Geriatr Psychiatry 2016 Sep;31(9):1075-1083. [doi: 10.1002/gps.4433] [Medline: 26765199]
10. Rigby T, Ashwill R, Johnson D, Galvin J. Differences in the experience of caregiving between spouse and adult child caregivers in Dementia with lewy bodies. Innov Aging 2019 Jul;3(3):igz027 [FREE Full text] [doi: 10.1093/geroni/igz027] [Medline: 31528714]
11. Goetz CG, Stebbins GT. Mortality and hallucinations in nursing home patients with advanced Parkinson's disease. Neurology 1995 Apr 01;45(4):669-671. [doi: 10.1212/wnl.45.4.669] [Medline: 7723953]
12. Leggett AN, Zarit S, Taylor A, Galvin JE. Stress and burden among caregivers of patients with lewy body dementia. Gerontologist 2011 Feb;51(1):76-85. [doi: 10.1093/geront/gnq055] [Medline: 20667944]
13. Boersma I, Jones J, Carter J, Bekelman D, Miyasaki J, Kutner J, et al. Parkinson disease patients' perspectives on palliative care needs. Neurol Clin Pract 2016 Apr 01;6(3):209-219. [doi: 10.1212/cpj.0000000000000233]
14. Balzer-Geldsetzer M, Ferreira J, Odin P, Bloem BR, Meissner WG, Lorenzl S, et al. Study protocol: Care of Late-Stage Parkinsonism (CLaSP): a longitudinal cohort study. BMC Neurol 2018 Nov 05;18(1):185 [FREE Full text] [doi: 10.1186/s12883-018-1184-3] [Medline: 30396331]
15. Yang W, Hamilton JL, Kopil C, Beck JC, Tanner CM, Albin RL, et al. Current and projected future economic burden of Parkinson's disease in the U.S. NPJ Parkinsons Dis 2020;6:15 [FREE Full text] [doi: 10.1038/s41531-020-0117-1] [Medline: 32665974]
16. Kruse C, Kretschmer S, Lipinski A, Verheyen M, Mengel D, Balzer-Geldsetzer M, et al. Resource utilization of patients with parkinson's disease in the late stages of the disease in Germany: data from the CLaSP study. Pharmacoeconomics 2021 May;39(5):601-615 [FREE Full text] [doi: 10.1007/s40273-021-01011-y] [Medline: 33738776]
17. McCrone P. Capturing the costs of end-of-life care: comparisons of multiple sclerosis, Parkinson's disease, and dementia. J Pain Symptom Manage 2009 Jul;38(1):62-67 [FREE Full text] [doi: 10.1016/j.jpainsymman.2009.04.006] [Medline: 19615628]
18. DeCherrie LV, Soriano T, Hayashi J. Home-based primary care: a needed primary-care model for vulnerable populations. Mt Sinai J Med 2012 Jul 11;79(4):425-432. [doi: 10.1002/msj.21321] [Medline: 22786732]

19. Reckrey JM, Soriano TA, Hernandez CR, DeCherrie LV, Chavez S, Zhang M, et al. The team approach to home-based primary care: restructuring care to meet individual, program, and system needs. J Am Geriatr Soc 2015 Mar 30;63(2):358-364 [FREE Full text] [doi: 10.1111/jgs.13196] [Medline: 25645568]
20. Dalby DM, Sellors JW, Fraser FD, Fraser C, van Ineveld C, Howard M. Effect of preventive home visits by a nurse on the outcomes of frail elderly people in the community: a randomized controlled trial. Can Med Asso J 2000 Mar 22;162(4):497-500 [FREE Full text] [Medline: 10701382]
21. Cassel JB, Kerr KM, McClish DK, Skoro N, Johnson S, Wanke C, et al. Effect of a home-based palliative care program on healthcare use and costs clasp study. J Am Geriatr Soc 2016 Nov 02;64(11):2288-2295 [FREE Full text] [doi: 10.1111/jgs.14354] [Medline: 27590922]
22. Kono A, Kanaya Y, Tsumura C, Rubenstein LZ. Effects of preventive home visits on health care costs for ambulatory frail elders: a randomized controlled trial. Aging Clin Exp Res 2013 Oct 15;25(5):575-581 [FREE Full text] [doi: 10.1007/s40520-013-0128-4] [Medline: 23949975]
23. Liimatta HA, Lampela P, Kautiainen H, Laitinen-Parkkonen P, Pitkala KH. The effects of preventive home visits on older people's use of health care and social services and related costs. J Gerontol A Biol Sci Med Sci 2020 Jul 13;75(8):1586-1593. [doi: 10.1093/gerona/glz139] [Medline: 31139827]
24. Bulamu NB, Kaambwa B, Ratcliffe J. Economic evaluations in community aged care: a systematic review. BMC Health Serv Res 2018 Dec 14;18(1):967 [FREE Full text] [doi: 10.1186/s12913-018-3785-3] [Medline: 30547788]
25. Boult C, Green AF, Boult LB, Pacala JT, Snyder C, Leff B. Successful models of comprehensive care for older adults with chronic conditions: evidence for the Institute of Medicine's "retooling for an aging America" report. J Am Geriatr Soc 2009 Dec;57(12):2328-2337. [doi: 10.1111/j.1532-5415.2009.02571.x] [Medline: 20121991]
26. Reckrey JM, Gettenberg G, Ross H, Kopke V, Soriano T, Ornstein K. The critical role of social workers in home-based primary care. Soc Work Health Care 2014 Apr 09;53(4):330-343 [FREE Full text] [doi: 10.1080/00981389.2014.884041] [Medline: 24717182]
27. Gomes B, Calanzani N, Curiale V, McCrone P, Higginson IJ. Effectiveness and cost-effectiveness of home palliative care services for adults with advanced illness and their caregivers. Cochrane Database Syst Rev 2013 Jun 06(6):CD007760 [FREE Full text] [doi: 10.1002/14651858.CD007760.pub2] [Medline: 23744578]
28. Stall N, Nowaczynski M, Sinha SK. Systematic review of outcomes from home-based primary care programs for homebound older adults. J Am Geriatr Soc 2014 Dec;62(12):2243-2251. [doi: 10.1111/jgs.13088] [Medline: 25371236]
29. Wajnberg A, Wang KH, Aniff M, Kunins HV. Hospitalizations and skilled nursing facility admissions before and after the implementation of a home-based primary care program. J Am Geriatr Soc 2010 Jun;58(6):1144-1147. [doi: 10.1111/j.1532-5415.2010.02859.x] [Medline: 20487075]
30. Beales JL, Edes T. Veteran's affairs home based primary care. Clin Geriatr Med 2009 Mar;25(1):149-154. [doi: 10.1016/j.cger.2008.11.002] [Medline: 19217499]
31. Vickers LF, O'Neill CM. An interdisciplinary home healthcare program for patients with Parkinson's disease. Rehabil Nurs 1998;23(6):286-299. [doi: 10.1002/j.2048-7940.1998.tb01806.x] [Medline: 10223029]
32. Hack N, Akbar U, Monari EH, Eilers A, Thompson-Avila A, Hwynn NH, et al. Person-centered care in the home setting for Parkinson's disease: operation house call quality of care pilot study. Parkinsons Dis 2015;2015:639494 [FREE Full text] [doi: 10.1155/2015/639494] [Medline: 26078912]
33. Fleisher J, Barbosa W, Sweeney MM, Oyler SE, Lemen AC, Fazl A, et al. Interdisciplinary home visits for individuals with advanced Parkinson's disease and related disorders. J Am Geriatr Soc 2018 Jul 02;66(6):1226-1232 [FREE Full text] [doi: 10.1111/jgs.15337] [Medline: 29608779]
34. Fleisher J, Sweeney M, Oyler S, Meisel T, Friede N, Di Rocco A, et al. Disease severity and quality of life in homebound people with advanced Parkinson disease. Neurol Clin Pract 2019 Sep 05;10(4):277-286. [doi: 10.1212/cpj.0000000000000716]
35. Fleisher JE, Klostermann EC, Hess SP, Lee J, Myrick E, Chodosh J. Interdisciplinary palliative care for people with advanced Parkinson's disease: a view from the home. Ann Palliat Med 2020 Feb;9(Suppl 1):80-89 [FREE Full text] [doi: 10.21037/apm.2019.09.12] [Medline: 31735037]
36. Okun MS, Siderowf A, Nutt JG, O'Conner GT, Bloem BR, Olmstead EM, et al. Piloting the NPF data-driven quality improvement initiative. Parkinsonism Relat Disord 2010 Sep;16(8):517-521. [doi: 10.1016/j.parkreldis.2010.06.005] [Medline: 20609611]
37. Oguh O, Kwasny M, Carter J, Stell B, Simuni T. Caregiver strain in Parkinson's disease: national Parkinson Foundation Quality Initiative study. Parkinsonism Relat Disord 2013 Nov;19(11):975-979. [doi: 10.1016/j.parkreldis.2013.06.015] [Medline: 23871587]
38. McLean S, Sheikh A, Cresswell K, Nurmatov U, Mukherjee M, Hemmi A, et al. The impact of telehealthcare on the quality and safety of care: a systematic overview. PLoS One 2013 Aug 19;8(8):e71238 [FREE Full text] [doi: 10.1371/journal.pone.0071238] [Medline: 23977001]
39. Barlow J, Singh D, Bayer S, Curry R. A systematic review of the benefits of home telecare for frail elderly people and those with long-term conditions. J Telemed Telecare 2007 Jun 23;13(4):172-179. [doi: 10.1258/135763307780908058] [Medline: 17565772]

40. Choi NG, Wilson NL, Sirrianni L, Marinucci ML, Hegel MT. Acceptance of home-based telehealth problem-solving therapy for depressed, low-income homebound older adults: qualitative interviews with the participants and aging-service case managers. Gerontologist 2014 Aug;54(4):704-713 [FREE Full text] [doi: 10.1093/geront/gnt083] [Medline: 23929664]
41. Hughes AJ, Daniel SE, Kilford L, Lees AJ. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. J Neurol Neurosurg Psychiatry 1992 Mar;55(3):181-184 [FREE Full text] [doi: 10.1136/jnnp.55.3.181] [Medline: 1564476]
42. Medicare and home health care. U.S. Department of Health and Human Services - Centers for Medicare & Medicaid Services. 2020. URL: https://www.medicare.gov/Pubs/pdf/10969-medicare-and-home-health-care.pdf [accessed 2021-07-29]
43. Alzheimer's Association. Research consent for cognitively impaired adults: recommendations for institutional review boards and investigators. Alzheimer Dis Assoc Disord 2004;18(3):171-175. [doi: 10.1097/01.wad.0000137520.23370.56] [Medline: 15494623]
44. Safarpour D, Thibault DP, DeSanto CL, Boyd CM, Dorsey ER, Racette BA, et al. Nursing home and end-of-life care in Parkinson disease. Neurology 2015 Jul 02;85(5):413-419. [doi: 10.1212/wnl.0000000000001715]
45. Olanow CW, Stern MB, Sethi K. The scientific and clinical basis for the treatment of Parkinson disease (2009). Neurology 2009 May 26;72(21 Suppl 4):1-136. [doi: 10.1212/WNL.0b013e3181a1d44c] [Medline: 19470958]
46. Stull D. The Multidimensional Caregiver Strain Index (MCSI): Its measurement and structure. J Clin Geropsychol 1996;2(3):175-196 [FREE Full text]
47. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983 Jun;67(6):361-370. [doi: 10.1111/j.1600-0447.1983.tb09716.x] [Medline: 6880820]
48. Fortinsky RH, Kercher K, Burant CJ. Measurement and correlates of family caregiver self-efficacy for managing dementia. Aging Ment Health 2002 May;6(2):153-160. [doi: 10.1080/13607860220126763] [Medline: 12028884]
49. Mcmurtry SL, Hudson WW. The Client Satisfaction Inventory: Results of an initial validation study. Res Soc Work Pract 2017 Sep 29;10(5):644-663. [doi: 10.1177/104973150001000506]
50. Martinez-Martin P, Jeukens-Visser M, Lyons KE, Rodriguez-Blazquez C, Selai C, Siderowf A, et al. Health-related quality-of-life scales in Parkinson's disease: critique and recommendations. Mov Disord 2011 Nov;26(13):2371-2380. [doi: 10.1002/mds.23834] [Medline: 21735480]
51. Goetz CG, Fahn S, Martinez-Martin P, Poewe W, Sampaio C, Stebbins GT, et al. Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Process, format, and clinimetric testing plan. Mov Disord 2007 Jan;22(1):41-47. [doi: 10.1002/mds.21198] [Medline: 17115387]
52. Abdolahi A, Scoglio N, Killoran A, Dorsey ER, Biglan KM. Potential reliability and validity of a modified version of the Unified Parkinson's Disease Rating Scale that could be administered remotely. Parkinsonism Relat Disord 2013 Mar;19(2):218-221 [FREE Full text] [doi: 10.1016/j.parkreldis.2012.10.008] [Medline: 23102808]
53. Goetz CG, Poewe W, Rascol O, Sampaio C, Stebbins GT, Counsell C, Movement Disorder Society Task Force on Rating Scales for Parkinson's Disease. Movement Disorder Society Task Force report on the Hoehn and Yahr staging scale: status and recommendations. Mov Disord 2004 Sep;19(9):1020-1028. [doi: 10.1002/mds.20213] [Medline: 15372591]
54. Jenkinson C, Fitzpatrick R. Cross-cultural evaluation of the short form 8-item Parkinson's Disease Questionnaire (PDQ-8): results from America, Canada, Japan, Italy and Spain. Parkinsonism Relat Disord 2007 Mar;13(1):22-28. [doi: 10.1016/j.parkreldis.2006.06.006] [Medline: 16931104]
55. Dorsey ER, Achey MA, Beck CA, Beran DB, Biglan KM, Boyd CM, et al. National randomized controlled trial of virtual house calls for people with Parkinson's disease: interest and barriers. Telemed J E Health 2016 Jul;22(7):590-598 [FREE Full text] [doi: 10.1089/tmj.2015.0191] [Medline: 26886406]
56. Achey MA, Beck CA, Beran DB, Boyd CM, Schmidt PN, Willis AW, et al. Virtual house calls for Parkinson disease (Connect.Parkinson): study protocol for a randomized, controlled trial. Trials 2014 Nov 27;15:465 [FREE Full text] [doi: 10.1186/1745-6215-15-465] [Medline: 25431346]
57. Mauskopf JA, Sullivan SD, Annemans L, Caro J, Mullins CD, Nuijten M, et al. Principles of good practice for budget impact analysis: report of the ISPOR Task Force on good research practices--budget impact analysis. Value Health 2007 Sep;10(5):336-347 [FREE Full text] [doi: 10.1111/j.1524-4733.2007.00187.x] [Medline: 17888098]
58. Peto V, Jenkinson C, Fitzpatrick R. PDQ-39: a review of the development, validation and application of a Parkinson's disease quality of life questionnaire and its associated measures. J Neurol 1998 May 24;245 Suppl 1(S1):10-14. [doi: 10.1007/pl00007730] [Medline: 9617716]
59. Peto V, Jenkinson C, Fitzpatrick R. Determining minimally important differences for the PDQ-39 Parkinson's disease questionnaire. Age Ageing 2001 Jul;30(4):299-302. [doi: 10.1093/ageing/30.4.299] [Medline: 11509307]
60. Fitzpatrick R, Norquist JM, Jenkinson C. Distribution-based criteria for change in health-related quality of life in Parkinson's disease. J Clin Epidemiol 2004 Jan;57(1):40-44. [doi: 10.1016/j.jclinepi.2003.07.003] [Medline: 15019009]
61. Carod-Artal FJ, Martinez-Martin P, Vargas AP. Independent validation of SCOPA-psychosocial and metric properties of the PDQ-39 Brazilian version. Mov Disord 2007 Jan;22(1):91-98. [doi: 10.1002/mds.21216] [Medline: 17094102]
62. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009 Apr;42(2):377-381 [FREE Full text] [doi: 10.1016/j.jbi.2008.08.010] [Medline: 18929686]

63. Soobader M, LeClere FB, Hadden W, Maury B. Using aggregate geographic data to proxy individual socioeconomic status: does size matter? Am J Public Health 2001 Apr;91(4):632-636. [doi: 10.2105/ajph.91.4.632] [Medline: 11291379]
64. Geronimus AT, Bound J. Use of census-based aggregate variables to proxy for socioeconomic group: evidence from national samples. Am J Epidemiol 1998 Sep 01;148(5):475-486. [doi: 10.1093/oxfordjournals.aje.a009673] [Medline: 9737560]
65. Miller MD, Paradis CF, Houck PR, Mazumdar S, Stack JA, Rifai A, et al. Rating chronic medical illness burden in geropsychiatric practice and research: application of the Cumulative Illness Rating Scale. Psychiatry Res 1992 Mar;41(3):237-248. [doi: 10.1016/0165-1781(92)90005-n]
66. King LA, Priest KC, Nutt J, Chen Y, Chen Z, Melnick M, et al. Comorbidity and functional mobility in persons with Parkinson disease. Arch Phys Med Rehabil 2014 Nov;95(11):2152-2157 [FREE Full text] [doi: 10.1016/j.apmr.2014.07.396] [Medline: 25102383]
67. Garrido MM, Deb P, Burgess JF, Penrod JD. Choosing models for health care cost analyses: issues of nonlinearity and endogeneity. Health Serv Res 2012 Dec 23;47(6):2377-2397 [FREE Full text] [doi: 10.1111/j.1475-6773.2012.01414.x] [Medline: 22524165]
68. Basu A, Manning WG, Mullahy J. Comparing alternative models: log vs Cox proportional hazard? Health Econ 2004 Aug 17;13(8):749-765. [doi: 10.1002/hec.852] [Medline: 15322988]
69. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. J Am Med Assoc 2013 Nov 27;310(20):2191-2194. [doi: 10.1001/jama.2013.281053] [Medline: 24141714]
70. Rickham PP. Code of ethics of the World Medical Association. Declaration of Helsinki. Br Med J 1964 Jul 18;2(5402):177 [FREE Full text] [doi: 10.1136/bmj.2.5402.177] [Medline: 14150898]
71. Guo L, Jiang Y, Yatsuya H, Yoshida Y, Sakamoto J. Group education with personal rehabilitation for idiopathic Parkinson's disease. Can J Neurol Sci 2009 Jan 02;36(1):51-59. [doi: 10.1017/s0317167100006314] [Medline: 19294889]
72. Biglan KM, Voss TS, Deuel LM, Miller D, Eason S, Fagnano M, et al. Telemedicine for the care of nursing home residents with Parkinson's disease. Mov Disord 2009 May 15;24(7):1073-1076. [doi: 10.1002/mds.22498] [Medline: 19353687]
73. Dorsey ER, Deuel LM, Voss TS, Finnigan K, George BP, Eason S, et al. Increasing access to specialty care: a pilot, randomized controlled trial of telemedicine for Parkinson's disease. Mov Disord 2010 Aug 15;25(11):1652-1659. [doi: 10.1002/mds.23145] [Medline: 20533449]
74. van Houwelingen CT, Ettema RG, Antonietti MG, Kort HS. Understanding older people's readiness for receiving telehealth: mixed-method study. J Med Internet Res 2018 Apr 06;20(4):e123 [FREE Full text] [doi: 10.2196/jmir.8407] [Medline: 29625950]
75. Roque NA, Boot WR. A new tool for assessing mobile device proficiency in older adults: The Mobile Device Proficiency Questionnaire. J Appl Gerontol 2018 Feb;37(2):131-156. [doi: 10.1177/0733464816642582] [Medline: 27255686]
76. Rocker C, Cappelletti L, Marshall C, Meunier CC, Brooks DW, Sherer T, et al. Use of an online portal to facilitate clinical trial recruitment: a preliminary analysis of Fox Trial Finder. J Parkinsons Dis 2015;5(1):55-66. [doi: 10.3233/JPD-140522] [Medline: 25624422]
77. Wildenbos GA, Peute L, Jaspers M. Facilitators and barriers of electronic health record patient portal adoption by older adults: a literature study. Stud Health Technol Inform 2017;235:308-312. [Medline: 28423804]
78. Fabbri M, Kauppila LA, Ferreira JJ, Rascol O. Challenges and perspectives in the management of late-stage Parkinson's disease. J Parkinsons Dis 2020;10(s1):75-83 [FREE Full text] [doi: 10.3233/JPD-202096] [Medline: 32568114]
79. Read J, Cable S, Löfqvist C, Iwarsson S, Bartl G, Schrag A. Experiences of health services and unmet care needs of people with late-stage Parkinson's in England: a qualitative study. PLoS One 2019 Dec 30;14(12):e0226916 [FREE Full text] [doi: 10.1371/journal.pone.0226916] [Medline: 31887175]
80. Rosqvist K, Hagell P, Iwarsson S, Nilsson MH, Odin P. Satisfaction with care in late stage Parkinson's disease. Parkinsons Dis 2019;2019:2593547. [doi: 10.1155/2019/2593547] [Medline: 31281630]

Abbreviations

CSI-SF: Client Satisfaction Inventory-Short Form
EMR: electronic medical record
HIPAA: Health Insurance Portability and Accountability Act
HY: Hoehn and Yahr
IN-HOME-PD: Interdisciplinary Home Visits for Parkinson’s Disease
MCSI: Multidimensional Caregiver Strain Index
MMSE: Mini-Mental State Examination
MoCA: Montreal Cognitive Assessment
PD: Parkinson disease
PDQ-8: Parkinson’s Disease Questionnaire-Short Form
PDQ-39: Parkinson’s Disease Questionnaire
PDQ-SI: Parkinson’s Disease Questionnaire-Summary Index

PF: Parkinson's Foundation
POP: Parkinson's Outcome Project
QoL: quality of life
REDCap: Research Electronic Data Capture
SI: summary index
UPDRS: Unified Parkinson's Disease Rating Scale

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Protocol

The Food Equity and Environmental Data Sovereignty (FEEDS) Project: Protocol for a Quasi-Experimental Study Evaluating a Digital Platform for Climate Change Preparedness

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Abstract

Background: Despite having the tools at our disposal to enable an adequate food supply for all people, inequities in food acquisition, distribution, and most importantly, food sovereignty, worsen food insecurity. The detrimental impact of climate change on food systems and mental health is further exacerbated by a lack of food sovereignty. We urgently require innovative solutions to enable food sovereignty, minimize food insecurity, and address climate change–related mental distress (ie, solastalgia). Indigenous communities have a wealth of Traditional Knowledge for climate change adaptation and preparedness to strengthen food systems. Traditional Knowledge combined with Western methods can revolutionize ethical data collection, engagement, and knowledge mobilization.

Objective: The Food Equity and Environmental Data Sovereignty (FEEDS) Project takes a participatory action, citizen science approach for early detection and warning of climate change impacts on food sovereignty, food security, and solastalgia. The aim of this project is to develop and implement a sustainable digital platform that enables real-time decision-making to mitigate climate change–related impacts on food systems and mental well-being.

Methods: Citizen science enables citizens to actively contribute to all aspects of the research process. The FEEDS Project is being implemented in five phases: participatory project planning, digital climate change platform customization, community-led evaluation, digital platform and project refinement, and integrated knowledge translation. The project is governed by a Citizen Scientist Advisory Council comprising Elders, Traditional Knowledge Keepers, key community decision makers, youth, and FEEDS Project researchers. The Council governs all phases of the project, including coconceptualizing a climate change platform, which consists of a smartphone app and a digital decision-making dashboard. Apart from capturing environmental and health-related big data (eg, weather, permafrost degradation, fire hazards, and human movement), the custom-built app uses artificial intelligence to engage and enable citizens to report on environmental hazards, changes in biodiversity or wildlife, and related food and mental health issues in their communities. The app provides citizens with valuable information to mitigate health-related risks and relays big data in real time to a digital dashboard.

Results: This project is currently in phase 1, with the subarctic Métis jurisdiction of Île-à-la-Crosse, Saskatchewan, Canada.

Conclusions: The FEEDS Project facilitates Indigenous Peoples' self-determination, governance, and data sovereignty. All citizen data are anonymous and encrypted, and communities have ownership, access, control, and possession of their data. The digital dashboard system provides decision makers with real-time data, thereby increasing the capacity to self-govern. The

participatory action research approach, combined with digital citizen science, advances the cocreation of knowledge and multidisciplinary collaboration in the digital age. Given the urgency of climate change, leveraging technology provides communities with tools to respond to existing and emerging crises in a timely manner, as well as scientific evidence regarding the urgency of current health and environmental issues.

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KEYWORDS

food security; food sovereignty; food equity; mental health; solastalgia; climate change impacts; climate change preparedness; digital health; digital dashboards; Indigenous health; mobile phone

Introduction

Background

Climate change poses an existential threat, with inevitable consequences for human health and food systems [1-6]. The global impact of climate change is well established and is commonly classified into direct and indirect effects, ranging from extreme heat and poor air quality to extreme weather events that damage infrastructure and increase health risks [7-9]. The complex and nuanced effects of climate change on food security and sovereignty warrant special attention as we strive for inclusive and equitable climate action.

Food systems include interlinked systems of production, processing, distribution, and consumption [5,10,11]. Indigenous food systems are particularly sensitive to climate change, as many Indigenous communities live in areas experiencing rapid environmental changes. Moreover, competing demands for land due to expanding resource extraction have adversely impacted the subsistence of Indigenous communities [12-16]. As a result, even subtle changes in the environment can have a disproportionately greater impact on Indigenous Peoples' food security and sovereignty [17-19].

Food security exists "when all people, at all times, have physical, social, and economic access to sufficient, safe, and nutritious food which meets their dietary needs and food preferences for a healthy, active life" [20]. For many Indigenous communities, the issue of food sovereignty is as critical to their survival as having adequate food supply [21-26]. Food sovereignty refers to the "right of local peoples to control their own food systems, including markets, ecological resources, food cultures, and production modes" [27]. This includes the right to define their own food systems, the ability to make decisions about consumption, harvesting practices, and relationship with the land [24,25,28-30]. Food sovereignty is a necessary component of cultural food security—a distinct but overlapping concept [24]. Households or communities can have food security without food sovereignty; however, there is no sovereignty without food security [21-24,31].

Despite having the tools at our disposal to enable adequate food supply for all, inequities in income, food access and distribution, and most importantly, food sovereignty, worsen food insecurity [30,32-34]. The detrimental impact of climate change on food systems is further exacerbated by a lack of food sovereignty [23,35-38]. Failure of these systems is linked to a troubling decline in mental health [39,40] and diet-related chronic disease (ie, type 2 diabetes, obesity, and hypertension) [41,42], particularly among Indigenous and racialized communities. These communities also face the brunt of climate change impacts and have the least control over their food access [13,43-48]. Solastalgia, which refers to the mental distress caused by environmental degradation and changes, is of increasing concern as environmental disasters and biodiversity loss have become more frequent and severe due to climate change [49]. Solastalgia may include ecological grief or eco-anxiety resulting from unanticipated ecological losses and uncertainty about the changing environment [49].

In rural and remote communities, climate change–related risks and their interplay with food systems and solastalgia can be consistently monitored using sophisticated early warning and response systems to improve the management of food and related mental health crises [1,50,51]. Such advanced monitoring can be facilitated through real-time engagement via ubiquitous digital devices such as smartphones. Smartphones can serve as tools of equity by amplifying the voices of isolated citizens and communities, as well as providing citizens with timely access to resources and information [52-54]. Community-based data collection improves monitoring and adaptation to environmental changes as Indigenous communities have a wealth of knowledge and experience in coping with environmental changes [1,55-57]. The integration of Western methods and Traditional Knowledge using Two-Eyed Seeing approaches is critical for developing and implementing climate change solutions in partnership with Indigenous communities [1,58-62].

Objective

We urgently require innovative solutions to enable food sovereignty and minimize food insecurity and solastalgia. In the digital age, citizen science can revolutionize ethical data collection, engagement, and knowledge mobilization. The Food Equity and Environmental Data Sovereignty (FEEDS) Project takes a participatory action, citizen science approach for early detection and warning of climate change impacts on food security, sovereignty, and solastalgia. The objective of this project is to customize and implement a sustainable digital platform that enables real-time decision-making and engagement among community members, decision makers, and researchers. On the basis of the principles of Two-Eyed Seeing [60], this study aims to partner with Indigenous communities for early detection and management of climate change as it relates to probable impacts on food systems and human health using a digital rapid response platform. This paper describes the FEEDS

Project protocol and its application in a subarctic Indigenous community in Canada.

Methods

Study Design

The FEEDS study is being implemented using a quasi-experimental design, which enables exploration of the links between environment, mental health, and food systems. The primary goal is to understand how early detection of climate change risks influences decision-making to improve management of solastalgia, food access and acquisition practices. The quasi-experimental design allows for the capture of natural experiments (ie, food system impacts resulting from environmental changes such as early ice road thaw) and pre- and posttests to assess the influence of specific climate change adaptation strategies. Pre- and posttests will include collecting data at baseline (before the implementation of a climate change preparedness or adaptation strategy) and at several time points after the implementation of a strategy. These data will elucidate changes in the knowledge or perceptions of community members about climate change impacts, changes in preparedness and adaptation behaviors, and specific effects of strategies on outcomes including food security status, food sovereignty, and solastalgia. Overall, this study design provides the flexibility required to adapt to emerging community needs over time.

FEEDS is part of the Smart Platform (DEPtH Lab) [53], a digital epidemiological and citizen science initiative that enables ethical surveillance, integrated knowledge translation, and behavioral and policy interventions. This platform is informed by the Smart Framework, a theoretical framework [52] that integrates citizen science, community-based participatory research, and systems science to conduct population health research in the digital age.

Citizen science facilitates active citizen participation in all phases of research, and when combined with community-based research methods, it can enable local solutions to global problems [52]. When added to systems science, this approach offers a unique opportunity to capture a holistic perspective and unpack underlying mechanisms for complex problems using big data [52]. More importantly, in partnership with Indigenous researchers, the platform integrates the Smart Framework with the principles of Ownership, Control, Access, and Possession [63] to not only coconceptualize features and cocreate knowledge but also to ensure data sovereignty through community ownership of data. The FEEDS study highlights Traditional Knowledge about the environment and food systems, Indigenous research methods, and Western digital citizen science methods to facilitate Two-Eyed Seeing.

Setting

This project is being implemented first in a subarctic community with road access in northwest Saskatchewan, Canada, the Northern Village of Île-à-la-Crosse. Sakitawak, the Cree name for Île-à-la-Crosse, translates to *the place where the river flows out* [64]. Sakitawak represents the geographic location of the community on the lake of Île-à-la-Crosse, which made it a strategic location for the fur trade. Established in 1778, Île-à-la-Crosse is the second oldest community in Saskatchewan, with a population of approximately 1300 [64]. The median age of residents was 29 years in 2016, with approximately 65% of residents aged 15 to 64 years. Île-à-la-Crosse is a predominantly Métis community (77%), and Northern Michif is the traditional language [65]. The community celebrates the heritages of both European and First Nations. Commercial fishing, wild rice harvesting, forestry, a hospital, and a school are the primary sources of employment in the community. Mobile and Wi-Fi internet plans provide data access to community members, with most citizens aged ≥13 years owning smartphones. Moreover, the presence of a cell tower in Île-à-la-Crosse offers reliable access to cellular data. Wi-Fi and cellular data access vary widely within and between communities; hence, it is not always the case that remote communities have lower access.

Citizen Scientist Recruitment and Engagement

Citizen science can range from contribution and collaboration to the cocreation of knowledge with citizens [52]. This project was coconceptualized with the Île-à-la-Crosse Citizen Scientist Advisory Council, which includes youth, Elders, Indigenous Knowledge Keepers, and decision makers of the jurisdiction of Île-à-la-Crosse. The primary role of the Advisory Council is to represent the interests of the community members and guide the governance of project development, implementation, and evaluation. All Council members are provided with Can $150 (US $119.30) as honoraria for each meeting to respect their time and guidance.

The Council leads the citizen recruitment strategy. Community members aged 13 years and older are invited to participate in the project as citizen scientists. Citizen scientists can actively engage in the research process from data collection to knowledge translation [52,53,66]. Citizen scientists determine their level of participation, but unlike traditional research projects, they can contribute to cocreating project objectives as community needs change. This participatory approach ensures that citizens are not passively providing data and can instead engage with researchers and decision makers to shape solutions or outcomes of interest. For example, citizens can anonymously and directly communicate information about a community emergency with decision makers through a front-end mobile app via a user-triggered messaging system. Citizen science also plays an important role in facilitating self-determination and self-governance, as citizens are stewards of their own data and decision-making in the community.

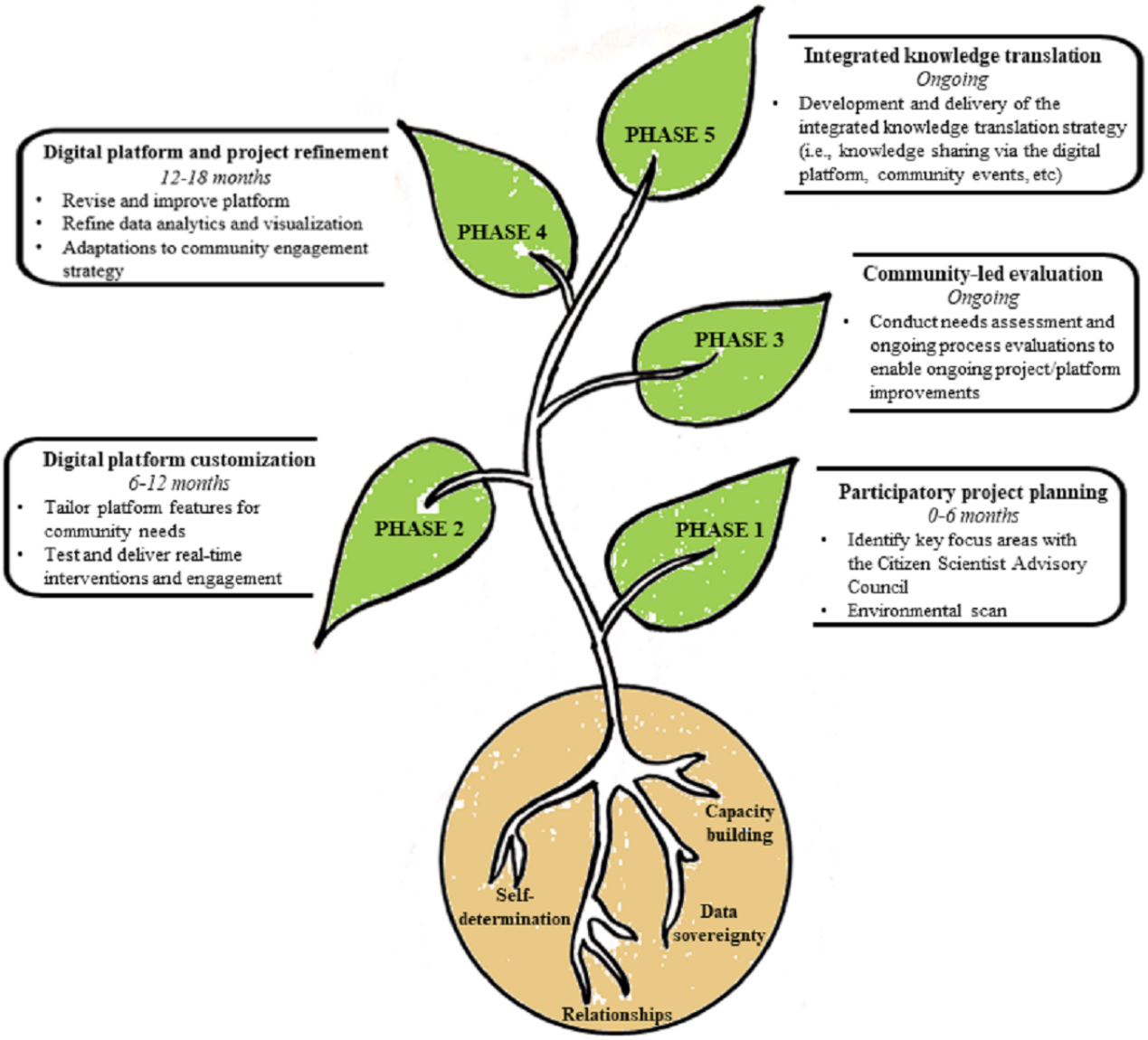
To obtain a representative community sample, the recruitment and engagement strategy aims to enroll citizens across various sociodemographic, gender, and digital literacy categories. Key decision makers and knowledge keepers are first approached to identify appropriate venues for engagement to invite citizens to the FEEDS Project. Inclusion criteria includes citizens aged ≥13 years who own or have access to smartphones. Citizens are recruited by disseminating project information through social media, the community radio station, the office of the Mayor, and the email list of the school board. Given the urgent and sensitive nature of addressing climate change impacts on mental health and food systems, the Advisory Council does not consider it ethical to randomize or limit citizen participation in this project [67].

Study Protocol

Overview

This study is being implemented in five iterative phases in partnership with the Northern Village of Île-à-la-Crosse. The phases include: (1) participatory project planning, (2) digital platform customization, (3) community-led evaluation, (4) digital platform and project refinement, and (5) integrated knowledge translation. Figure 1 summarizes the FEEDS Project phases (leaves), associated tasks and timelines, and the core principles (roots) of self-determination, relationships with communities, data sovereignty, and capacity building.

Figure 1. The Food Equity and Environmental Data Sovereignty Project overview.



Phase 1: Participatory Project Planning (0 to 6 Months)

The project is currently in phase 1, with the Advisory Council convening with the lead FEEDS researchers once every 2 months. The main agenda for the Council meetings revolves around the following themes: (1) rapid response to environmental disasters or hazards; (2) sustainability of the digital platform; (3) food and data sovereignty; (4) real-time intervention design for mental wellness; (5) citizen engagement features of the smartphone app; and (6) decision-making dashboard features and functionality. As part of this process, the Council has identified existing and emerging needs to address climate change–related impacts on community health. In phase 1, we are completing an environmental scan to create an inventory of available resources and programming for food security and sovereignty, solastalgia, and mental wellness, as well as climate change adaptation and preparedness strategies in the community. The findings from this scan will inform digital climate change platform customization.

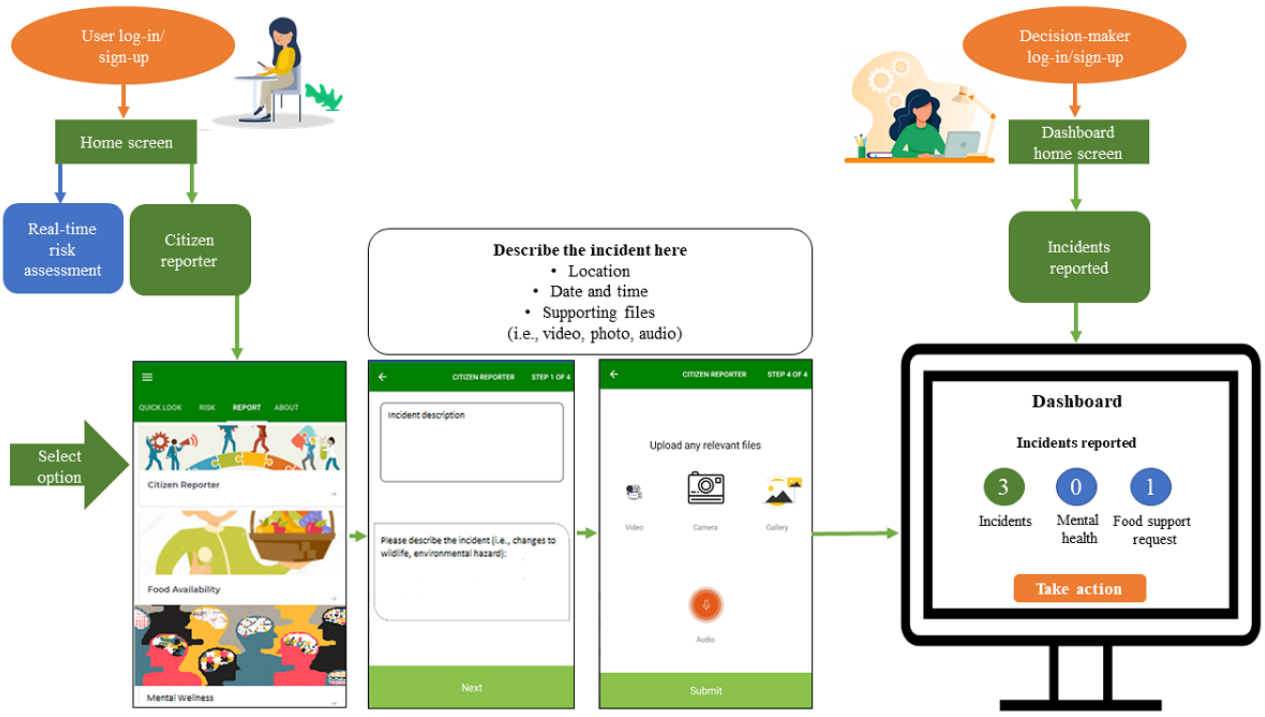
Phase 2: Digital Climate Change Platform Customization (6-12 Months)

As part of the Smart Platform [53], a digital platform has been developed to address existing and emerging population health crises. Using citizen-owned smartphones, a mobile app can be downloaded by citizens to share information about relevant community issues. Data from this app are relayed in real time

to a digital decision-making dashboard that is securely accessed by the Mayor of Île-à-la-Crosse.

Given the increasing concern over the adverse impacts of climate change on food systems and health, this digital platform is being adapted to capture relevant environmental, food, and solastalgia-related data in the community of Île-à-la-Crosse (Figure 2). The Advisory Council is leading the conversation regarding customization of digital platform features to address three key objectives: (1) ethical monitoring of risk that is conducted by engaging citizens in real time, (2) real-time interventions to mitigate risk by providing citizens with community-specific alerts, and (3) implementation of a digital decision-making dashboard to facilitate Indigenous self-governance and data sovereignty. There are three guiding principles that will enable the achievement of these objectives: (1) citizen empowerment and data ownership to maximize active engagement, (2) privacy to ensure that sensitive data such as citizen location are not stored in external servers [52,53], and (3) security and scalability to replicate the platform across multiple jurisdictions. The office of the Mayor is leading the development and coordination of rapid response strategies in the community.

Figure 2. Prototype of the digital dashboard for decision-making.



Phase 3: Community-Led Evaluation (Ongoing)

After an initial needs assessment, process evaluations will be conducted throughout the project to ensure that the app and dashboard are designed with relevant features for citizens and decision makers. Textbox 1 summarizes the key questions to be addressed by each evaluation type. The timeline of the evaluations is set by the Advisory Council; however, a needs assessment was conducted at the beginning of the project, with process evaluations scheduled annually. A consistent evaluation will ensure that updates and improvements are made to the platform in a timely manner.

Textbox 1. Summary of evaluation activities.

Needs assessment (year 1)

- What are the key concerns of the community regarding?
  - Food security and sovereignty
  - Climate change and environmental events or hazards
  - Existing and emerging mental health issues as they relate to climate change (ie, solastalgia and eco-anxiety)
- What types of programming, services, or resources are available to address?
  - Food insecurity and sovereignty (including but not limited to food access, availability, and traditional food acquisition practices)
  - Climate change and/or environmental events (ie, environmental hazards and changes in biodiversity and/or wildlife)
  - Community mental health
- What technology, if any, is the community currently using to address concerns above?
- What services, resources, and knowledge would help improve the community's response to concerns above?
- How does the community envision the digital platform (app+dashboard) to address climate change, food systems, and related mental health issues?
- What features would be useful in the digital platform?

Engagement or evaluation activity

- Environmental scan
- Advisory Council consultation
- Key informant interviews
  - Indigenous Knowledge Keepers
  - Community Mayor

Process evaluation (annually)

- To what extent has the digital platform helped the community address issues related to?
  - Food security and sovereignty
  - Climate change and environmental events or hazards
  - Related mental health issues
- To what extent has the digital dashboard helped decision makers respond to issues related to the concerns above?
- What are some areas of improvement for the digital platform (app+dashboard)?
- Are there differences between app users and nonusers?
- Are certain subgroups more or less likely to use certain app features?

Engagement or evaluation activity

- Key informant interviews
- Evaluation survey administered via smartphone app (modified Mobile App Rating Scale [68] and Knowledge Uptake and Utilization Tool [69])
- Focus groups with citizens (groups of 6-8 people with representation from sex- and gender-diverse citizens, across age groups, as well as app user and nonuser groups)

Phase 4: Digital Platform and Project Refinement (12-18 Months)

Consistent, evidence-based adaptation of the digital platform will be conducted using big data ethically sourced from citizens. These adaptations ensure that both dashboard data analytics and app-based engagement are continuously enhanced. As digital dashboards are designed in close collaboration with the decision makers, the evaluation activities will engage decision makers at regular intervals to obtain their feedback to advance data analytics based on their needs. This process is also part of the overarching phase of integrated knowledge translation.

Real-time engagement is a critical part of this project; thus, the engagement strategy will be adapted and refined throughout the project to encourage citizen participation. Using human-centered

artificial intelligence and citizen science, the platform improves engagement continuously by refining the app based on citizen input. As engagement will depend on behaviors, emotions, expectations, and perceptions of the citizens, human-centered artificial intelligence will develop solutions that will capture the context and intention of these factors to further human-machine (app) interactions. For example, if a particular citizen is engaging more during the early morning due to their work schedule, the platform will develop algorithms to engage that citizen in the morning. This approach will enhance evidence-based engagement, improve the reliability and validity of artificial intelligence algorithms, and continuously refine the product codeveloped with citizens.

Overarching Phase: Integrated Knowledge Translation (Ongoing)

The success of this platform will depend on the overarching phase of integrated knowledge translation that integrates the Smart Framework [52] with Traditional Knowledge to ensure Two-Eyed Seeing [60] in the project conceptualization, development, implementation, evaluation, and refinement. The Smart Platform combines citizen science, community-based participatory research, and systems science to conduct population health intervention research in the digital age [52,53]. By integrating this approach of the framework with the Traditional Knowledge of Indigenous communities, we are working to decolonize how big data and artificial intelligence are used in advancing equity. Integrated knowledge translation ultimately promotes community input for climate adaptation strategies at every phase and is critical for vertical (to larger communities) and horizontal (increasing platform features) scale-up.

Knowledge translation activities include knowledge sharing via the digital platform with citizens and decision makers, web-based and in-person events, social media, local radio, as well as reports and publications. An important aspect of data sovereignty is the control of where, with whom, how, and when project data are shared. Hence, the data collected through the FEEDS Project belong to the citizens and community where the project is based, and Île-à-la-Crosse along with the Citizen Scientist Advisory Council guides data governance.

Data Collection and Analysis

This project collects quantitative and qualitative data by engaging citizens through the FEEDS app. In particular, data on environmental changes, hazards, and events are collected to track the environmental impacts on community food systems and mental health. Food-specific data, including food availability, access, acquisition practices, and connections to environmental conditions, are used to identify resources, programming, or policy solutions within the community. Impacts on health are also tracked by asking citizens about their mental, physical, spiritual, and emotional well-being. These time-stamped big data include both subjective ecological momentary assessments and objective sensor data [52].

Traditional Knowledge, citizen perspectives, and decision maker feedback are critical to understanding knowledge uptake and use, as well as designing and delivering culturally responsive interventions for climate change preparedness, food sovereignty, and solastalgia. The smartphone app, focus group discussions, and key informant interviews will capture relevant contextual information to understand specific issues in the community, barriers to, and opportunities for climate change adaptation and preparedness. Qualitative data collection, particularly digital storytelling, can play an important role in passing Traditional Knowledge to future generations in the community.

Big data from FEEDS can be linked with data from other databases, including repositories of climate change (ie, Arctic observatories) and weather data (ie, Environment and Climate Change Canada) to leverage existing sources that have historical and prospective data that will enhance prediction models.

All citizen data will be anonymized; however, citizens have the option to identify themselves to community decision makers to seek help. Before data collection, citizens provide informed consent using the app. To ensure confidentiality, data are encrypted before being stored on smartphones and streamed to servers when the devices establish a Wi-Fi connection. Permissions built into the app are restricted so that the app cannot access personally identifiable information that is present on smartphones (eg, contact lists or network sites visited). MAC address anonymization is used to protect citizen scientists' data. Citizens are also introduced to the *pause* functionality—a key privacy component—which allows participants to disable monitoring for a set duration. In the case of lost or stolen phones, participants do not have to worry about data breaches, as study data on phones are strongly encrypted. Once data have been uploaded, they are stored on the secure University of Saskatchewan servers for 10 years.

All citizen scientists will have the option to drop out of the study through the app anytime they wish. Moreover, citizens will be provided with study emails to contact the investigators with questions and concerns and to remove themselves from the study anytime they wish.

Mixed methods analyses will be conducted immediately after data collection to ensure timely dissemination of findings, which may impact app features and/or community decision-making. Each short- and long-term objective will be assessed beginning with descriptive analyses to generate accurate population or subpopulation profiles. This will enable all further regression analyses to consider the intersection of multiple identities and sex and gender variations. Profiles that reflect the behavior or outcomes of subpopulations will be constructed. For example, sex and gender differences in the perception of app features and usefulness in association with age and digital literacy status (urban, rural, and remote) will be delineated to enable refinement of the platform. Missing data will be rigorously explored and addressed appropriately to ensure maximum use of objective and subjective data. Missing patterns will be explored before applying imputation or deletion strategies for different mechanisms: ignorable missing (random missing) and nonignorable missing [70]. Comprehensive exploration will also be conducted to identify potential ignorable missing (random) or nonignorable missing data across the intersection of sex and gender spectra. As variation in app use is expected among citizens, understanding and addressing missing data

through imputation or deletion strategies will be critical to address the project objectives [70].

Results

The FEEDS Project is currently in phase 1. The Advisory Council is comprised of 8 citizen scientists, including 4 youth, 2 Elders, and 2 decision makers. Other communities in the north will be invited to collaborate and customize the digital platform as part of the FEEDS scale-up. The FEEDS Project was approved by the research ethics boards of the University of Regina and the University of Saskatchewan through a synchronized review protocol (REB# 2017-29).

Discussion

Food equity and environmental data sovereignty are key components of climate justice. Food equity includes the right for all people to consume, grow, and acquire healthy and affordable food and involves eliminating systemic barriers within food systems [27,28,71,72]. Food equity requires food security and food sovereignty and promotes the ability of citizens to participate in decision-making about food systems [73,74]. The sovereignty of environmental and health data within this study is critical, especially for Indigenous communities to enable self-governance.

The FEEDS Project takes a decolonized approach to research using the Smart Framework and principles of Two-Eyed Seeing. The unique digital platform promotes data sovereignty, as communities are the stewards of their own data. The issues of climate change, food inequity, and solastalgia require innovative solutions. The rapid response enabled via digital platforms combined with the wealth of Traditional Knowledge about the environment and food systems is essential not only to address these issues in partnership with Indigenous communities but also for conversations about climate action and justice, globally.

Citizen science has played a vital role in the ecological sciences and has great potential to combat existing and emerging health crises if citizens' data can be anonymized and effectively shared with citizens and their communities [52]. The FEEDS Project demonstrates how advancing citizen science can enable big data generation to address complex issues that intersect multiple disciplines and sectors.

For this initiative to be successful, capacity building is critical for ongoing work with the jurisdiction of Île-à-la-Crosse. The FEEDS Project provides a digital infrastructure for monitoring, managing, and eventually mitigating adverse climate change–related impacts on local food systems and mental health. Ultimately, community capacity will ensure the sustainability of this infrastructure. The Advisory Council provides a space for community members, including youth and Elders, to meet and learn from one another. In Île-à-la-Crosse, adjacent initiatives, including digital literacy programs, are being set up to ensure accessibility and inclusion of community members across all age groups. The FEEDS Project can be adapted and scaled up to other northern communities facing similar environmental and food system challenges.

In addition to the data ownership and privacy concerns covered in the *Methods* section, another contextual consideration for project success is addressing internet inequity. Internet inequity refers to differential access to the internet based on the wealth of a country (high-, low-, or middle-income), geographic region (urban, rural, or remote), and socioeconomic status, gender, age, or ethnicity of the citizens [52]. Rural and remote communities facing barriers to internet connectivity are arguably the most adversely impacted by climate change and food insecurity, so it is important to consider whom we may be leaving out by going digital. The digital divide is a complex phenomenon; however, countries such as Canada are pledging resources to enable equitable access to rural and remote areas [75-78]. Although it is beyond the scope of this project to address these systemic issues, we are working with policymakers and communities as part of the Smart Platform to improve internet access for citizens. For example, we are providing smartphones and data plans to enable citizen participation and working with local community organizations to provide venues for free Wi-Fi access.

The FEEDS Project takes a novel digital citizen science approach to understand and address climate change, food equity, and solastalgia in the 21st century. Climate change is taking an inevitable toll on food systems, with remote, Indigenous communities disproportionately impacted in Canada. Combining the principles of Two-Eyed Seeing and the Smart Framework, the FEEDS Project provides early detection and potential for mitigation of adverse environmental, food system, and mental health impacts, while enabling data sovereignty and self-governance.

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Conflicts of Interest

None declared.

References

1. Lam S, Dodd W, Skinner K, Papadopoulos A, Zivot C, Ford J, et al. Community-based monitoring of Indigenous food security in a changing climate: global trends and future directions. Environ Res Lett 2019 Jul 05;14(7):073002. [doi: 10.1088/1748-9326/ab13e4]
2. Kovats S, Hales S, Campbell-Lendrum D, Rocklov J, Honda Y, Lloyd S. Global risk assessment of the effect of climate change on selected causes of death in 2030s and 2050s. ISEE Conference Abstracts 2015 Aug 20;2015(1):1204. [doi: 10.1289/isee.2015.2015-1204]
3. Harper S, Cunsolo A, Babujee A, Coggins S, De Jongh E, Rusnak T, et al. Trends and gaps in climate change and health research in North America. Environ Res 2021 Aug;199:111205 [FREE Full text] [doi: 10.1016/j.envres.2021.111205] [Medline: 33961824]
4. Vermeulen SJ, Campbell BM, Ingram JS. Climate change and food systems. Annu Rev Environ Resour 2012 Nov 21;37(1):195-222. [doi: 10.1146/annurev-environ-020411-130608]
5. Watts N, Adger WN, Ayeb-Karlsson S, Bai Y, Byass P, Campbell-Lendrum D, et al. The Lancet Countdown: tracking progress on health and climate change. Lancet 2017 Mar 18;389(10074):1151-1164. [doi: 10.1016/S0140-6736(16)32124-9] [Medline: 27856085]
6. Myers SS, Smith MR, Guth S, Golden CD, Vaitla B, Mueller ND, et al. Climate change and global food systems: potential impacts on food security and undernutrition. Annu Rev Public Health 2017 Mar 20;38(1):259-277. [doi: 10.1146/annurev-publhealth-031816-044356] [Medline: 28125383]
7. McMichael A, Campbell-Lendrum D, Corvalan C, Ebi K, Githeko A, Scheraga J, et al. Climate Change and Human Health: Risks and Responses. Geneva: World Health Organization; 2003.
8. Climate effects on health. Centers for Disease Control and Prevention. URL: https://www.cdc.gov/climateandhealth/effects/default.htm [accessed 2021-06-05]
9. Shukla PR, Skea J, Buendia EC, Masson-Delmotte V, Pörtner HO, Roberts DC, et al. IPCC, 2019: Climate Change and Land: an IPCC special report on climate change, desertification, land degradation, sustainable land management, food security, and greenhouse gas fluxes in terrestrial ecosystems. Intergovernmental Panel on Climate Change (IPCC). URL: https://www.ipcc.ch/srccl/ [accessed 2021-06-05]
10. Saxena AK, Fuentes XC, Herbas RG, Humphries DL. Indigenous food systems and climate change: impacts of climatic shifts on the production and processing of native and traditional crops in the Bolivian Andes. Front Public Health 2016 Mar 03;4:20 [FREE Full text] [doi: 10.3389/fpubh.2016.00020] [Medline: 26973824]
11. Nutrition Division. Indigenous Peoples' Food Systems: the many dimensions of culture, diversity and environment for nutrition and health. Food and Agriculture Organization of the United Nations. 2009. URL: http://www.fao.org/documents/card/en/c/250ee74b-9c3f-5dc1-8086-6e0b78b22795/ [accessed 2021-06-05]
12. Kuhnlein HV, Erasmus B, Spigelski D, Burlingame B, editors. Indigenous Peoples' Food Systems & Well-being: Interventions & Polices for Healthy Communities. Rome, Italy: Food and Agriculture Organization of the United Nations; 2013:1-437.
13. Ford JD. Indigenous health and climate change. Am J Public Health 2012 Jul;102(7):1260-1266. [doi: 10.2105/AJPH.2012.300752] [Medline: 22594718]
14. Turner NJ, Berkes F, Stephenson J, Dick J. Blundering intruders: extraneous impacts on two indigenous food systems. Hum Ecol 2013 Jun 9;41(4):563-574. [doi: 10.1007/s10745-013-9591-y]
15. Myette E, Riva M. Surveying the complex social-ecological pathways between resource extraction and Indigenous Peoples' health in Canada: A scoping review with a realist perspective. The Extractive Industries and Society 2021 Jun;8(2):100901. [doi: 10.1016/j.exis.2021.100901]
16. Jalbert K, Willow A, Casagrande D, Paladino S, editors. Extractive industries in global economies. In: ExtrACTION: Impacts, Engagements, and Alternative Futures. New York: Routledge; 2017:1-266.
17. Barber M, Jackson S, Dambacher J, Finn M. The persistence of subsistence: qualitative social-ecological modeling of indigenous aquatic hunting and gathering in tropical Australia. Ecol Soc 2015;20(1):200160. [doi: 10.5751/es-07244-200160]
18. Furgal C, Seguin J. Climate change, health, and vulnerability in Canadian northern Aboriginal communities. Environ Health Perspect 2006 Dec;114(12):1964-1970 [FREE Full text] [doi: 10.1289/ehp.8433] [Medline: 17185292]
19. Lemke S, Delormier T. Indigenous Peoples' food systems, nutrition, and gender: Conceptual and methodological considerations. Matern Child Nutr 2017 Nov 22;13 Suppl 3:e12499 [FREE Full text] [doi: 10.1111/mcn.12499] [Medline: 29359433]
20. Food and Agriculture Organization. Rome Declaration on World Food Security and World Food Summit Plan of Action. World Food Summit 13-17 November 1996. Rome, Italy: Food and Agriculture Organization of the United Nations; 1996:1-43.
21. Cidro J, Adekunle B, Peters E, Martens T. Beyond food security: understanding access to cultural food for urban Indigenous People in Winnipeg as Indigenous food sovereignty. Can J Urban Res 2015;24(1):24-43 [FREE Full text]
22. Delormier T, Marquis K. Building healthy community relationships through food security and food sovereignty. Curr Devel Nutr 2018;3(2):25-31. [doi: 10.1093/cdn/nzy088]
23. Desmarais AA, Wittman H. Farmers, foodies and First Nations: getting to food sovereignty in Canada. J Peasant Stud 2014 Jan 17;41(6):1153-1173. [doi: 10.1080/03066150.2013.876623]

24. Rocha C, Liberato RS. Food Sovereignty for Cultural Food Security. Food Cult Soc 2015 Apr 29;16(4):589-602. [doi: 10.2752/175174413x13673466712047]
25. Settee P, Shukla S. Indigenous Food Systems: Concepts, Cases, and Conversations. Toronto, Ontario: Canadian Scholars; 2020.
26. Wendimu MA, Desmarais AA, Martens TR. Access and affordability of "healthy" foods in northern Manitoba? The need for Indigenous food sovereignty. Can Food Studies 2018 May 23;5(2):44-72. [doi: 10.15353/cfs-rcea.v5i2.302]
27. Desmarais AA, Wiebe N, Wittman H. Food Sovereignty in Canada: Creating Just and Sustainable Food Systems. Black Point, Nova Scotia: Fernwood Publishing; 2011:1-232.
28. Wittman H, Desmarais AA, Wiebe N. Why should Canada pursue food sovereignty? – nurturing food sovereignty in Canada. Food Sover Can Creat Just Sustain Food Syst 2012 Jun 08:1-15. [doi: 10.22230/cjnser.2012v3n1a103]
29. Thompson S, Kamal AG, Alam MA, Wiebe J. Community development to feed the family in northern manitoba communities: evaluating food activities based on their food sovereignty, food security, and sustainable livelihood outcomes. Can J Nonprof Soc Econ Res 2012 Dec 07;3(2):43-66. [doi: 10.22230/cjnser.2012v3n2a121]
30. Ratima M, Martin D, Castleden H, Delormier T. Indigenous voices and knowledge systems - promoting planetary health, health equity, and sustainable development now and for future generations. Glob Health Promot 2019 Apr 09;26(S3):3-5. [doi: 10.1177/1757975919838487] [Medline: 30964406]
31. Clapp J. Food security and food sovereignty. Dialogues in Human Geography 2014 Jun 25;4(2):206-211. [doi: 10.1177/2043820614537159]
32. D'Odorico P, Carr J, Davis K, Dell'Angelo J, Seekell D. Food inequality, injustice, and rights. Bioscience 2019 Mar 01;69(3):180-190 [FREE Full text] [doi: 10.1093/biosci/biz002] [Medline: 30899122]
33. Hossain MB, Long MA, Stretesky PB. Welfare state spending, income inequality and food insecurity in affluent nations: a cross-national examination of OECD countries. Sustainability 2020 Dec 31;13(1):324. [doi: 10.3390/su13010324]
34. Leventon J, Laudan J. Local food sovereignty for global food security? Highlighting interplay challenges. Geoforum 2017 Oct;85:23-26. [doi: 10.1016/j.geoforum.2017.07.002]
35. Darma R, Rahmadanih R, Tenriawaru N, Amandaria R. Climate change adaptation in the perspectives of food, energy crisis, and environmental degradation for food sovereignty in Indonesia. Int J Agricult Sys 2014;2(1):77-89. [doi: 10.20956/ijas.v1i1.24]
36. Panikkar B, Lemmond B. Being on land and sea in troubled times: climate change and food sovereignty in Nunavut. Land 2020 Dec 10;9(12):508. [doi: 10.3390/land9120508]
37. Conversi D. Sovereignty in a changing world: from Westphalia to food sovereignty. Globalizations 2016 Feb 24;13(4):484-498. [doi: 10.1080/14747731.2016.1150570]
38. Edelman M, Weis T, Baviskar A, Borras SM, Holt-Giménez E, Kandiyoti D, et al. Introduction: critical perspectives on food sovereignty. J Peasant Studies 2014 Oct 15;41(6):911-931. [doi: 10.1080/03066150.2014.963568]
39. Jones AD. Food insecurity and mental health status: a global analysis of 149 countries. Am J Prev Med 2017 Aug;53(2):264-273 [FREE Full text] [doi: 10.1016/j.amepre.2017.04.008] [Medline: 28457747]
40. Pourmotabbed A, Moradi S, Babaei A, Ghavami A, Mohammadi H, Jalili C, et al. Food insecurity and mental health: a systematic review and meta-analysis. Public Health Nutr 2020 Mar 16;23(10):1778-1790. [doi: 10.1017/s136898001900435x]
41. Nagata JM, Palar K, Gooding HC, Garber AK, Bibbins-Domingo K, Weiser SD. Food insecurity and chronic disease in US young adults: findings from the national longitudinal study of adolescent to adult health. J Gen Intern Med 2019 Dec;34(12):2756-2762 [FREE Full text] [doi: 10.1007/s11606-019-05317-8] [Medline: 31576509]
42. Laraia B. Food insecurity and chronic disease. Adv Nutr 2013 Mar 01;4(2):203-212 [FREE Full text] [doi: 10.3945/an.112.003277] [Medline: 23493536]
43. Hall NL, Crosby L. Climate change impacts on health in remote indigenous communities in Australia. Int J Environ Health Res 2020 Jun 16:1-16. [doi: 10.1080/09603123.2020.1777948] [Medline: 32543219]
44. My fear is losing everything: the climate crisis and First Nations' right to food in Canada. Human Rights Watch. 2020. URL: https://www.hrw.org/report/2020/10/21/my-fear-losing-everything/climate-crisis-and-first-nations-right-food-canada [accessed 2021-06-15]
45. Morello-Frosch R, Pastor M, Sadd J, Shonkoff S. The climate gap: inequalities in how climate change hurts Americans and how to close the gap. PERE Publications. 2009. URL: https://dornsife.usc.edu/pere/climategap/ [accessed 2021-06-18]
46. Hoerner J, Robinson N. A climate of change: African Americans, global warming, and a just climate policy for the U.S. Reimagine. URL: https://www.reimaginerpe.org/cj/research/climateofchangeafricanamericans [accessed 2021-06-05]
47. White-Newsome JL. A policy approach toward climate justice. Black Schol 2016 Sep 22;46(3):12-26. [doi: 10.1080/00064246.2016.1188353]
48. Gonzalez C. Racial capitalism, climate justice, and climate displacement. Onati Soc Leg Ser 2020 Feb 04;11(1):108-147. [doi: 10.35295/osls.iisl/0000-0000-0000-1137]
49. Galway L, Beery T, Jones-Casey K, Tasala K. Mapping the solastalgia literature: a scoping review study. Int J Environ Res Public Health 2019 Jul 25;16(15):2662 [FREE Full text] [doi: 10.3390/ijerph16152662] [Medline: 31349659]
50. Food Security Monitoring Systems (FSMS) - Technical guidance sheet. World Food Programme. 2014. URL: https://www.wfp.org/publications/monitoring-food-security-technical-guidance-sheet [accessed 2021-08-17]

51. Beddington JR, Asaduzzaman M, Clark ME, Bremauntz A, Guillou MD, Jahn MM, et al. The role for scientists in tackling food insecurity and climate change. Agric Food Secur 2012;1(1):10. [doi: 10.1186/2048-7010-1-10]
52. Katapally TR. The SMART Framework: Integration of citizen science, community-based participatory research, and systems science for population health science in the digital age. JMIR Mhealth Uhealth 2019 Aug 30;7(8):e14056 [FREE Full text] [doi: 10.2196/14056] [Medline: 31471963]
53. Katapally TR, Bhawra J, Leatherdale ST, Ferguson L, Longo J, Rainham D, et al. The SMART study, a mobile health and citizen science methodological platform for active living surveillance, integrated knowledge translation, and policy interventions: longitudinal study. JMIR Public Health Surveill 2018 Mar 27;4(1):e31 [FREE Full text] [doi: 10.2196/publichealth.8953] [Medline: 29588267]
54. Canada's most vulnerable: Improving health care for First Nations, Inuit and Métis seniors. Canadian Health Workforce Network (CHWN). 2013. URL: https://tinyurl.com/3u8648et [accessed 2021-06-04]
55. Pollock RM, Whitelaw GS. Community-based monitoring in support of local sustainability. Loc Environ 2005 Jun;10(3):211-228. [doi: 10.1080/13549839.2005.9684248]
56. Johnson N, Alessa L, Behe C, Danielsen F, Gearheard S, Gofman-Wallingford V, et al. The Contributions of Community-Based Monitoring and Traditional Knowledge to Arctic Observing Networks: Reflections on the State of the Field. ARCTIC 2015 Jan;68(5):28 [FREE Full text] [doi: 10.14430/arctic4447]
57. Kipp A, Cunsolo A, Gillis D, Sawatzky A, Harper SL. The need for community-led, integrated and innovative monitoring programmes when responding to the health impacts of climate change. Int J Circumpolar Health 2019 May 08;78(2):1517581 [FREE Full text] [doi: 10.1080/22423982.2018.1517581] [Medline: 31066653]
58. Abu R, Reed MG, Jardine TD. Using two-eyed seeing to bridge Western science and Indigenous knowledge systems and understand long-term change in the Saskatchewan River Delta, Canada. Int J Water Res Develop 2019 Jan 21;36(5):757-776. [doi: 10.1080/07900627.2018.1558050]
59. Bartlett C, Marshall M, Marshall A. Two-Eyed Seeing and other lessons learned within a co-learning journey of bringing together indigenous and mainstream knowledges and ways of knowing. J Environ Stud Sci 2012 Aug 16;2(4):331-340. [doi: 10.1007/s13412-012-0086-8]
60. Iwama M, Marshall M, Marshall A, Bartlett C. Two-eyed seeing and the language of healing in community-based research. Can J Native Educ 2009;32(2):3-23 [FREE Full text]
61. Martin D. Two-eyed seeing: a framework for understanding indigenous and non-indigenous approaches to indigenous health research. Can J Nurs Res 2012 Jun;44(2):20-42. [Medline: 22894005]
62. Fressigne L, Ahmad A, Coates K, Holroyd C. Hyperlocal northern food systems: cool ideas to address northern food insecurity. Northern Policy Analytics. 2020. URL: https://www.northernpolicyanalytics.com/npa-projects/hyperlocal-northern-food-systems [accessed 2021-06-05]
63. Understanding OCAP. First Nations Information Governance Centre. 2020. URL: https://fnigc.ca/ocap-training/ [accessed 2021-06-04]
64. Patuanak - English River First Nation. Cameco Northern Saskatchewan. 2020. URL: https://www.cameconorth.com/community/community-profiles/patuanak-english-river-first-nation [accessed 2021-06-05]
65. Healthy aging in place environmental scan île-à-la-crosse. Saskatchewan Population Health and Evaluation Research Unit (SPHERU). 2013. URL: https://spheru.ca/ [accessed 2021-05-30]
66. Silvertown J. A new dawn for citizen science. Trends Ecol Evol 2009 Sep;24(9):467-471. [doi: 10.1016/j.tree.2009.03.017] [Medline: 19586682]
67. Leatherdale ST. Natural experiment methodology for research: a review of how different methods can support real-world research. Int J Soc Res Methodol 2018 Jul 02;22(1):19-35. [doi: 10.1080/13645579.2018.1488449]
68. Stoyanov SR, Hides L, Kavanagh DJ, Zelenko O, Tjondronegoro D, Mani M. Mobile app rating scale: a new tool for assessing the quality of health mobile apps. JMIR Mhealth Uhealth 2015 Mar 11;3(1):e27 [FREE Full text] [doi: 10.2196/mhealth.3422] [Medline: 25760773]
69. Skinner K. Developing a tool to measure knowledge exchange outcomes. Can J Program Eval 2007;22(1):49-73 [FREE Full text]
70. Little R, Rubin D. Statistical Analysis with Missing Data, Second Edition. Hoboken, New Jersey, United States: John Wiley & Sons; 2002.
71. Mui Y, Khojasteh M, Judelsohn A, Sirwatka A, Kelly S, Gooch P, et al. Planning for regional food equity. J Am Plan Asso 2021 Jan 22;87(3):354-369. [doi: 10.1080/01944363.2020.1845781]
72. Desmarais A. PEASANTS SPEAK - The Vía Campesina: Consolidating an international peasant and farm movement. J Peasant Studies 2010 Sep 14;29(2):91-124. [doi: 10.1080/714003943]
73. Wittman H. Reframing agrarian citizenship: Land, life and power in Brazil. J Rural Stud 2009 Jan;25(1):120-130. [doi: 10.1016/j.jrurstud.2008.07.002]
74. Wittman H. Reworking the metabolic rift: La Vía Campesina, agrarian citizenship, and food sovereignty. J Peasant Studies 2009 Nov 19;36(4):805-826. [doi: 10.1080/03066150903353991]

75. Report of the Special Rapporteur on the promotion and protection of the right to freedom of opinion and expression, Frank La Rue. Office of the United Nations High Commissioner for Human Rights. 2011. URL: https://www2.ohchr.org/english/bodies/hrcouncil/docs/17session/A.HRC.17.27_en.pdf [accessed 2021-06-20]
76. Broadband Fund: Closing the digital device in Canada. Government of Canada. 2021. URL: https://crtc.gc.ca/eng/internet/internet.htm [accessed 2021-06-05]
77. Stepping up internet services in rural and remote locations. National Research Council Canada. 2020. URL: https://nrc.canada.ca/en/stories/stepping-internet-services-rural-remote-locations [accessed 2021-06-04]
78. We are helping over 800 rural and Indigenous communities improve their internet. Canadian Internet Registration Authority (CIRA). 2020. URL: https://www.cira.ca/blog/state-internet/helping-rural-and-indigenous-communities [accessed 2021-06-11]

Abbreviations

FEEDS: Food Equity and Environmental Data Sovereignty

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Corrigenda and Addenda

Correction: Combined Use of Web-Based and In-Person Education on Ill Health Self-management Skills in Adults With Bipolar Disorder: Protocol for a Mixed Methods Study

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In “Combined Use of Web-Based and In-Person Education on Ill Health Self-management Skills in Adults With Bipolar Disorder: Protocol for a Mixed Methods Study” (JMIR Res Protoc 2021;10(9):e25168) one error was noted.

One author's name was displayed as:

Andreas Hatzittofis

It has now been corrected to:

Andreas Chatzittofis

The correction will appear in the online version of the paper on the JMIR Publications website on September 15, 2021, together with the publication of this correction notice. Because this was made after submission to PubMed, PubMed Central, and other full-text repositories, the corrected article has also been resubmitted to those repositories.

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Protocol

Health Equity in Artificial Intelligence and Primary Care Research: Protocol for a Scoping Review

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Abstract

Background: Though artificial intelligence (AI) has the potential to augment the patient-physician relationship in primary care, bias in intelligent health care systems has the potential to differentially impact vulnerable patient populations.

Objective: The purpose of this scoping review is to summarize the extent to which AI systems in primary care examine the inherent bias toward or against vulnerable populations and appraise how these systems have mitigated the impact of such biases during their development.

Methods: We will conduct a search update from an existing scoping review to identify studies on AI and primary care in the following databases: Medline-OVID, Embase, CINAHL, Cochrane Library, Web of Science, Scopus, IEEE Xplore, ACM Digital Library, MathSciNet, AAAI, and arXiv. Two screeners will independently review all abstracts, titles, and full-text articles. The team will extract data using a structured data extraction form and synthesize the results in accordance with PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews) guidelines.

Results: This review will provide an assessment of the current state of health care equity within AI for primary care. Specifically, we will identify the degree to which vulnerable patients have been included, assess how bias is interpreted and documented, and understand the extent to which harmful biases are addressed. As of October 2020, the scoping review is in the title- and abstract-screening stage. The results are expected to be submitted for publication in fall 2021.

Conclusions: AI applications in primary care are becoming an increasingly common tool in health care delivery and in preventative care efforts for underserved populations. This scoping review would potentially show the extent to which studies on AI in primary care employ a health equity lens and take steps to mitigate bias.

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KEYWORDS

artificial intelligence; health information technology; health informatics; electronic health records; big data; data mining; primary care; family medicine; decision support; diagnosis; treatment; scoping review; health equity; health disparity

Introduction

Artificial intelligence (AI) is a field of computer science that aims to create systems that are capable of independent reasoning [1,2]. Despite tremendous gains in some industries, ranging from the perfection of recommendation systems [3] and optimizing supply chains [4] to self-driving cars and collaborative robotics [5], AI has continued to marginalize minority populations. One such example involves NorthPointe's COMPAS Core solution, an algorithm that seeks to assess the risk that recent convicts would recommit a crime [6]. The algorithm has a demonstrated bias toward labeling Black individuals as being at a high risk for recommitting a crime when compared to their White counterparts, when in reality the former were half as likely to commit the crime. While this case represents a case of algorithm bias, the bias intrinsic to other AI applications may be more subtle and therefore more likely to stay undetected.

Vulnerable populations in health care, such as women and transgender individuals, Black and Latinx populations, and those with low socioeconomic status, represent cohorts of individuals who experience significant baseline health disparities and are at heightened risk of being affected by algorithmic bias [6-8]. Pre-existing and unintended biases in the development pipeline, whether they take the form of historical, representation, or aggregation bias [9], have the potential to perpetuate deeply rooted stigma, poor cohort representation, and ineffective treatment modalities in the end-product that may further discriminate against these groups through these AI systems. For example, Obermeyer et al [10] showed that a popular health care risk–scoring algorithm recommended fewer health care assessments for Black patients than for White patients, likely because the algorithm was trained from a data set where the health care system itself contained unequal access to and lower levels of care for Black patients. Such studies reflect the need for research into fairness and AI within health care.

Primary care is the cornerstone of health care delivery and serves, in theory, as the entry point for most patients into the health care setting [11]. Historically, primary care leads medicine to recognize and attend to social determinants of health, which are strong drivers of inequitable health outcomes in vulnerable populations [12,13]. Primary care includes a wide spectrum of disease and many diverse care tasks for patients, which makes augmenting clinical practice with AI tools particularly appealing and useful. Using AI for routine tasks may allow primary care clinicians to focus on complex diagnostic and therapeutic tasks and cultivate stronger patient-physician relationships [14]. To our knowledge, only 1 other scoping review has identified current AI applications in primary care [15]. We build on their work by focusing specifically on health equity. As such, this systematic scoping review aims to (1) assess the baseline representation of these vulnerable populations in the AI applications for primary care, (2) determine whether studies are cognizant of potential biases in their results, and (3) understand how, if at all, these studies address the manner in which these biases affect the model's impact on vulnerable populations, either positively or negatively, in the primary care setting.

Methods

Scoping Review

We selected a scoping review as the best method for assessing the research landscape of AI and health equity in primary care because it offers a way to systematically identify key research gaps, opportunities, evidence, and concepts in this understudied space. This type of review differs from systematic reviews and meta-analyses in that it does not narrow the parameters of the review to a specific quality assessment. Instead, it is a systematic approach to examine the landscape of a research field using broad questions to examine both empirical and conceptual aspects [16,17]. This is particularly important in the fields of health equity, primary care, and AI, where much of the literature is currently focused on specific outcomes or aspects of care [18-21]. Equity considerations extend across multiple outcomes and therefore require a scoping review to draw overall conclusions. Our protocol, developed on the basis of seminal work by Arksey and O'Malley [16], includes six stages: (1) identification of the research question; (2) identification of relevant studies; (3) study selection; (4) data extraction; (5) collation, summarization, and reporting of the results; and (6) consultation of knowledge users. We followed the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Scoping Reviews) checklist [22] and registered our protocol with the Open Science Framework (digital object identifier: 10.17605/OSF.IO/WGSB3). To identify articles of interest, we conducted a search update on the basis of a previous study by Kueper et al [15], who conducted a systematic scoping review of AI and primary care research in May 2020.

Step 1: Identifying the Research Question

A committee of medical professionals at different levels (medical students and attending physicians) with multiple domain expertise (AI, primary care, and fairness in machine learning) and training in recognition of health care disparities led the scope of this study. We used the methodology of Arksey and O'Malley [16] and Levac et al [23] to guide the discussions for determining the research questions we sought to investigate. We considered vulnerable populations on the basis of the PROGRESS (place of residence, race/ethnicity/culture/language, occupation, gender/sex, religion, education, socioeconomic status, and social capital) criteria [8], which include the following variables to ascertain vulnerabilities: place of residence; race, ethnicity, and culture; occupation; gender; religion; education; socioeconomic status; and social capital. We identified three key domains for assessment: representation of vulnerable populations in the underlying data set relative to the intended target population, as assessed, for example, by subgroup prevalence; author reporting of the types of bias outlined by Suresh et al [9]; and whether these studies attempt to mitigate these pre-existing biases in their systems upstream of, during, or downstream of model development (Table 1).

Table 1. Research questions.

Research questions	Operational definitions
What is the representation of vulnerable individuals in the intended target population for any study on artificial intelligence within primary care?	Vulnerable populations are defined as those with known disparities as described by the following categories: • Place of residence (eg, rural) • Race, ethnicity (eg, Black) • Occupation (eg, coal miners) • Gender, sex (eg, transgender) • Religion (eg, Amish) • Education (eg, high-school only) • Socioeconomic status (eg, low income) • Social capital (eg, isolation)
How well do current studies on artificial intelligence in primary care report different types of bias that may be perpetuated as health disparities by their systems?	Data extraction elements (Table 2)
What interventions do current studies on artificial intelligence in primary care use to address harmful effects of pre-existing biases in their systems?	Example interventions are listed below: • Preprocessing • Modified data sources • Preprocessing data for fairness • Model development • Demographic parity • Equalized odds/opportunity • Disparity regularization • Counterfactual fairness • Postprocessing • Subgroup analysis • Meta-regression • Quality assurance

Steps 2 and 3: Identify Relevant Studies and Study Selection

Steps Overview

To guide the search strategy for our scoping review, we have developed a number of protocols and parameters. We will use Covidence [24] to manage our records and data throughout the review.

To retrieve all AI and primary care literature, we will use a similar search strategy and eligibility criteria documented by Kuepfer et al [15], in which a team of interdisciplinary experts iteratively refined search terms for 11 databases to reliably and robustly retrieve literature spanning AI and primary care globally. This study screened over 7900 articles to amass a total of 405 eligible articles at this domain intersection (Multimedia Appendix 1). Our populations of interest are vulnerable patients (who may or may not be explicitly recognized by the study of interest in our search strategy); we will include any AI intervention; the comparison will be the current standard of care without the AI intervention; and we will include any patient-level outcome of interest in primary care. Rather than combining vulnerable population search terms, we allow our search query to broadly include AI literature that addresses vulnerable populations implicitly (eg, only ensuring demographic parity for a primary clinical outcome) or, equally importantly, fails to do so at all. For example, Hannun et al [25] used a corpus of ambulatory electrocardiograhs and trained a deep learning model to predict arrhythmias, which may have strong implications of use in primary care, but provide no context on the demographic representation and comorbidity burden in their data sets. To confirm that we applied the methodology appropriately, 2 independent reviewers (JW and SS) will extract a random sample of 4% of titles from their initial search. Then, they will apply the title and abstract screening and full-text screening process, resolving disputes with a third reviewer. Cohen κ will then be calculated between the studies we select and those selected by Kueper et al [15]. This will be repeated until a Cohen κ of >0.80 is achieved. We will then include the 405 studies that were selected by Kueper et al [15].

We will also apply the search strategy and screening criteria applied to any new articles since Kueper et al [15]'s initial search on April 6, 2018 (Multimedia Appendix 1). Two independent reviewers (JW and SS) will first review all titles and abstracts on the basis of the defined eligibility criteria. Full-text versions of all identified articles will be independently reviewed by these 2 independent reviewers for inclusion after initial screening of titles and abstracts to determine whether any other further refinements to the eligibility criteria should be made. Disagreements will be resolved by an independent reviewer through discussion, and the selection process will be adjusted to reflect these subsequent changes. Articles for which no consensus can be reached will be included in the review. Based on guidelines from Cochrane Methods, the search strategy will be utilized once again if 12 months have passed since the initial search strategy and the date of publication [26].

Once this process is complete, a final PRISMA flow diagram [27] will be submitted to document the number of articles at

each step of identification, screening, eligibility, and inclusion. For now, a PRISMA flow diagram containing the number of queried and screened articles is available in Multimedia Appendix 2.

Databases

In line with Kueper et al [15], we searched the following databases: Medline-OVID, Embase, CINAHL, Cochrane Library, Web of Science, Scopus, IEEE Xplore, ACM Digital Library, MathSciNet, AAAI, and arXiv; these will capture published studies predominantly in the fields of medicine, computer science, and the intersection of both fields.

Step 4: Extracting the Data

We built a preliminary data framework in accordance with the suggestions of Daudt et al [28] to align data extraction with the initial research question (Table 2). One category we extracted is measuring compliance with existing AI ethics guidelines developed for the European Commission. This category was chosen after examining multiple other AI ethical guidelines, including those of the House of Lords [29] and IEEE [30]. The European Commission's guidelines were chosen because of the comprehensible key requirements, orientation toward conceptual, higher-level evaluation (rather than technical specificities), and wide adoption across the AI community [31-33]. Two authors (JW and SS) will independently extract data from the first 10 included studies and meet to determine whether the framework is specific enough for consistency and the data are sufficient for research questions outlined initially. During this process and in prior stages, it is likely that additional categories and adjustments will be made to our data extraction framework, at which time we shall consult with the research team to guide decisions on how to appropriately modify the framework. Once the reviewers reach a consensus using the data extraction framework, it will be circulated among the research team and consultation team for final comments and suggestions. Following this, additional reviewers may be brought on, in which case they are expected to match the data extracted from these first 10 included studies in order to take part in the data collection (Cohen κ>0.8). For any disputes on data extraction, a third reviewer will be involved in settling the discussion, and appropriate adjustments to the data extraction framework will be made.

Table 2. Data extraction elements.

Category	Elements appraised
Reviewer information	• Reviewer name • Reviewer comments
Bibliometrics	• First and last name of the first author • Title • Source • Year of publication • Country • Status of publication
Primary care function (adapted from Kueper et al [15])	• Diagnostic decision support: artificial intelligence–assisted diagnostics • Treatment decision support: artificial intelligence–assisted treatment, including remote management of care • Referral support: artificial intelligence–assisted support for any portion of the referral process, especially for direct referrals of patients to specialist services • Scheduling assistance: models for optimizing clinic schedules and overbooking • Future state prediction: artificial intelligence offering predictions about the future state, such as consult service utilization or prognosis of existing conditions. (this excludes predictions of one's chances of developing a health condition in the near term, which falls under diagnostic decision support) • Health care utilization analyses: artificial intelligence extracts information retrospectively to understand more about the current processes or interactions within a health care system • Knowledge base and ontology construction or use • Information extraction: artificial intelligence extracts knowledge from structured or unstructured data sources • Descriptive information provision: Artificial intelligence summarizes existing data in interpretable or useful ways • Other: function not represented above, but specifics of function will still be recorded in case a new category emerges
Author-reported intended end-users	• The intended user of the artificial intelligence product, including but not limited to patients, physicians, nurses, nurse practitioners, administrators, researchers, others, and unknown (if an end-user is not specified as the tool was still in development, a researcher was designated)
Target health condition (adapted from Kueper et al [15])	• General • Diabetes • Cancer, non-skin • Heart valves, murmurs • Musculoskeletal/joint • Dementia, cognitive impairment • Lung apnea, chronic obstructive pulmonary disease • Chronic disease, frailty • Skin cancer • Stroke, neurological • Psychiatric • Coronary artery disease • Heart failure • Hypertension • Other cardiovascular disease • Gastrointestinal/liver • Ear, nose, and throat • Eye and retina • Trauma, emergency surgery • Infection • Metabolic • Kidney and urinary tract • Immunization, reactions • Skin disorders • Obesity • Pediatric/developmental • Other

Category	Elements appraised

Data set	• Size: number of unique patients
	• Time period if applicable
	• Source of data:
	  • Electronic health record
	  • National registry
	  • Claims
	  • Remote monitoring devices (ie, smart watch or mobile phone)
	  • Other (specified)
	  • Unknown
	• Number of institutions: single or multiple
	• Setting (urban, rural, both, or unknown): We use the United States Census' County Classification Lookup Table [34] to determine whether a certain area was urban or rural. If there were multiple locations, we selected both.

Compliance with "Ethics Guidelines for Trustworthy AI" [35]: which of the 7 elements were addressed (yes/no)?	• Human agency and oversight: how well does the algorithm support human decision-making and permit oversight on its predictions? • Technical robustness and safety: how well-suited is the algorithm for its intended use? How well does it mitigate harm? • Privacy and data governance: how well does the algorithm's data ingestion and analysis pipeline respect patient privacy (eg, HIPAA compliance) and enforce safeguards against unpermitted access? • Transparency: does the artificial intelligence algorithm explain reasons for its outputs in a traceable and interpretable way? • Diversity, nondiscrimination, and fairness: how biased is the algorithm with regard to its performance? How easy is it for stakeholders to provide feedback on the algorithm's performance for its continuous development? • Societal and environmental well-being: what are the societal (eg, dehumanizing relationships) and ecological (eg, energy consumption) impacts of the algorithm? • Accountability: who is held responsible to ensure the algorithm's development, outcomes, harm, and regulation?
Model fairness and focus on health equity: is the main purpose of the study specifically outlined to improve health for a vulnerable population (yes/no)?	Must be explicitly stated in the introduction or abstract as motivation for the paper to focus on at least 1 vulnerable population (though there may be other populations studied as well) defined by any of the following categories which are largely based off of the NIMHD Research Framework [36]: • Place of residence (eg, rural) • Race, ethnicity (eg, Black African American or Latinx) • Occupation (eg, coal miners) • Gender, sex (eg, transgender) • Religion (eg, Amish) • Education (eg, low) • Socioeconomic status (eg, low income) • Social capital (eg, isolation) • Does the study include key variables that could reflect disparities across protected classes (eg, age, sex, or race/ethnicity)? • If reported, do they include these variables in their evaluation (eg, subgroup analysis to demonstrate equal performance)? • Existing biases: does the study discuss biases or potential repercussions related to vulnerable populations? [9] • Historical bias (ie, data retrieval) • Representation bias (ie, population representation) • Measurement bias • Aggregation bias • Evaluation bias • Deployment bias • Bias mitigation: does the study attempt to reduce existing biases, either explicitly or implicitly? If so, what methodology do they employ? • Preoutput (changes to the algorithm or input data) • Postoutput (user education, transparency, and specifying the use case) • Other
Stage of the study	

Category	Elements appraised
	• Methodological development: generation of novel artificial intelligence methods or modification of existing artificial intelligence methods to accomplish a task relevant to primary care. • Retrospective data analysis or model development: developed an artificial intelligence model trained on retrospectively collected data to identify trends or perform a task that awaits prospective validation. • Evaluation: artificial intelligence implemented in the intended setting as part of a pilot study, such as a prospective cohort study or randomized controlled trial. • Postimplementation: assessing the impact of an artificial intelligence implementation after officially deployed in its intended setting.

Step 5: Collating, Summarizing, and Reporting the Results

Our analysis will involve both a descriptive numerical summary and an interpretive synthesis. While our approach in stage 5 will be an iterative process, we will use this section to first provide descriptive tables, frequency tables, and visual representation of the results. Further synthesis will be performed to identify current obstacles, gaps, and opportunities in the literature.

Step 6: Consultation

Our scoping review will include consultation with other AI researchers in academia, nonprofit, and industry to enhance the perspective, applicability, and purpose of our study and ultimately offer more practical recommendations. We will engage with stakeholders at three timepoints: (1) prior to the submission of this protocol, (2) during the finalization of the data collection framework, and (3) at the end of the study during the collation, summarization, and reporting of the results.

Results

Electronic database searches were conducted in October 2020, and title and abstract screening are currently underway. We expect to complete the remaining steps of the scoping review, including publication, by fall 2021.

Discussion

Principal Findings

To our knowledge, this will be the first scoping review that applies an equity lens to the existing literature on AI in primary care. Primary care has a large potential to reduce costs and improve quality of life, especially for underserved populations [37]. Many experts have lauded AI's potential to affect primary care [14] and issues in vulnerable patient care management. By understanding AI's current place in primary care through the lens of health care equity, researchers can develop AI interventions that address the field's existing gaps and opportunities.

After completing this scoping review, we will write a briefing paper to address the implications of the findings in a narrative. We will also develop a manuscript and PRISMA-ScR checklist to submit for publication.

Limitations

Our scoping review will not incorporate a peer review process for our search strategy despite being recommended in Peer Review of Electronic Search Strategies [38]. This is typically conducted for systematic reviews rather than for scoping reviews and is not feasible with the time and resource constraints we have to achieve this review [23]. Additionally, we do not engage with community members or underserved populations themselves for consultation or feedback. We believe this is important for any study related to health equity as it improves the quality and applicability of studies for the populations they hope to serve [23,39]. However, identifying and consulting with these groups has been difficult and costly to incorporate into the protocol, which has been a recurring problem in this field of research. Instead, we rely on expert stakeholders to guide our critical appraisal of the existing literature. Considering the design of this study, we also will not conduct a rigorous assessment of the included articles beyond an inequity lens [16]. Additionally, scoping reviews do not provide a clear understanding of the efficacy of current interventions in practice as systematic reviews do, which is offset by the benefit of providing breadth from a large number of studies [16]. We also limit our work to English language articles, and no proprietary research is captured in this review.

Conclusions

AI has immense potential to improve the patient-physician relationship by augmenting physician capabilities. Primary care is an especially viable area for the integration of AI, given its early entry point, broad scope of vulnerable populations, the heavy toll these socioeconomic factors have on patient care, and the need to address these factors to manage disease more effectively. However, algorithms are susceptible to performance disparities across different subgroups, which may further reinforce pre-existing health inequities if not rigorously assessed before deployment. With this scoping review protocol, we aim to provide a process to assess the state of AI in primary care for vulnerable populations.

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Conflicts of Interest

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Multimedia Appendix 1
Search strategy and overview for Kueper et al [<xref ref-type="bibr" rid="37ref15">15</xref>].
[PDF File (Adobe PDF File), 3605 KB - resprot_v10i9e27799_app1.pdf]

Multimedia Appendix 2
PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) flow diagram from Kueper et al [<xref ref-type="bibr" rid="37ref15">15</xref>].
[PPT File (Microsoft PowerPoint Presentation), 184 KB - resprot_v10i9e27799_app2.ppt]

References

1. Kok J. Artificial Intelligence. Paris: EOLSS Publications; 2009.
2. Baştanlar Y, Özuysal M. Introduction to Machine Learning. In: miRNomics: MicroRNA Biology and Computational Analysis. Totowa, NJ: Humana Press; 2014:105-128.
3. Covington P, Adams J, Sargin E. Deep Neural Networks for YouTube Recommendations. 2016 Presented at: RecSys '16: Tenth ACM Conference on Recommender Systems; September 15-19, 2016; Boston, MA. [doi: 10.1145/2959100.2959190]
4. Carbonneau R, Laframboise K, Vahidov R. Application of machine learning techniques for supply chain demand forecasting. Eur J Oper Res 2008 Feb;184(3):1140-1154. [doi: 10.1016/j.ejor.2006.12.004]
5. Pierson HA, Gashler MS. Deep learning in robotics: a review of recent research. Adv Robot 2017 Aug 21;31(16):821-835. [doi: 10.1080/01691864.2017.1365009]
6. Rudin C, Ustun B. Optimized Scoring Systems: Toward Trust in Machine Learning for Healthcare and Criminal Justice. Interfaces 2018 Oct;48(5):449-466. [doi: 10.1287/inte.2018.0957]
7. Frohlich KL, Potvin L. Transcending the known in public health practice: the inequality paradox: the population approach and vulnerable populations. Am J Public Health 2008 Feb;98(2):216-221. [doi: 10.2105/AJPH.2007.114777] [Medline: 18172133]
8. O'Neill J, Tabish H, Welch V, Petticrew M, Pottie K, Clarke M, et al. Applying an equity lens to interventions: using PROGRESS ensures consideration of socially stratifying factors to illuminate inequities in health. J Clin Epidemiol 2014 Jan;67(1):56-64. [doi: 10.1016/j.jclinepi.2013.08.005] [Medline: 24189091]
9. Suresh H, Guttag JV. A Framework for Understanding Sources of Harm throughout the Machine Learning Life Cycle. arXiv. Preprint posted online January 28, 2019. [FREE Full text]
10. Obermeyer Z, Powers B, Vogeli C, Mullainathan S. Dissecting racial bias in an algorithm used to manage the health of populations. Science 2019 Oct 25;366(6464):447-453. [doi: 10.1126/science.aax2342] [Medline: 31649194]
11. Donaldson MS, Yordy KD, Lohr KN, Vanselow NA. Defining Primary Care. In: Primary Care: America's Health in a New Era. Washington, DC: National Academies Press; 1996:27-51.
12. Katz A, Chateau D, Enns JE, Valdivia J, Taylor C, Walld R, et al. Association of the Social Determinants of Health With Quality of Primary Care. Ann Fam Med 2018 May;16(3):217-224 [FREE Full text] [doi: 10.1370/afm.2236] [Medline: 29760025]
13. Khanassov V, Pluye P, Descoteaux S, Haggerty JL, Russell G, Gunn J, et al. Organizational interventions improving access to community-based primary health care for vulnerable populations: a scoping review. Int J Equity Health 2016 Oct 10;15(1):168 [FREE Full text] [doi: 10.1186/s12939-016-0459-9] [Medline: 27724952]

14. Lin SY, Mahoney MR, Sinsky CA. Ten Ways Artificial Intelligence Will Transform Primary Care. J Gen Intern Med 2019 Aug;34(8):1626-1630 [FREE Full text] [doi: 10.1007/s11606-019-05035-1] [Medline: 31090027]
15. Kueper JK, Terry AL, Zwarenstein M, Lizotte DJ. Artificial Intelligence and Primary Care Research: A Scoping Review. Ann Fam Med 2020 May;18(3):250-258 [FREE Full text] [doi: 10.1370/afm.2518] [Medline: 32393561]
16. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. Int J Soc Res Methodol 2005 Feb;8(1):19-32. [doi: 10.1080/1364557032000119616]
17. Graham ID. Knowledge synthesis and the Canadian Institutes of Health Research. Syst Rev 2012 Feb 09;1:6 [FREE Full text] [doi: 10.1186/2046-4053-1-6] [Medline: 22587985]
18. Entezarjou A, Bonamy AE, Benjaminsson S, Herman P, Midlöv P. Human- Versus Machine Learning-Based Triage Using Digitalized Patient Histories in Primary Care: Comparative Study. JMIR Med Inform 2020 Sep 03;8(9):e18930 [FREE Full text] [doi: 10.2196/18930] [Medline: 32880578]
19. Weng SF, Reps J, Kai J, Garibaldi JM, Qureshi N. Can machine-learning improve cardiovascular risk prediction using routine clinical data? PLoS One 2017;12(4):e0174944 [FREE Full text] [doi: 10.1371/journal.pone.0174944] [Medline: 28376093]
20. Zhou S, Fernandez-Gutierrez F, Kennedy J, Cooksey R, Atkinson M, Denaxas S, UK Biobank Follow-up and Outcomes Group, et al. Defining Disease Phenotypes in Primary Care Electronic Health Records by a Machine Learning Approach: A Case Study in Identifying Rheumatoid Arthritis. PLoS One 2016;11(5):e0154515 [FREE Full text] [doi: 10.1371/journal.pone.0154515] [Medline: 27135409]
21. Abràmoff MD, Lavin PT, Birch M, Shah N, Folk JC. Pivotal trial of an autonomous AI-based diagnostic system for detection of diabetic retinopathy in primary care offices. NPJ Digit Med 2018;1:39 [FREE Full text] [doi: 10.1038/s41746-018-0040-6] [Medline: 31304320]
22. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Ann Intern Med 2018 Oct 02;169(7):467-473 [FREE Full text] [doi: 10.7326/M18-0850] [Medline: 30178033]
23. Levac D, Colquhoun H, O'Brien KK. Scoping studies: advancing the methodology. Implement Sci 2010 Sep 20;5:69 [FREE Full text] [doi: 10.1186/1748-5908-5-69] [Medline: 20854677]
24. Better systematic review management. Covidence. URL: https://www.covidence.org/ [accessed 2020-09-10]
25. Hannun AY, Rajpurkar P, Haghpanahi M, Tison GH, Bourn C, Turakhia MP, et al. Cardiologist-level arrhythmia detection and classification in ambulatory electrocardiograms using a deep neural network. Nat Med 2019 Jan;25(1):65-69 [FREE Full text] [doi: 10.1038/s41591-018-0268-3] [Medline: 30617320]
26. Methodological Expectations of Cochrane Intervention Reviews. Cochrane Methods. URL: https://methods.cochrane.org/methodological-expectations-cochrane-intervention-reviews [accessed 2020-11-27]
27. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 2009 Jul 21;6(7):e1000097 [FREE Full text] [doi: 10.1371/journal.pmed.1000097] [Medline: 19621072]
28. Daudt H, van Mossel C, Scott S. Enhancing the scoping study methodology: a large, inter-professional team's experience with Arksey and O'Malley's framework. BMC Med Res Methodol 2013 Mar 23;13:48 [FREE Full text] [doi: 10.1186/1471-2288-13-48] [Medline: 23522333]
29. Artificial Intelligence Committee. AI in the UK: ready, willing and able? UK Parliament. 2017. URL: https://publications.parliament.uk/pa/ld201719/ldselect/ldai/100/10002.htm [accessed 2021-04-19]
30. IEEE Ethics in Action in Autonomous and Intelligent Systems. IEEE. URL: https://ethicsinaction.ieee.org/ [accessed 2021-04-14]
31. Hagendorff T. The Ethics of AI Ethics: An Evaluation of Guidelines. Minds Mach 2020 Feb 01;30(1):99-120. [doi: 10.1007/s11023-020-09517-8]
32. Rességuier A, Rodrigues R. AI ethics should not remain toothless! A call to bring back the teeth of ethics. Big Data Soc 2020 Jul 22;7(2):205395172094254. [doi: 10.1177/2053951720942541]
33. Jobin A, Ienca M, Vayena E. The global landscape of AI ethics guidelines. Nat Mach Intell 2019 Sep 02;1(9):389-399. [doi: 10.1038/s42256-019-0088-2]
34. Urban and Rural. US Census Bureau. URL: https://www.census.gov/programs-surveys/geography/guidance/geo-areas/urban-rural.html [accessed 2020-10-13]
35. Communication: Building Trust in Human Centric Artificial Intelligence. European Commission. URL: https://digital-strategy.ec.europa.eu/en/library/communication-building-trust-human-centric-artificial-intelligence [accessed 2020-10-13]
36. Overview. National Institute of Minority Health and Health Disparities. URL: https://www.nimhd.nih.gov/about/overview/ [accessed 2021-04-09]
37. Morelli V. An Introduction to Primary Care in Underserved Populations: Definitions, Scope, and Challenges. Prim Care 2017 Mar;44(1):1-9. [doi: 10.1016/j.pop.2016.09.002] [Medline: 28164809]
38. McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C. PRESS Peer Review of Electronic Search Strategies: 2015 Guideline Statement. J Clin Epidemiol 2016 Jul;75:40-46 [FREE Full text] [doi: 10.1016/j.jclinepi.2016.01.021] [Medline: 27005575]

39. Kilbourne AM, Switzer G, Hyman K, Crowley-Matoka M, Fine MJ. Advancing health disparities research within the health care system: a conceptual framework. Am J Public Health 2006 Dec;96(12):2113-2121. [doi: 10.2105/AJPH.2005.077628] [Medline: 17077411]

Abbreviations

AI: artificial intelligence
PRISMA-ScR: Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews.

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Protocol

Analyzing Evidence on Interventions to Strengthen the Clinical Support for Midwifery Students in Clinical Placements: Protocol for a Systematic Scoping Review

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Abstract

Background: The benefits of clinical support are evident in various mentorship, preceptorship, or clinical supervision models. Poor collaboration between lecturers and clinical staff, lack of confidence about student support, large student intakes coupled with core demands create negative attitudes toward student supervision, and this poses a huge challenge to midwifery students who are expected to become competent in the process.

Objective: This study aims to identify and analyze interventions, strategies, and/or mechanisms in order to strengthen the clinical support for midwifery students in clinical practice areas from a global perspective.

Methods: This review will follow the Arksey and O'Malley framework (2005). The search strategy will include primary studies searched for in electronic databases such as EBSCOhost (CINAHL, MEDLINE, and Health Source: Nursing/Academic edition), PubMed, Google, and Google Scholar. Keywords such as "midwifery students," "midwifery education," and "clinical support" will be used to search for related articles. The search will include articles from the cited by search, as well as citations from the reference list of included articles. All title-screened articles will be exported to an EndNote library, and duplicate studies will be removed. Two independent reviewers will concurrently carry out the abstract and full-text article screening according to the eligibility criteria. Extracted data will highlight the aims, geographical setting, and level of training; intervention outcomes; and the most relevant and most significant findings. This review will also include a mixed methods quality appraisal check. A narrative summary of data extracted will be analyzed using content analysis.

Results: Interventions to strengthen the clinical support for midwifery students in practice will be extracted from this review, and data will be analyzed and extracted to develop a comprehensive guide or framework for clinical mentorship. As of August 2021, the electronic search, the data extraction, and the analysis have been completed. The results paper is expected to be published within the next 6 months.

Conclusions: It is expected that this review will contribute to midwifery education by identifying quality evidence on clinical support interventions available to midwifery students globally, as well as best practice methods, procedures, or interventions that can be used to develop a midwifery mentorship training program.

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KEYWORDS

midwifery students; registered midwives; clinical support interventions; midwives; midwifery; students; mentorship; clinical supervision; collaboration; clinician attitudes

Introduction

The clinical support for midwifery students is critical to the quality of graduates produced at higher education institutions. A significant concern for lecturers and registered midwives is to produce graduates who are safe and competent practitioners [1-3]. Midwifery students spend 50% of module time in clinical placements for work-integrated learning. Therefore, a registered midwife who supports students in clinical placements has an extremely important role to create and maintain a positive working experience, increasing students' enthusiasm and ensuring their retention in the profession [4-6].

Midwifery students value the clinical support they receive during their transition from a student to a confident midwife practitioner. The benefits of clinical support are evident in various mentorship, preceptorship, or clinical supervision models, and it is supported widely in the literature [7-9]. However, literature on the perceptions of mentors or preceptors concurs that clinical staff feel unprepared in their roles to support students in clinical placements [10-15]. Furthermore, time constraints and the core function of registered midwives, which is to deliver patient care, hampers opportunities to support students during clinical placement for learning [15].

Findings from other studies also showed positive outcomes in the student-mentor relationship, even more so when mentoring is undertaken in a planned method [3,6]. In addition, providing support and training to registered midwives to take on the role of a clinical mentor or preceptor is highly recommended in many developed countries such as New Zealand, Scotland, and the United Kingdom [15-18]. Very few studies conducted in African countries relate to the clinical support for midwifery students [2,19]. One study called the MOMENTUM project was conducted in Uganda and supported by the Royal College of Midwives (United Kingdom). The project aimed to address the poor quality of mentorship for midwifery students by developing a context-specific model for mentorship in Uganda [19].

In South Africa, registered midwives working in clinical placements assume the role of clinical mentors. These clinical mentors do not receive any formal support or training and, therefore, experience conflicts in their roles and expectations. Poor collaboration between lecturers and clinical staff, negative feelings, lack of confidence about student support, and large student intakes create negative attitudes toward clinical supervision [2,20]. Currently, in South Africa, there are no known support structures for registered midwives who support students in clinical practice. Hence, the quality of midwifery mentorship is questionable, and the need to train and support registered midwives to mentor students in maternity care units has become necessary.

Identifying and analyzing the interventions to support mentorship training on a global capacity has not been previously conducted in South Africa. There are also no scoping reviews on clinical support structures or interventions to strengthen midwifery clinical support. The results of this systematic scoping review will identify interventions to strengthen the clinical support for midwifery students; subsequently, through data analysis, these results could help in developing a comprehensive mentorship training guide for midwifery clinical practice.

Methods

Study Design

This systematic scoping review will focus on retrieving and reviewing studies on clinical support interventions available to midwifery students globally. The review will follow the Arksey and O'Malley (2005) framework [21] using the following steps: (1) identifying the research question; (2) identifying the relevant studies; (3) study selection; (4) charting the data; (5) collating, summarizing, and reporting the results; and (6) consultation (optional).

Objectives

The objective for this systematic scoping review is to identify and analyze best practice guidelines, interventions, strategies, and/or mechanisms in order to support midwifery students in clinical practice areas on a global perspective.

Identifying the Research Question

What evidence is available on interventions to strengthen the current clinical support for midwifery students globally?

Eligibility of the Research Question

The review will use the population, concept, context (PCC) framework, as described by Levac et al [22,23], to determine the research question's eligibility criteria. Table 1 shows the eligibility criteria and the elements to be used in the review.

Table 1. The population, concept, context framework.

Eligibility criteria	Elements of the study
Population	Studies that include training of midwifery undergraduate and/or postgraduate students. Studies that include the perspectives of mentors and mentees.
Concept	To strengthen clinical support for midwifery students. Clinical support terms such as "clinical supervision," "mentorship," and "preceptorship" are used interchangeably in nursing and midwifery practice.
Context	Midwifery education and training, globally.

Identifying Relevant Studies

This scoping review will select preliminary studies using qualitative, quantitative, and mixed methods related to clinical support for midwifery students. Electronic platforms such as EBSCOhost (CINAHL, MEDLINE, Health Source: Nursing/Academic Edition), PubMed, Science Direct, Google, and Google Scholar will be searched to find articles published in peer-reviewed journals and the grey literature. The search strategy involves using search terms such as "midwifery students," "clinical supervision OR mentorship OR preceptorship," and "midwifery education." The search will be limited to English-language articles and confined within the last 10 years (2010-2020) to identify support interventions and strategies that are up to date and current.

The review will include a manual search of the main published articles and citations from the "related literature" list. Eligibility criteria to ensure specific information relating to the research question will be used in the studies. It will include Boolean terms ("midwifery AND clinical support," OR "mentorship," OR "clinical supervision," OR "preceptorship"), medical subject headings (MESH) terms ("midwifery students AND clinical support interventions," "mentorship AND midwifery students," and "midwifery practice and clinical supervision models"). If full-text articles are unobtainable, the researchers will consult with the librarian for assistance. All researchers will maintain an electronic search record of all literature searched.

Study Selection

The researcher will design a form for abstract and full-text screening by using Google Forms. The search strategy will follow a 3-stage system of title screening, abstract screening, and full-text screening, as determined by the inclusion criteria mentioned below. All selected articles from the screening process will be saved in an EndNote software folder.

Inclusion Criteria

The following studies will be included: (1) studies that present evidence on midwifery students; (2) studies that present evidence on clinical support such as mentorship, preceptorship, and clinical supervision; (3) studies that present evidence on midwifery education; (4) studies conducted between 2010 and 2020; (5) studies that include a support intervention or strategy; and (6) peer-reviewed articles and studies from the grey literature, which may include governmental policies and guidelines.

Exclusion Criteria

The following studies will be excluded from the analysis: (1) studies that do not include midwifery students and (2) studies that do not include an intervention or strategy.

The Screening Process

The primary investigator will conduct a thorough title-screening process using relevant databases. All articles selected will be exported to an EndNote library. Duplicated articles will be extracted from the reference list. The primary investigator and an independent collaborator will screen all saved abstracts using a standardized Google Forms as a tool. Both the primary investigator and the independent collaborator will apply the inclusion criteria developed for the search. The eligible articles selected from the abstract-screening stage will then undergo a full-text article screening process using another standardized Google Forms. Both the primary investigator and the research collaborator will work independently. Both screeners will also compile a screening report for both the abstract and full-text screening. A third reviewer (the research supervisor) will resolve any discrepancies that may emerge.

Charting the Data

In this stage, the researcher will design a data charting tool using Google Forms. Textbox 1 shows the variables used in the data charting tool. The data charting tool will highlight the study's aims, intervention outcomes, the most relevant findings, and the most significant findings, and author comments.

All researchers will collectively conduct a content analysis to extract relevant outcomes. All emerging themes and variables will be used to answer the research question. The data charting tool will be updated continually.

Textbox 1. Variables used in the data charting stage.

Variables used in the data charting form:

- Author and date
- Full journal reference
- Study aims or research question
- Geographical setting
- Level of training
- Intervention outcomes (methods, procedures, evaluation, removal and monitoring, preferences, and acceptability)
- Most relevant findings
- Most significant findings
- Comments

Quality Appraisal

This study will include a quality check as recommended by Levac et al [23]. A mixed methods quality appraisal tool designed by Pluye et al [24] will be used to assess the methodological quality of studies retrieved. According to the mixed methods quality appraisal tool, there are 4 different criteria used in both qualitative and quantitative study designs and 3 criteria used in the mixed methods section. A scoring metrics system will present all outcomes according to the number of criteria met. Table 2 shows an example summary of the scoring metric, presented according to the study design, the number of criteria met, and the percentage score; the corresponding descriptors will be recorded alongside.

A score of 75% and higher indicates a high-quality outcome and will be included in the study. A score of 25% and below indicates a low-quality outcome and will not be included in the study.

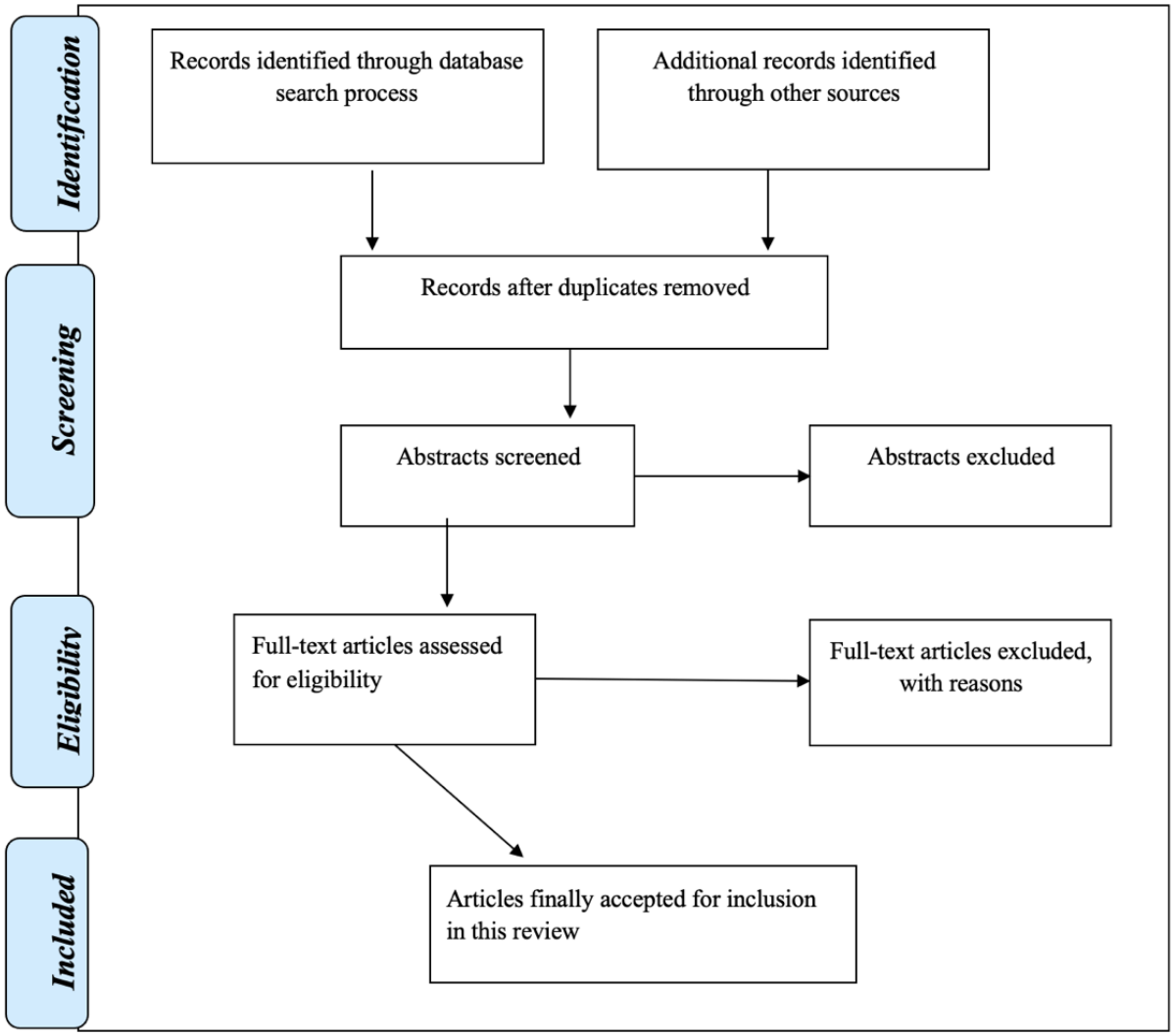
Table 2. Scoring metrics summary (example).

Study design and number of criteria met	Score (%)	Descriptors
Qualitative and quantitative studies		
1	25	*
2	50	**
3	75	***
4	100	****
Mixed method studies		
0	25	*
1	50	**
2	75	***
3	100	****

Collating, Summarizing, and Reporting the Results

A narrative summary of data extracted will be analyzed using content analysis. Only the most relevant and most significant data in line with the research question will be included in the study. The results of the systematic scoping review will be mapped in a 2009 PRISMA (Preferred Reporting Items for Systematic reviews and Meta-analyses) flow diagram, as shown in Figure 1. Once the protocol is accepted, the systematic scoping review findings will be published in an accredited journal in an electronic format. Results will also be presented at midwifery and nursing education conferences nationally and/or internationally.

Figure 1. PRISMA (Preferred Reporting Items for Systematic reviews and Meta-analyses) flow diagram presenting screening results.



Ethics Approval and Consent to Participate

The study was approved by the affiliated university's ethics committee for Human Social Science (Ethics approval no. HSS/1509/018M).

Availability of Data and Materials

All data generated and analyzed from this study will be included in the published systematic review article and will be available on request.

Results

Interventions to strengthen the clinical support for midwifery students in practice will be extracted from this review, and data will be carefully analyzed to develop a comprehensive guide or framework for clinical mentorship. As of August 2021, the electronic search, the data extraction, and the analysis have been completed. The results paper is expected to be published within the next 6 months.

Discussion

The quality of clinical support for midwifery students in placement learning is well debated as some clinical staff feel unprepared to instruct new students [12,13]. Mentors play a vital role in shaping students as qualified midwives, and the mentor-student relationship affects confidence in practice [25,26]. Thus, the poor support received during clinical practice may lead to inadequately prepared graduates who contribute to the high maternal mortality rates, especially in African countries such as Botswana, Lesotho, Swaziland, Zimbabwe, Malawi, Namibia, Mozambique, Angola, and South Africa.

According to the 2008 Nursing and Midwifery Council (NMC) requirements, trained mentors undertake assessments and provide feedback on preregistration midwifery students' proficiencies. This expectation can be especially useful in the South African context, as students have to fulfill long hours in clinical placements to achieve clinical requirements and hours. However, contrary findings were found in other studies using the same, abovementioned requirements. Studies found that

mentors had difficulties assessing, supervising, supporting, and guiding students in practice [11,27-29].

The fundamental aim of midwifery education is to develop a safe and competent practitioner who will resume full responsibility and accountability for practice [30]. Ensuring that midwifery students are equipped with the necessary skills to provide high standards of care remains a challenge for lecturers and clinical mentors. Therefore, reviewing and analyzing best practice interventions, strategies, or models that strengthen clinical support for midwifery students is urgently needed.

This systematic scoping review aims to review and analyze the current clinical support systems available to midwifery students globally and identify a suitable intervention to strengthen clinical support for midwifery students in South Africa.

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Authors' Contributions

HA conceptualized and prepared the protocol under the guidance of CM. HA and CM contributed to reviewing of the draft manuscript. All authors read and approved the final version of the manuscript.

Conflicts of Interest

None declared.

References

1. Andrews M, Brewer M, Buchan T, Denne A, Hammond J, Hardy G, et al. Implementation and sustainability of the nursing and midwifery standards for mentoring in the UK. Nurse Educ Pract 2010 Oct;10(5):251-255. [doi: 10.1016/j.nepr.2009.11.014] [Medline: 20022562]
2. Phuma-Ngaiyaye E, Bvumbwe T, Chipeta MC. Using preceptors to improve nursing students' clinical learning outcomes: a Malawian students' perspective. Int J Nurs Sci 2017 May 10;4(2):164-168 [FREE Full text] [doi: 10.1016/j.ijnss.2017.03.001] [Medline: 31406737]
3. Sayani AH, Jan R, Lennox S, Mohammad YJ, Awan S. Evaluating the results of mentorship training for community midwives in Sindh, Pakistan. Br J Midwifery 2017 Aug 02;25(8):511-518. [doi: 10.12968/bjom.2017.25.8.511]
4. Bradshaw C, Murphy Tighe S, Doody O. Midwifery students' experiences of their clinical internship: a qualitative descriptive study. Nurse Educ Today 2018 Oct;68:213-217. [doi: 10.1016/j.nedt.2018.06.019] [Medline: 29966883]
5. Gilmour C, McIntyre M, McLelland G, Hall H, Miles M. Exploring the impact of clinical placement models on undergraduate midwifery students. Women Birth 2013 Mar;26(1):e21-e25. [doi: 10.1016/j.wombi.2012.06.004] [Medline: 22819545]
6. Gray M, Malott A, Davis BM, Sandor C. A scoping review of how new midwifery practitioners transition to practice in Australia, New Zealand, Canada, United Kingdom and The Netherlands. Midwifery 2016 Dec;42:74-79. [doi: 10.1016/j.midw.2016.09.018] [Medline: 27769012]
7. Hilli Y, Salmu M, Jonsén E. Perspectives on good preceptorship: A matter of ethics. Nurs Ethics 2014 Aug 30;21(5):565-575. [doi: 10.1177/0969733013511361] [Medline: 24380890]
8. McSharry E, Lathlean J. Clinical teaching and learning within a preceptorship model in an acute care hospital in Ireland; a qualitative study. Nurse Educ Today 2017 May;51:73-80. [doi: 10.1016/j.nedt.2017.01.007] [Medline: 28130976]
9. Sidebotham M, Fenwick J. Midwifery students' experiences of working within a midwifery caseload model. Midwifery 2019 Jul;74:21-28. [doi: 10.1016/j.midw.2019.03.008] [Medline: 30921548]
10. Bennett M, McGowan B. Assessment matters-mentors need support in their role. Br J Nurs 2014 May 09;23(9):454-458. [doi: 10.12968/bjon.2014.23.9.454] [Medline: 24820808]
11. Casey DC, Clark L. Roles and responsibilities of the student nurse mentor: an update. Br J Nurs 2011 Aug 11;20(15):933-937. [doi: 10.12968/bjon.2011.20.15.933] [Medline: 21841658]
12. Jokelainen M, Turunen H, Tossavainen K, Jamookeeah D, Coco K. A systematic review of mentoring nursing students in clinical placements. J Clin Nurs 2011 Oct;20(19-20):2854-2867. [doi: 10.1111/j.1365-2702.2010.03571.x] [Medline: 21429055]
13. Myall M, Levett-Jones T, Lathlean J. Mentorship in contemporary practice: the experiences of nursing students and practice mentors. J Clin Nurs 2008 Jul;17(14):1834-1842. [doi: 10.1111/j.1365-2702.2007.02233.x] [Medline: 18578757]
14. Mead D, Hopkins A, Wilson C. Views of nurse mentors about their role. Nurs Manag (Harrow) 2011 Oct 27;18(6):18-23. [doi: 10.7748/nm2011.10.18.6.18.c8716] [Medline: 22017148]
15. Moran M, Banks D. An exploration of the value of the role of the mentor and mentoring in midwifery. Nurse Educ Today 2016 May;40:52-56. [doi: 10.1016/j.nedt.2016.02.010] [Medline: 27125150]

16. Dixon L, Calvert S, Tumilty E, Kensington M, Gray E, Lennox S, et al. Supporting New Zealand graduate midwives to stay in the profession: An evaluation of the Midwifery First Year of Practice programme. Midwifery 2015 Jul;31(6):633-639. [doi: 10.1016/j.midw.2015.02.010] [Medline: 25819705]
17. Hogan R, Fox D, Barratt-See G. Peer to peer mentoring: Outcomes of third-year midwifery students mentoring first-year students. Women Birth 2017 Jul;30(3):206-213. [doi: 10.1016/j.wombi.2017.03.004] [Medline: 28366500]
18. Tweedie K, Yerrell J, Crozier K. Collaborative coaching and learning in midwifery clinical placements. Br J Midwifery 2019 May 02;27(5):324-329. [doi: 10.12968/bjom.2019.27.5.324]
19. Kemp J, Shaw E, Musoke MG. Developing a model of midwifery mentorship for Uganda: The MOMENTUM project 2015-2017. Midwifery 2018 May;59:127-129. [doi: 10.1016/j.midw.2018.01.013] [Medline: 29425895]
20. The National Strategic Plan for nurse education, Training and Practice 2012/3-2016/7. 2013 Mar. URL: https://www.hst.org.za/publications/NonHST%20Publications/Strategic_Plan_for_Nurse_Education_Training_and_Practice.pdf [accessed 2021-08-26]
21. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. Int J Soc Res Methodol 2005 Feb;8(1):19-32. [doi: 10.1080/1364557032000119616]
22. Colquhoun HL, Levac D, O'Brien KK, Straus S, Tricco AC, Perrier L, et al. Scoping reviews: time for clarity in definition, methods, and reporting. J Clin Epidemiol 2014 Dec;67(12):1291-1294. [doi: 10.1016/j.jclinepi.2014.03.013] [Medline: 25034198]
23. Levac D, Colquhoun H, O'Brien KK. Scoping studies: advancing the methodology. Implement Sci 2010 Oct 20;5:69 [FREE Full text] [doi: 10.1186/1748-5908-5-69] [Medline: 20854677]
24. Pluye P, Robert E, Cargo M, Bartlett G, O'Cathain A. Proposal: A mixed methods appraisal tool for systematic mixed studies reviews. Montreal: McGill University; 2011. URL: http://mixedmethodsappraisaltoolpublic.pbworks.com/w/file/fetch/84371689/MMAT%202011%20criteria%20and%20tutorial%202011-06-29updated2014.08.21.pdf [accessed 2021-08-31]
25. Hughes AJ, Fraser DM. "There are guiding hands and there are controlling hands": student midwives experience of mentorship in the UK. Midwifery 2011 Aug;27(4):477-483. [doi: 10.1016/j.midw.2010.03.006] [Medline: 20462677]
26. Sundler AJ, Björk M, Bisholt B, Ohlsson U, Engström AK, Gustafsson M. Student nurses' experiences of the clinical learning environment in relation to the organization of supervision: a questionnaire survey. Nurse Educ Today 2014 May;34(4):661-666. [doi: 10.1016/j.nedt.2013.06.023] [Medline: 23850574]
27. Carter AG, Wilkes E, Gamble J, Sidebotham M, Creedy DK. Midwifery students experiences of an innovative clinical placement model embedded within midwifery continuity of care in Australia. Midwifery 2015 Aug;31(8):765-771. [doi: 10.1016/j.midw.2015.04.006] [Medline: 25921953]
28. Gray O, Brown D. Evaluating a nurse mentor preparation programme. Br J Nurs 2016;25(4):212-217. [doi: 10.12968/bjon.2016.25.4.212] [Medline: 26911167]
29. Veeramah V. Effectiveness of the new NMC mentor preparation course. Br J Nurs 2012 Apr 12;21(7):413-6, 418. [doi: 10.12968/bjon.2012.21.7.413] [Medline: 22585019]
30. The Nursing and Midwifery Council. URL: https://www.nmc.org.uk/ [accessed 2021-08-26]

Abbreviations

NMC: Nursing and Midwifery Council
PCC: population, concept, context
PRISMA: Preferred Reporting Items for Systematic reviews and Meta-analyses

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