
JMIR Research Protocols

Impact Factor (2022): 1.7

Volume 8 (2019), Issue 11 ISSN 1929-0748 Editor in Chief: Xiaomeng (Simone) Ma, PhDc, MS, BS

Contents

Protocols

| | |
|---|----|
| The Effects of Resistance Exercise With Blood Flow Restriction on Flow-Mediated Dilation and Arterial Stiffness in Elderly People With Low Gait Speed: Protocol for a Randomized Controlled Trial (e14691) Samuel Amorim, Hans Degens, Alexandra Passos Gaspar, Luciana De Matos. | 4 |
| Home-Based Cardiac Rehabilitation in Brazil's Public Health Care: Protocol for a Randomized Controlled Trial (e13901) Ana Lima, Isabella Nascimento, Anne Oliveira, Thiago Martins, Danielle Pereira, Raquel Britto. | 13 |
| HIV Prevention Via Mobile Messaging for Men Who Have Sex With Men (M-Cubed): Protocol for a Randomized Controlled Trial (e16439) Patrick Sullivan, Ryan Zahn, Sarah Wiatrek, Cristian Chandler, Sabina Hirshfield, Rob Stephenson, Jose Bauermeister, Mary Chiasson, Martin Downing Jr, Deborah Gelaude, Aaron Siegler, Keith Horvath, Erin Rogers, Ana Alas, Evelyn Olansky, Heather Saul, Eli Rosenberg, Gordon Mansergh. | 21 |
| Remotely Monitored Gamification and Social Incentives to Improve Glycemic Control Among Adults With Uncontrolled Type 2 Diabetes (iDiabetes): Protocol for a Randomized Controlled Trial (e14180) Michael Fortunato, Joseph Harrison, Ai Oon, Dylan Small, Victoria Hilbert, Charles Rareshide, Mitesh Patel. | 32 |
| Social Media Intervention to Promote Smoking Treatment Utilization and Cessation Among Alaska Native People Who Smoke: Protocol for the Connecting Alaska Native People to Quit Smoking (CAN Quit) Pilot Study (e15155) Pamela Sinicrope, Kathryn Koller, Judith Prochaska, Christine Hughes, Martha Bock, Paul Decker, Christie Flanagan, Zoe Merritt, Crystal Meade, Abbie Willetto, Ken Resnicow, Timothy Thomas, Christi Patten. | 42 |
| Delivering a Post-Partum Weight Loss Intervention via Facebook or In-Person Groups: Protocol for a Randomized Feasibility Pilot Trial (e15530) Molly Waring, Brooke Libby, Tiffany Moore Simas, Madison Bracken, Jessica Bibeau, Valeria Herrera, Justin Wang, Sherry Pagoto. | 57 |
| Comparing the Impact of an Implicit Learning Approach With Standard Care on Recovery of Mobility Following Stroke: Protocol for a Pilot Cluster Randomized Controlled Trial (e14222) Louise Johnson, Jane Burridge, Sara Demain, Sean Ewings. | 71 |
| A Mobile Health App to Improve HIV Medication Adherence: Protocol for a Pilot Randomized Controlled Trial (e15356) Susan Ramsey, Evan Ames, Julia Uber, Samia Habib, Seth Clark. | 81 |
| Factors in Randomized Controlled Trials Reported to Impact the Implementation of Patient-Reported Outcome Measures Into Routine Care: Protocol for a Systematic Review (e14579) Natasha Roberts, Kimberly Alexander, David Wyld, Monika Janda. | 92 |

| | |
|---|-----|
| <p>Prevalence of Malnutrition Among Elderly People in Iran: Protocol for a Systematic Review and Meta-Analysis (e15334) Homeira Khoddam, Sepideh Eshkevarlaji, Mahin Nomali, Mahnaz Modanloo, Abbas Keshtkar.</p> | 99 |
| <p>Allegiance Bias and Treatment Quality as Moderators of the Effectiveness of Humanistic Psychotherapy: Protocol for a Systematic Review and Meta-Analysis (e15140) Olivia Schünemann, Alessa Jansen, Ulrike Willutzki, Nina Heinrichs.</p> | 107 |
| <p>Time-Limited Trials Among Critically Ill Patients With Advanced Medical Illnesses to Reduce Nonbeneficial Intensive Care Unit Treatments: Protocol for a Multicenter Quality Improvement Study (e16301) Dong Chang, Jennifer Parrish, Nader Kamangar, Janice Liebler, May Lee, Thanh Neville.</p> | 115 |
| <p>Improving Team-Based Decision Making Using Data Analytics and Informatics: Protocol for a Collaborative Decision Support Design (e16047) Don Roosan, Anandi Law, Mazharul Karim, Moom Roosan.</p> | 125 |
| <p>Feasibility of Point-of-Care Testing for Influenza Within a National Primary Care Sentinel Surveillance Network in England: Protocol for a Mixed Methods Study (e14186) Simon de Lusignan, Uy Hoang, Harshana Liyanage, Ivelina Yonova, Filipa Ferreira, Javier Diez-Domingo, Tristan Clark.</p> | 139 |
| <p>Implementing a Digital HIV Care Navigation Intervention (Health eNav): Protocol for a Feasibility Study (e16406) Sean Arayasirikul, Dillon Trujillo, Caitlin Turner, Victory Le, Erin Wilson.</p> | 144 |
| <p>Real-Time Detection of Behavioral Anomalies of Older People Using Artificial Intelligence (The 3-PEGASE Study): Protocol for a Real-Life Prospective Trial (e14245) Antoine Piau, Benoit Lepage, Carole Bernon, Marie-Pierre Gleizes, Fati Nourhashemi.</p> | 155 |
| <p>Evidence on User-Led Innovation in Diabetes Technology (The OPEN Project): Protocol for a Mixed Methods Study (e15368) Shane O'Donnell, Dana Lewis, María Marchante Fernández, Mandy Wäldchen, Bryan Cleal, Timothy Skinner, Klemens Raile, Adrian Tappe, Tebbe Ubben, Ingrid Willaing, Bastian Hauck, Saskia Wolf, Katarina Braune.</p> | 163 |
| <p>Development of an Early Warning System to Prevent Crises in the Palliative Home Care Setting of Patients and Their Informal Caregivers: Protocol for a Mixed Method Study (e13933) André Fringer, Eleonore Arrer, Edith Maier, Wilfried Schnepf, Tom Ulmer.</p> | 172 |
| <p>Developing Strategies to Reduce Unnecessary Services in Primary Care: Protocol for User-Centered Design Charrettes (e15618) Mandi Klamerus, Laura Damschroder, Jordan Sparks, Sarah Skurla, Eve Kerr, Timothy Hofer, Tanner Caverly.</p> | 191 |
| <p>Monitoring of Vedolizumab Infusion Therapy (MOVE-IT) Response With Fecal Inflammation Markers, Ultrasound, and Trough Serum Level in Patients With Ulcerative Colitis: Protocol for a Multicentric, Prospective, Noninterventonal Study (e14335) Jimmi Cording, Margit Blömacher, Berit Wiebe, Jost Langhorst, Torsten Kucharzik, Andreas Sturm, Stefan Schreiber, Ulf Helwig.</p> | 214 |
| <p>A National Behavioral and Clinical Surveillance System of Adults With Diagnosed HIV (The Medical Monitoring Project): Protocol for an Annual Cross-Sectional Interview and Medical Record Abstraction Survey (e15453) Linda Beer, Christopher Johnson, Jennifer Fagan, Emma Frazier, Margaret Nyaku, Jason Craw, Catherine Sanders, Ruth Luna-Gierke, R Shouse.</p> | 221 |

Action Ethnography of Community Reintegration for Veterans and Military Service Members With Traumatic Brain Injury: Protocol for a Mixed Methods Study ([e14170](#))
Christine Melillo, Kiersten Downs, Christina Dillahunt-Aspillaga, Jason Lind, Karen Besterman-Dahan, Bridget Hahm, Nicole Antinori, Christine Elnitsky, Angelle Sander, Heather Belanger, Peter Toyinbo, Gail Powell-Cope. 229

Original Papers

Nutritional Assessment of Childhood Cancer Survivors (the Swiss Childhood Cancer Survivor Study-Nutrition): Protocol for a Multicenter Observational Study ([e14427](#))
Fabiën Belle, Maja Beck Popovic, Marc Ansari, Maria Otth, Claudia Kuehni, Murielle Bochud. 179

Impact of Perinatal Different Intrauterine Environments on Child Growth and Development: Planning and Baseline Data for a Cohort Study ([e12970](#))
Isabel Werlang, Juliana Bernardi, Marina Nunes, Thiago Marcelino, Vera Bosa, Mariana Michalowski, Clécio da Silva, Marcelo Goldani. 204

Group Sex Events Among Cisgender Men Who Have Sex With Men: Cross-Sectional and Longitudinal Survey Study to Explore Participation and Risk-Taking Behaviors ([e15426](#))
Lauren Violette, Lisa Niemann, Vanessa McMahan, David Katz, Pollyanna Chavez, Hollie Clark, Andy Cornelius-Hudson, Steven Ethridge, Sarah McDougal, George Ure II, Joanne Stekler, Kevin Delaney. 241

Protocol

The Effects of Resistance Exercise With Blood Flow Restriction on Flow-Mediated Dilation and Arterial Stiffness in Elderly People With Low Gait Speed: Protocol for a Randomized Controlled Trial

Samuel Amorim¹; Hans Degens^{2,3,4}, PhD; Alexandra Passos Gaspar¹, PhD; Luciana Diniz Nagem Janot De Matos¹, PhD

¹Hospital Israelita Albert Einstein, São Paulo, Brazil

²Research Centre for Musculoskeletal Science & Sports Medicine, Manchester Metropolitan University, Manchester, United Kingdom

³Lithuanian Sports University, Kaunas, Lithuania

⁴University of Medicine, Pharmacy, Science and Technology of Targu Mures, Targu Mures, Romania

Corresponding Author:

Luciana Diniz Nagem Janot De Matos, PhD
Hospital Israelita Albert Einstein
Avenida Albert Einstein 627, Bloco D, 3 Andar
São Paulo, 05651901
Brazil
Phone: 55 (11) 2151 1100
Email: luciana.matos@einstein.br

Abstract

Background: During aging, a significant loss of muscle mass, strength, and power is associated with a decline in daily functional capacities. Traditionally, resistance training is prescribed to prevent or reverse the skeletal muscle weakness, but the required training intensity may be too demanding for older people with poor physical performance. Resistance exercise with blood flow moderation (KAATSU training), originally developed in Japan, combines resistance exercise with blood flow restriction. It has been reported that KAATSU training enhances muscle hypertrophy in many populations. However, few studies have evaluated the effects of resistance exercises with blood flow restriction in elderly people and how this affects vascular structure and function.

Objective: The aim of this study was to evaluate (1) the acute and chronic effects of resistance exercise with blood flow restriction on vascular health in elderly people with low gait speed and (2) whether low-load resistance training with blood flow restriction elicits similar strength and gait speed gains to those elicited by conventional resistance training without blood flow restriction.

Methods: This is an ongoing randomized controlled trial in elderly people with low gait speed. Overall, two study arms of 13 participants each perform resistance exercise with and without blood flow restriction. The 2 groups are as follows: the control group will perform conventional resistance exercise (60% of 1 repetition maximum) and the KAATSU group will perform the low-load resistance exercise with blood flow restriction (20% of 1 repetition maximum) for 12 weeks. Pulse wave velocity, venous occlusion plethysmography, and flow-mediated dilation are used to assess arterial stiffness, muscle blood flow, and endothelial function, respectively. The secondary outcomes are gait speed, strength, and quality of life. All measures will be performed before and after the training program.

Results: This research study is in progress. Recruitment has started, and data collection is expected to finish in August 2020.

Conclusions: The findings of this study will have important implications for the rehabilitation of elderly people.

Trial Registration: ClinicalTrials.gov NCT03272737; <https://clinicaltrials.gov/ct2/show/NCT03272737>

International Registered Report Identifier (IRRID): DERR1-10.2196/14691

(*JMIR Res Protoc* 2019;8(11):e14691) doi:[10.2196/14691](https://doi.org/10.2196/14691)

KEYWORDS

blood flow restriction; arterial stiffness; elderly people

Introduction

Background

According to the World Health Organization, many countries, including China, Thailand, and Brazil, will see an increase in the percentage of the population over 65 years, from 7% in 2000 to 14% in the 2030s [1].

This increase in the proportion of older people represents a huge challenge for health care as aging is accompanied by decrements in cardiovascular function, skeletal muscle weakness, and changes in blood coagulation, all of which have a negative impact on the functional capacity of the elderly person [2,3].

Therefore, strategies that can prevent, minimize, or even reverse these effects of aging are imperative to maintain mobility and the ability to perform activities of daily living that are fundamental for the autonomy of elderly people [4].

Senescence and Skeletal Muscle System

One of the major factors contributing to the age-related muscle wasting is disuse; however, even master athletes show aging-related muscle wasting and weakness, suggesting that other factors, such as an inherent aging process, must also contribute [5].

Elderly people with muscle weakness have 2.6 times higher risk of severe mobility limitation, 4.6 times higher risk of low gait speed, and 2.1 times higher risk of mortality compared with elderly people without muscle weakness [6].

Senescence and the Cardiovascular System

Progressive loss of cardiomyocytes, reduction of the β_1 -adrenergic response, and degenerative alterations in the sinus node are all hallmarks of the aging heart. In parallel, there is an increased deposition of collagen that will contribute to diastolic dysfunction of the heart [7].

In addition to these cardiac changes, aortic stiffness is increased and atheromatous plaques and endothelial dysfunction develop [8]. Levels of coagulation factors are elevated and those of anticoagulants are decreased, increasing the underlying incidence of thrombosis, especially above the age of 70 years [9,10].

Physical Exercise and the Cardiovascular System

Many questions related to the effect of physical training on the health of older people still need to be answered, such as the most appropriate type and the best form of training to enhance functional gains without secondary vascular impairment. Aerobic training improves the cardiovascular system, increases muscle blood flow, arterial compliance, and endothelial function that reduce the risk of comorbidities [11]. However, the use of this exercise modality in elderly people with reduced gait speed is limited [12].

Resistance exercise is a potent tool to gain and maintain strength and skeletal muscle mass in sarcopenic older people with diminished gait speed [13,14], but high intensities (>60% of 1 repetition maximum [RM]) are required for gains in skeletal muscle mass [15]. However, older people may not be able to

cope with such loads and should avoid this type of exercise as it may cause undue stress on the cardiovascular system [16].

Recently, it was reported that low-intensity resistance exercise with blood flow restriction (BFR) may be able to induce gains in strength and muscle mass in older people [17]. Typically, BFR training uses low loads (20%-30% of 1RM) and short periods of training [18], a load that is better coped with and may thus be more applicable to elderly people, especially those who are sarcopenic. However, so far there are no studies evaluating the safety of BFR training for the cardiovascular system in this population [19].

Study Aim and Hypotheses

The aim of this study is to evaluate (1) the acute and chronic effects of resistance exercise with BFR on vascular health in elderly people with low gait speed and (2) whether low-load resistance training with BFR elicits similar gait speed and strength gains to those elicited by conventional resistance training without BFR. Specifically, we will investigate the effect of the 2 training modalities on arterial stiffness, muscle blood flow, endothelial function, gait speed, and muscle strength in this population.

Our hypotheses are that low-load resistance exercise with BFR elicits the same increase in strength and improvement in quality of life as conventional resistance training and that it has no detrimental effect on arterial stiffness, muscle blood flow, and endothelial function. The findings of this trial may inform future recommendations for training of the elderly population.

Methods

Study Design

This study is designed as a randomized, blind, controlled intervention trial.

Ethical Approval

The study received ethical approval from the ethical committee of the Hospital Israelita Albert Einstein and is registered on the ClinicalTrials.gov website. Participants are only included after signing the informed consent form.

Identifiable elements, including names, phone numbers, street addresses, city or state, zip code, email addresses, and date of birth will be collected but maintained under strict confidentiality. Screening materials will be kept for the participants recruited in the study and destroyed for those that do not meet the criteria or decide not to take part. Authorization for use and disclosure of the participants' personal health information is restricted to this specific study, and data will be kept for 5 years after publication.

Sample Size and Power Calculation

The sample size was calculated with Stata software (StataCorp LP) for both the acute and chronic protocols based on previous reports. It has been reported that flow-mediated dilation (FMD) was on average 4.3% (SD 3.1%) and arterial stiffness was on average 9.2 m/s (SD 1.1 m/s) [20].

Power analysis indicated that we need 10 participants per group to detect a difference in FMD of 3.1% and arterial stiffness on average 1.1 m/s between groups at a statistical power of 0.80 and an alpha of .05.

Owing to the conditions and frailty of elderly people, up to 20% dropouts are expected, and therefore, we are recruiting 13 participants per group.

Eligibility

The eligibility criteria for participation in the study are provided in [Textbox 1](#).

Textbox 1. Inclusion and exclusion criteria.

Inclusion criteria:

- Elderly people aged ≥ 65 years
- Gait speed < 0.9 m/s

Exclusion criteria:

- Smoking < 6 months
- Previous deep venous thrombosis
- Uncontrolled arterial hypertension (blood pressure $> 160/100$ mm Hg)
- Uncontrolled dyslipidemia (total cholesterol > 220 mg/dL)
- Infections within the past 1 month
- Osteoarticular or neurological problems that prevent training
- Use of oral anticoagulants
- Symptomatic peripheral obstructive arterial disease or ankle-brachial index < 0.9
- History of anemia, cerebrovascular disease, or myocardial infarction in the last 6 months
- Elderly people with uncontrolled diabetes mellitus or peripheral neuropathy
- Use of double antiplatelet agents: aspirin, Aggrenox, cilostazol, eptifibatide, ticlopidine, and tirofiban

Participant Information and Informed Consent

Eligible participants are recruited primarily based on the results of a gait speed test. They consult with a cardiologist and a physiatrist to assess their health and determine whether they can participate in the study. In addition, medical records of the participants will be filled in for later analysis. Eligible participants are informed of their rights, and the procedures of the study and will be allowed to participate only if they provide written informed consent. Relatives are informed about the details of the tests and exercise sessions, if necessary.

Recruitment

Participants are recruited from the Vila Mariana Unit of the Hospital Israelita Albert Einstein and elderly care centers in São Paulo.

Randomization

Using a website [21], participants are randomized into two groups, each with 13 participants:

1. Low-load resistance exercise group (20% of 1RM) with BFR (resistance exercise with blood flow moderation, KAATSU);
2. Conventional resistance exercise (CRE) group (60% of 1RM).

The block sizes and randomized sequences are hidden from those who recruit or allocate participants to prevent

predictability of the next assignment [22]. The participants must be aged 65 years or above.

Blinding

Research team members administering clinical assessments are blinded from participant allocation. Participant allocation will not be revealed during the study.

Exercise and Training Intervention

Acute Protocol: Resistance Exercise Session

Participants are instructed to consume a light meal before the training sessions and drink water. They should avoid physical activity and alcohol consumption 48 hours before the sessions. In addition, 24 hours before the first clinical tests, they should avoid consuming caffeine, chocolate, and tea.

Before the experimental exercise session, all participants undergo 2 familiarization sessions and 1RM tests to standardize the resistance exercise intensity. The KAATSU group participants perform bilateral seated knee extension and leg press exercises: 3 sets of 15 repetitions with 20 seconds rest between sets and 60 seconds between exercises at 20% of 1RM (Table 1). There is a 72-hour rest interval between sessions. Then, cuffs are inflated to a pressure that does not cause pain or discomfort during the warm-up and resistance exercises. This protocol is based on the study that evaluated KAATSU training in patients with metabolic diseases [23].

The CRE group individuals perform bilateral seated knee extension and leg press exercises: 3 sets of 15 repetitions with 60 seconds of rest between both sets and exercises, at 60% of 1RM.

Blood pressure and heart rate are evaluated before and 15 min, 30 min, and 60 min after the acute exercise session. Arterial stiffness, muscle blood flow, and vascular endothelial function are measured before and 60 min after the exercise session (Figure 1).

Table 1. Resistance exercise protocol of the acute study (session 1).

| Groups | Series | Repetitions | Exercises | % of 1 repetition maximum | Lifting cadence (s) | Interval between sets (s) | Session duration (min) | Cuff size (mm) |
|----------------------------------|--------|-------------|-------------------------------------|---------------------------|---------------------|---------------------------|------------------------|----------------|
| Conventional resistance exercise | 3 | 15 | KE ^a and LP ^b | 60 | 1-1 ^c | 60 | 10 | — ^d |
| KAATSU | 3 | 15 | KE and LP | 20 | 1-1 | 20 | 10 | 50 |

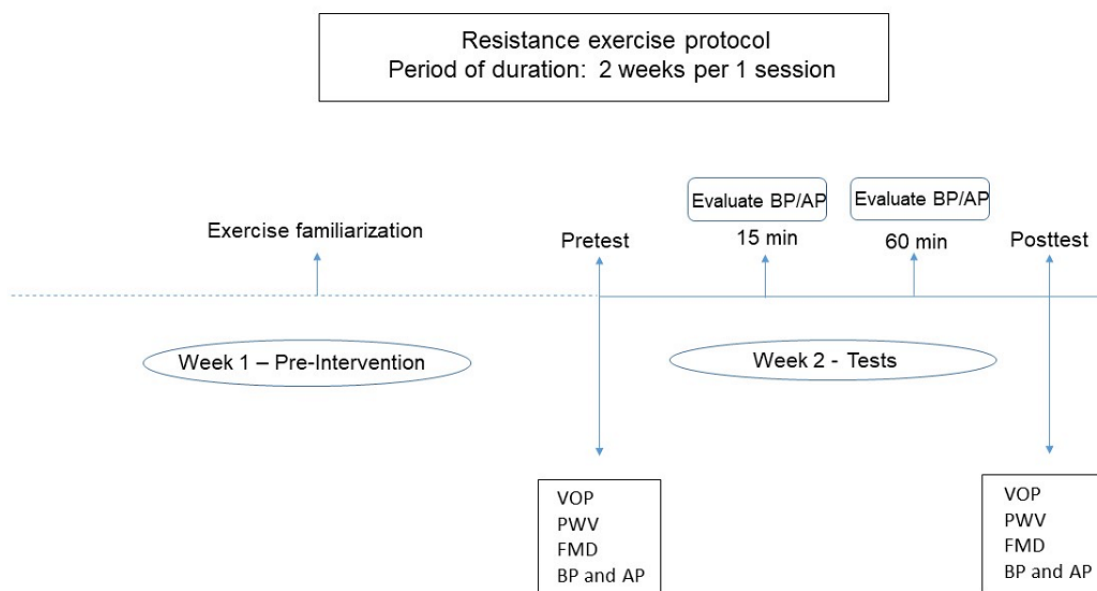
^aKE: knee extension.

^bLP: leg press.

^c1-1: 1.0 s concentric and 1.0 s eccentric lifting cadence.

^dNot applicable.

Figure 1. The sequence of activities that will be developed during the acute study. AP: arterial pressure; BP: blood pressure; FMD: flow-mediated dilation; PWV: pulse wave velocity; VOP: venous occlusion plethysmography.



Chronic Protocol: Resistance Training Program

The protocol comprises 2 sessions per week for 12 weeks (Figure 2).

All groups are submitted to the same exercise protocol. The KAATSU group participants perform 2 sets of 15 repetitions at 20% of 1RM each time. The CRE group participants perform 2 sets with 15 repetitions at 60% of 1RM for each exercise in

the first 4 weeks. The rest interval between exercises is 60 seconds for both groups, and rest interval between sets is 60 seconds for the CRE group and 20 seconds for the KAATSU group. The exercise duration of each repetition is 2.0 seconds (1.0 second concentric and 1.0 second eccentric lifting cadence). The exercise volume is increased to 3 sets for both groups in the fifth week of training. A load adjustment is carried out in training sessions 9 and 18 (Table 2).

Figure 2. The sequence of activities that will be developed during the chronic study. AP: arterial pressure; BP: blood pressure; FMD: flow-mediated dilation; PWV: pulse wave velocity; VOP: venous occlusion plethysmography.

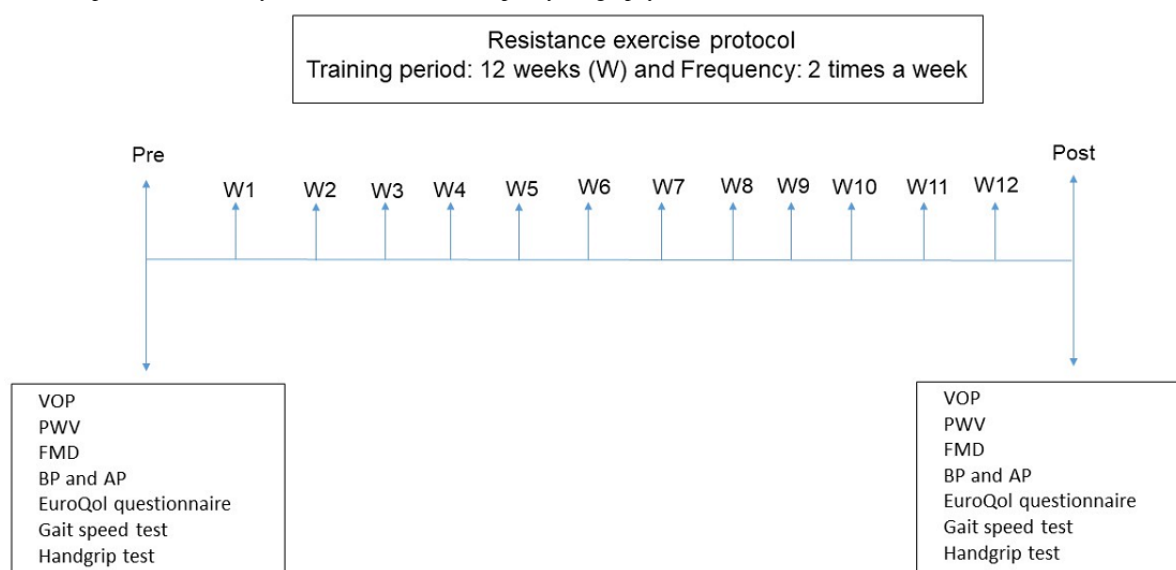


Table 2. Resistance exercise protocol of the chronic study.

| Sessions | Groups | Series | Repetitions | Exercises | % age of 1RM ^a | Lifting cadence (s) | Interval between sets (s) | Session duration (min) | Cuff size (mm) |
|----------|------------------|--------|-------------|-------------------------------------|---------------------------|---------------------|---------------------------|------------------------|----------------|
| 1-8 | CRE ^b | 2 | 15 | KE ^c and LP ^d | 60 | 1-1 ^e | 60 | 10 | — ^f |
| 1-8 | KAATSU | 2 | 15 | KE and LP | 20 | 1-1 | 20 | 10 | 50 |
| 9 | CRE and KAATSU | — | — | — | 1RM test | — | — | — | — |
| 10-17 | CRE | 3 | 15 | KE and LP | 60 | 1-1 | 60 | 10 | — |
| 10-17 | KAATSU | 3 | 15 | KE and LP | 20 | 1-1 | 20 | 10 | 50 |
| 18 | CRE and KAATSU | — | — | — | 1RM test | — | — | — | — |
| 19-24 | CRE | 3 | 15 | KE and LP | 60 | 1-1 | 60 | 10 | — |
| 19-24 | KAATSU | 3 | 15 | KE and LP | 20 | 1-1 | 20 | 10 | 50 |

^aRM: repetition maximum.

^bCRE: conventional resistance exercise.

^cKE: knee extension.

^dLP: leg press.

^e1-1: 1.0 s concentric and 1.0 s eccentric lifting cadence.

^fNot applicable.

Determination of Blood Flow Restriction Pressure

BFR is accomplished using the KAATSU Nano device (KAATSU Global) that automatically detects the pressure needed on the limbs to reduce blood flow.

First, baseline pressure is calculated according to the age and general physical condition of the participants. This is the pressure observed after manually tightening the pneumatic cuffs on the upper arms or upper legs. Second, the cuffs are placed around both upper limbs, and a cycle function is started that comprises 8 cycles of 20 seconds inflation and 5 seconds deflation of the cuffs. After this step, the instructor removes the cuffs and places the leg cuffs on both lower limbs and inflates

the cuffs up to the optimal pressure that does not cause pain or discomfort. The optimal pressure values result from a combination of age, level of fitness, limb circumference, and tests standardized by the methodology [24]. Participants remain with the cuffs on the lower limbs from the beginning to the end of the exercise session [23].

Data Management

Data from the trial are routinely scrutinized for omissions and errors. All manually entered data are entered twice, and the source of any inconsistency is explored and resolved. Electronic data are stored and copied to an external hard drive. Data are only accessible to the study researchers. Each participant in the

study is provided with an identification number, and the recorded data are coded using this number.

Primary Goals

Venous Occlusion Plethysmography Protocol

Muscle blood flow is evaluated with venous occlusion plethysmography. The participant's legs are elevated above the level of the heart to ensure adequate venous drainage. A mercury-filled silastic tube, connected to a low-pressure transducer and a plethysmograph (DE Hokanson), is placed around the largest circumference of the calf region. One cuff is placed around the ankle and another around the thigh. The ankle cuff is inflated to a suprasystolic pressure, 30 seconds before starting the measurements. At 15-second intervals, the cuff around the thigh is inflated above the venous pressure for a period of 7 to 8 seconds. Increased tension in the silastic tube reflects an increase in leg volume and vasodilation. The signal of the muscle blood flow wave is recorded on a polygraph and analyzed every minute, averaging 3 records per minute. The protocol is performed in a cycle of 5 min of rest, 3 min of isometric exercise, and 2 min of recovery [25].

Isometric Handgrip Exercise Protocol

In a supine position, the maximal voluntary handgrip force is determined as the highest force in 3 consecutive attempts using a Jamar hydraulic palmar dynamometer (Asimow Engineering). For the activation of the central command, mechanoreceptors, and muscular metaboreceptors, the individual performs, after 5 min of rest (baseline records), 3 min of exercise at 30% of maximal voluntary contraction. This maneuver isolates the activation of muscle metaboreceptors to observe their selective activation [26]. After the isometric handgrip exercise, there are 2 min for recovery to occur. Throughout the protocol, muscle blood flow, blood pressure, and heart rate are recorded.

Measurement of Arterial Stiffness—Pulse Wave Analysis and Velocity

Arterial stiffness is estimated from the carotid-femoral aortic pulse wave velocity [27]. The carotid-femoral aortic pulse waves are recorded by tonometry (SphygmoCor, AtCor Medical). At the same time, an electrocardiogram is registered to calculate the wave transit time. Overall, 2 distances are measured: the recording point between the carotid artery and the sternal furcula (distance 1), and between the sternal furcula and the recording point in the femoral artery (distance 2). The distance traveled by the pulse wave is calculated as $distance\ 2 - distance\ 1$. The carotid-femoral aortic pulse wave velocity is calculated as follows: $carotid-femoral\ aortic\ pulse\ wave\ velocity = \frac{1}{4}(\times)distance\ traveled\ by\ the\ pulse\ wave\ (m) / transit\ time\ (seconds)$.

Basal Blood Flow and Vasodilatory Capacity—Flow-Mediated Dilation

Basal blood flow and flow-mediated vasodilation are measured as previously described [28,29]. Images of the brachial artery are recorded by a 2-dimensional ultrasonography device with a spectral Doppler and linear transducer (Ultra-0122, Philips).

The participant is maintained in the supine position with the arm slightly abducted, for 20 min. After locating the brachial artery, the transducer is placed on the anteromedial aspect of the arm, perpendicular to the axis of the arm, 2 cm to 10 cm above the antecubital fold, over the artery. To confirm the location and quality of the arterial pulse obtained, Doppler is triggered. The resolution of contrast, depth, and gain is adjusted to optimize the longitudinal images of the lumen and arterial wall interface. The insonation angle is $\leq 60^\circ$. Blood flow velocity spectra are recorded simultaneously in the 10-MHz linear pulse mode. The diameter of the artery and the basal blood flow are recorded continuously over 120 seconds. After the baseline recording, a cuff on the forearm is inflated to 50 mm Hg above the systolic blood pressure. The occlusion is maintained for 5 min and then released quickly. The Doppler recordings are resumed 30 seconds before deflating the cuff and are continued for another 180 seconds. The diameter and the postocclusion blood flow are measured after release. The vasodilatory capacity is calculated as the percentage increase in the diameter of the brachial artery after occlusion.

Secondary Goals

Speed Gait Test

To measure their gait speed, participants walk 4.6 m and the time needed to cover this distance is recorded. The mean of 3 attempts is calculated and divided by the distance. The participants included must achieve an average of <0.9 m/s in the walking test [30,31].

One Repetition Maximum Test (Knee Extension and Seated Leg Press)

The dynamic force of the lower limb muscles is evaluated by the maximal repetition of knee extension and leg press exercise, according to the protocol presented in a previous study [32]. The participants perform a warm-up comprising 1 series with 10 unloaded repetitions. After this step, the mass to be lifted is progressively increased until the maximum load that can be lifted is reached, with a maximum limit of 5 attempts and a 3 min to 5 min interval between them. The test is conducted by a physical education professional who verbally encourages the participants throughout these steps and performs the load adjustment at weeks 5 and 10.

Heart Rate and Blood Pressure

Blood pressure and heart rate are evaluated with oscillometry (Dixtal DX 2020).

Anthropometric Assessment

Anthropometric measurements are registered before and after the training program following the International Society for Anthropometric Assessments standards [33]. Body mass is measured with an accuracy of 0.1 kg (Filizola). Stature is obtained by means of a stadiometer with an accuracy of 0.5 cm. Body mass index is calculated as body mass divided by height squared. The circumference of the quadriceps is measured using a tape measure (Seca) with a precision of 0.1 cm.

Quality of Life EuroQol-5 Domain

The questionnaire Quality of life Euro QoL-5 Domain s used to estimate the quality of life in participants before and after the study [34].

Benefits

The possible benefits of KAATSU training are improved muscle strength and gait speed in elderly people, without any detrimental effect on arterial stiffness, muscle blood flow, or endothelial function, and perhaps even an enhanced vascular function, all achieved at a lower training load with BFR than with conventional resistance training.

Adverse Events and Risks

BFR exercise may cause headache, red spots, redness, pain, and discomfort in lower limbs during or after exercise sessions.

Auditing

Auditing is carried out as per the policies of the sponsor and of those overseeing the sponsor.

Results

The last equipment for the study was obtained in January 2018. Recruitment and data collection were initiated in February 2018. Data collection is expected to be completed in January 2020, and the results are expected to be available in August 2020.

Discussion

Overview

This is the first time that the effects of BFR exercise on elderly people with low gait speed are evaluated utilizing the gold

standard cardiovascular assessment. All necessary support and funding to conduct our study have been received.

Studies that have analyzed the effects of BFR with resistance exercise on cardiovascular function in older people are scarce. Shimizu et al showed that BFR training improved endothelial function and blood circulation in active elderly people [35]. Similarly, Patterson et al reported that 4 weeks of unilateral plantar flexion with BFR enhanced limb blood flow in sedentary older people [36]. Yasuda et al demonstrated that 3 months of low-intensity resistance exercise with BFR did not change arterial stiffness and muscle blood flow in inactive seniors [37]. So far, there is thus no indication that BFR exercise has detrimental effects on vascular function, but no studies have been performed on elderly people with poor physical performance. Therefore, studies are necessary to assess the benefits and possible harm for cardiovascular function owing to BFR exercise in older people.

This protocol describes a collaborative co-design study focused on the application of a new treatment method to combat sarcopenia in the older population. The findings from this study will have important implications on the safety to prescribe this type of exercise to the elderly people.

Limitations

Finding eligible participants may be problematic, and the exclusion criteria limit our investigation in elderly people with low gait speed.

Conclusions

This trial will evaluate the effects of resistance training with or without BFR on muscle strength and gait speed and whether BFR during exercise has any detrimental or beneficial effects on arterial stiffness, muscle blood flow, and endothelial function in elderly people with low gait speed.

Acknowledgments

The project is funded by the São Paulo Research Foundation, which is not involved in any way in this study.

Authors' Contributions

SA, APG, and LDNJDM designed the study. All authors provided methodological suggestions and took part in editing the manuscript. SA wrote the first draft, and all authors have read and approved the final version of this manuscript.

Conflicts of Interest

None declared.

References

1. World Health Organization. 2012. Good Health Adds Life to Years: Global Brief for World Health Day 2012 URL: https://www.who.int/ageing/publications/whd2012_global_brief/en/ [accessed 2012-01-12]
2. Kovacic JC, Moreno P, Nabel EG, Hachinski V, Fuster V. Cellular senescence, vascular disease, and aging: part 2 of a 2-part review: clinical vascular disease in the elderly. *Circulation* 2011 May 3;123(17):1900-1910. [doi: [10.1161/CIRCULATIONAHA.110.009118](https://doi.org/10.1161/CIRCULATIONAHA.110.009118)] [Medline: [21537006](https://pubmed.ncbi.nlm.nih.gov/21537006/)]
3. Park DC, Yeo SG. Aging. *Korean J Audiol* 2013 Sep;17(2):39-44 [FREE Full text] [doi: [10.7874/kja.2013.17.2.39](https://doi.org/10.7874/kja.2013.17.2.39)] [Medline: [24653904](https://pubmed.ncbi.nlm.nih.gov/24653904/)]
4. Fielding RA, Rejeski WJ, Blair S, Church T, Espeland MA, Gill TM, LIFE Research Group. The lifestyle interventions and independence for elders study: design and methods. *J Gerontol A Biol Sci Med Sci* 2011 Nov;66(11):1226-1237 [FREE Full text] [doi: [10.1093/gerona/glr123](https://doi.org/10.1093/gerona/glr123)] [Medline: [21825283](https://pubmed.ncbi.nlm.nih.gov/21825283/)]

5. Piasecki M, Ireland A, Piasecki J, Degens H, Stashuk DW, Swiecicka A, et al. Long-term endurance and power training may facilitate motor unit size expansion to compensate for declining motor unit numbers in older age. *Front Physiol* 2019;10:449 [FREE Full text] [doi: [10.3389/fphys.2019.00449](https://doi.org/10.3389/fphys.2019.00449)] [Medline: [31080415](https://pubmed.ncbi.nlm.nih.gov/31080415/)]
6. Manini TM, Visser A, Won-Park S, Patel KV, Strotmeyer ES, Chen H, et al. Knee extension strength cutpoints for maintaining mobility. *J Am Geriatr Soc* 2007 Mar;55(3):451-457. [doi: [10.1111/j.1532-5415.2007.01087.x](https://doi.org/10.1111/j.1532-5415.2007.01087.x)] [Medline: [17341251](https://pubmed.ncbi.nlm.nih.gov/17341251/)]
7. Moore A, Mangoni AA, Lyons D, Jackson SH. The cardiovascular system. *Br J Clin Pharmacol* 2003 Sep;56(3):254-260 [FREE Full text] [doi: [10.1046/j.0306-5251.2003.01876.x](https://doi.org/10.1046/j.0306-5251.2003.01876.x)] [Medline: [12919173](https://pubmed.ncbi.nlm.nih.gov/12919173/)]
8. Nazari-Shafti TZ, Cooke JP. Telomerase therapy to reverse cardiovascular senescence. *Methodist Debakey Cardiovasc J* 2015;11(3):172-175 [FREE Full text] [doi: [10.14797/mdcj-11-3-172](https://doi.org/10.14797/mdcj-11-3-172)] [Medline: [26634025](https://pubmed.ncbi.nlm.nih.gov/26634025/)]
9. Esmon CT. Basic mechanisms and pathogenesis of venous thrombosis. *Blood Rev* 2009 Sep;23(5):225-229 [FREE Full text] [doi: [10.1016/j.blre.2009.07.002](https://doi.org/10.1016/j.blre.2009.07.002)] [Medline: [19683659](https://pubmed.ncbi.nlm.nih.gov/19683659/)]
10. Raskob G, Anghaisuksiri P, Blanco A, Buller H, Gallus A, Hunt B, ISTH Steering Committee for World Thrombosis Day. Thrombosis: a major contributor to global disease burden. *Arterioscler Thromb Vasc Biol* 2014 Nov;34(11):2363-2371. [doi: [10.1161/ATVBAHA.114.304488](https://doi.org/10.1161/ATVBAHA.114.304488)] [Medline: [25304324](https://pubmed.ncbi.nlm.nih.gov/25304324/)]
11. Campbell A, Grace F, Ritchie L, Beaumont A, Sculthorpe N. Long-term aerobic exercise improves vascular function into old age: a systematic review, meta-analysis and meta regression of observational and interventional studies. *Front Physiol* 2019;10:31 [FREE Full text] [doi: [10.3389/fphys.2019.00031](https://doi.org/10.3389/fphys.2019.00031)] [Medline: [30863313](https://pubmed.ncbi.nlm.nih.gov/30863313/)]
12. Reid KF, Fielding RA. Skeletal muscle power: a critical determinant of physical functioning in older adults. *Exerc Sport Sci Rev* 2012 Jan;40(1):4-12 [FREE Full text] [doi: [10.1097/JES.0b013e31823b5f13](https://doi.org/10.1097/JES.0b013e31823b5f13)] [Medline: [22016147](https://pubmed.ncbi.nlm.nih.gov/22016147/)]
13. Saeterbakken AH, Bårdstu HB, Brudeseth A, Andersen V. Effects of strength training on muscle properties, physical function, and physical activity among frail older people: a pilot study. *J Aging Res* 2018;2018:8916274 [FREE Full text] [doi: [10.1155/2018/8916274](https://doi.org/10.1155/2018/8916274)] [Medline: [29988285](https://pubmed.ncbi.nlm.nih.gov/29988285/)]
14. Gardner MM, Robertson MC, Campbell AJ. Exercise in preventing falls and fall related injuries in older people: a review of randomised controlled trials. *Br J Sports Med* 2000 Feb;34(1):7-17 [FREE Full text] [doi: [10.1136/bjism.34.1.7](https://doi.org/10.1136/bjism.34.1.7)] [Medline: [10690444](https://pubmed.ncbi.nlm.nih.gov/10690444/)]
15. Hunter GR, McCarthy JP, Bamman MM. Effects of resistance training on older adults. *Sports Med* 2004;34(5):329-348. [doi: [10.2165/00007256-200434050-00005](https://doi.org/10.2165/00007256-200434050-00005)] [Medline: [15107011](https://pubmed.ncbi.nlm.nih.gov/15107011/)]
16. Figueroa A, Okamoto T, Jaime S, Fahs C. Impact of high- and low-intensity resistance training on arterial stiffness and blood pressure in adults across the lifespan: a review. *Pflugers Arch* 2019 Mar;471(3):467-478. [doi: [10.1007/s00424-018-2235-8](https://doi.org/10.1007/s00424-018-2235-8)] [Medline: [30426247](https://pubmed.ncbi.nlm.nih.gov/30426247/)]
17. Centner C, Wiegel P, Gollhofer A, König D. Correction to: effects of blood flow restriction training on muscular strength and hypertrophy in older individuals: a systematic review and meta-analysis. *Sports Med* 2019 Jan;49(1):109-111. [doi: [10.1007/s40279-018-1013-2](https://doi.org/10.1007/s40279-018-1013-2)] [Medline: [30414044](https://pubmed.ncbi.nlm.nih.gov/30414044/)]
18. Horiuchi M, Okita K. Blood flow restricted exercise and vascular function. *Int J Vasc Med* 2012;2012:543218 [FREE Full text] [doi: [10.1155/2012/543218](https://doi.org/10.1155/2012/543218)] [Medline: [23133756](https://pubmed.ncbi.nlm.nih.gov/23133756/)]
19. Amorim S, Gaspar AP, Degens H, de Matos LD. The effects of blood flow restriction exercise on vascular function in the elderly: a systematic review. *Intergr Clin Med* 2019;3(1):1-6. [doi: [10.15761/ICM.1000140](https://doi.org/10.15761/ICM.1000140)]
20. Yasuda T, Fukumura K, Uchida Y, Koshi H, Iida H, Masamune K, et al. Effects of low-load, elastic band resistance training combined with blood flow restriction on muscle size and arterial stiffness in older adults. *J Gerontol A Biol Sci Med Sci* 2015 Aug;70(8):950-958. [doi: [10.1093/gerona/glu084](https://doi.org/10.1093/gerona/glu084)] [Medline: [24917178](https://pubmed.ncbi.nlm.nih.gov/24917178/)]
21. Randomization. URL: <http://randomization.com/> [accessed 2019-09-17]
22. Kim J, Shin W. How to do random allocation (randomization). *Clin Orthop Surg* 2014 Mar;6(1):103-109 [FREE Full text] [doi: [10.4055/cios.2014.6.1.103](https://doi.org/10.4055/cios.2014.6.1.103)] [Medline: [24605197](https://pubmed.ncbi.nlm.nih.gov/24605197/)]
23. Satoh I. Kaatsu training: application to metabolic syndrome. *Int J KAATSU Train Res* 2011;7(1):7-12. [doi: [10.3806/ijktr.7.7](https://doi.org/10.3806/ijktr.7.7)]
24. KAATSU Global. 2017. KAATSU User Manual: KAATSU Protocols for Training, Recovery, Rehabilitation, Fitness, and Wellness URL: https://www.kaatsu-global.com/Assets/Files/Presentations/KAATSU_User_Manual.pdf [accessed 2019-09-16]
25. Wythe S, Davies T, Martin D, Feelisch M, Gilbert-Kawai E. Getting the most from venous occlusion plethysmography: proposed methods for the analysis of data with a rest/exercise protocol. *Extrem Physiol Med* 2015;4:8 [FREE Full text] [doi: [10.1186/s13728-015-0027-8](https://doi.org/10.1186/s13728-015-0027-8)] [Medline: [26060573](https://pubmed.ncbi.nlm.nih.gov/26060573/)]
26. Ray CA, Rea RF, Clary MP, Mark AL. Muscle sympathetic nerve responses to dynamic one-legged exercise: effect of body posture. *Am J Physiol* 1993 Jan;264(1 Pt 2):H1-H7. [doi: [10.1152/ajpheart.1993.264.1.H1](https://doi.org/10.1152/ajpheart.1993.264.1.H1)] [Medline: [8430836](https://pubmed.ncbi.nlm.nih.gov/8430836/)]
27. David M, Malti O, AlGhatrif M, Al Ghatrif M, Wright J, Canepa M, et al. Pulse wave velocity testing in the Baltimore longitudinal study of aging. *J Vis Exp* 2014 Feb 7(84):e50817 [FREE Full text] [doi: [10.3791/50817](https://doi.org/10.3791/50817)] [Medline: [24561745](https://pubmed.ncbi.nlm.nih.gov/24561745/)]
28. Thijssen DH, Black MA, Pyke KE, Padilla J, Atkinson G, Harris RA, et al. Assessment of flow-mediated dilation in humans: a methodological and physiological guideline. *Am J Physiol Heart Circ Physiol* 2011 Jan;300(1):H2-12 [FREE Full text] [doi: [10.1152/ajpheart.00471.2010](https://doi.org/10.1152/ajpheart.00471.2010)] [Medline: [20952670](https://pubmed.ncbi.nlm.nih.gov/20952670/)]
29. Black MA, Cable NT, Thijssen DH, Green DJ. Importance of measuring the time course of flow-mediated dilatation in humans. *Hypertension* 2008 Feb;51(2):203-210. [doi: [10.1161/HYPERTENSIONAHA.107.101014](https://doi.org/10.1161/HYPERTENSIONAHA.107.101014)] [Medline: [18086954](https://pubmed.ncbi.nlm.nih.gov/18086954/)]

30. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Cardiovascular Health Study Collaborative Research Group. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001 Mar;56(3):M146-M156. [doi: [10.1093/gerona/56.3.m146](https://doi.org/10.1093/gerona/56.3.m146)] [Medline: [11253156](https://pubmed.ncbi.nlm.nih.gov/11253156/)]
31. Falsarella G, Gasparotto LP, Barcelos CC, Coimbra IB, Moretto MC, Pascoa MA, et al. Body composition as a frailty marker for the elderly community. *Clin Interv Aging* 2015;10:1661-1666 [FREE Full text] [doi: [10.2147/CIA.S84632](https://doi.org/10.2147/CIA.S84632)] [Medline: [26527868](https://pubmed.ncbi.nlm.nih.gov/26527868/)]
32. Brown LE, Weir JP. ASEP procedures recommendation I: accurate assessment of muscular strength and power. *J Exerc Physiol* 2001;4(3):1-21 [FREE Full text]
33. Stewart AD, Marfell-Jones M, Olds T, de Ridder JH. International Standards for Anthropometric Assessment. Australia: International Society for the Advancement of Kinanthropometry; 2001.
34. Janssen B. EuroQol. 2015. EQ-5D User Guide URL: <https://euroqol.org/publications/user-guides/> [accessed 2019-09-16]
35. Shimizu R, Hotta K, Yamamoto S, Matsumoto T, Kamiya K, Kato M, et al. Low-intensity resistance training with blood flow restriction improves vascular endothelial function and peripheral blood circulation in healthy elderly people. *Eur J Appl Physiol* 2016 Apr;116(4):749-757. [doi: [10.1007/s00421-016-3328-8](https://doi.org/10.1007/s00421-016-3328-8)] [Medline: [26822582](https://pubmed.ncbi.nlm.nih.gov/26822582/)]
36. Patterson SD, Ferguson RA. Enhancing strength and postocclusive calf blood flow in older people with training with blood-flow restriction. *J Aging Phys Act* 2011 Jul;19(3):201-213. [doi: [10.1123/japa.19.3.201](https://doi.org/10.1123/japa.19.3.201)] [Medline: [21727301](https://pubmed.ncbi.nlm.nih.gov/21727301/)]
37. Yasuda T, Fukumura K, Fukuda T, Uchida Y, Iida H, Meguro M, et al. Muscle size and arterial stiffness after blood flow-restricted low-intensity resistance training in older adults. *Scand J Med Sci Sports* 2014 Oct;24(5):799-806. [doi: [10.1111/sms.12087](https://doi.org/10.1111/sms.12087)] [Medline: [23730848](https://pubmed.ncbi.nlm.nih.gov/23730848/)]

Abbreviations

- BFR:** blood flow restriction
CRE: conventional resistance exercise
FMD: flow-mediated dilation
RM: repetition maximum

Edited by G Eysenbach; submitted 12.05.19; peer-reviewed by W Zhang, M Khazae-Pool; comments to author 31.07.19; accepted 07.08.19; published 01.11.19.

Please cite as:

Amorim S, Degens H, Passos Gaspar A, De Matos LDNJ

The Effects of Resistance Exercise With Blood Flow Restriction on Flow-Mediated Dilation and Arterial Stiffness in Elderly People With Low Gait Speed: Protocol for a Randomized Controlled Trial

JMIR Res Protoc 2019;8(11):e14691

URL: <https://www.researchprotocols.org/2019/11/e14691>

doi: [10.2196/14691](https://doi.org/10.2196/14691)

PMID: [31682588](https://pubmed.ncbi.nlm.nih.gov/31682588/)

©Samuel Amorim Amorim, Hans Degens, Alexandra Passos Gaspar, Luciana Diniz Nagem Janot De Matos. Originally published in JMIR Research Protocols (<http://www.researchprotocols.org>), 01.11.2019. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in JMIR Research Protocols, is properly cited. The complete bibliographic information, a link to the original publication on <http://www.researchprotocols.org>, as well as this copyright and license information must be included.

Protocol

Home-Based Cardiac Rehabilitation in Brazil's Public Health Care: Protocol for a Randomized Controlled Trial

Ana Paula Lima¹, MSc; Isabella Oliveira Nascimento¹, MSc; Anne Caroline A Oliveira¹, PT; Thiago Henrique S Martins¹, PT; Danielle A Gomes Pereira¹, PhD; Raquel Rodrigues Britto¹, PhD

Physical Therapy Department, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

Corresponding Author:

Danielle A Gomes Pereira, PhD

Physical Therapy Department

Universidade Federal de Minas Gerais

Av Antonio Carlos, 6627

Belo Horizonte, 31270-901

Brazil

Phone: 55 31991037415

Email: danielleufmg@gmail.com

Abstract

Background: Coronary artery disease (CAD) is among the main causes of hospitalization and death worldwide, therefore, the implementation of programs to reduce its impact is necessary. Supervised cardiac rehabilitation has been shown to have positive effects on CAD control. However, there are barriers to patient participation in the traditional, face-to-face cardiac rehabilitation programs, mainly in low-resource environments.

Objective: This study aimed to verify patient compliance to a home-based cardiac rehabilitation program, which includes unsupervised health education and physical exercises, guided by telephone. Moreover, we compare this new method to the traditional supervised cardiac rehabilitation offered in most hospital centers.

Methods: We present here a two-arm, single-blinded, and randomized controlled design protocol, which compares the traditional cardiac rehabilitation (CenterRehab) with the home-based cardiac rehabilitation (Home-Based) in 72 patients affected by CAD. The primary outcome is the compliance to the cardiac rehabilitation sessions. The secondary outcomes (to evaluate effectiveness) include measurable variables such as functional capacity, CAD risk factors (blood pressure, waist circumference, glycemic, cholesterol levels, depressive symptoms, and the level of physical activity), the patient's quality of life, the disease knowledge, and the morbidity rate. Parameters such as the program cost and the usability will also be evaluated. The programs will last 12 weeks, with a total of 60 rehabilitation and 6 educational sessions. Patients of the CenterRehab program will participate in 24 supervised sessions and 36 home sessions, while the patients of the Home-Based program will participate in 2 supervised sessions and 58 home sessions, guided by telephone. After the 12-week period all participants will be recommended to continue practicing physical exercises at home or at a community center, and they will be invited for re-evaluation after 3 months. The outcomes will be evaluated at baseline, and after 3 and 6 months.

Results: Participants are currently being recruited for the trial. Data collection is anticipated to be completed by October 2019.

Conclusions: This is the first study in Brazil comparing the traditional cardiac rehabilitation approach with a novel, home-based protocol that uses an accessible and low-cost technology. If positive results are obtained, the study will contribute to establish a new and viable model of cardiac rehabilitation.

Trial Registration: ClinicalTrials.gov NCT03605992; <https://clinicaltrials.gov/ct2/show/NCT03605992>

International Registered Report Identifier (IRRID): DERR1-10.2196/13901

(*JMIR Res Protoc* 2019;8(11):e13901) doi:[10.2196/13901](https://doi.org/10.2196/13901)

KEYWORDS

cardiac rehabilitation; coronary disease; exercise

Introduction

Background

Cardiovascular diseases (CVDs), including its main form, the coronary artery disease (CAD), are the leading cause of death worldwide [1]. CAD has a negative impact on morbidity, quality of life, and survival of the population [2]. In Brazil, CAD is among the main causes of hospitalization and death [3]; thus, the implementation of programs that minimize these impacts is necessary [4-6].

The World Health Organization defined cardiac rehabilitation (CR) as a set of activities and interventions necessary to ensure the best physical, mental, and social conditions for the patients with chronic or postacute CVD, to be able to preserve or return to their appropriate place in the society by their own efforts [7]. The main goal of CR is the education and training for self-care, with an emphasis on physical exercise, as its positive effects on improving the quality of life as well as reducing hospitalization and the risk of death in CAD patients have been thoroughly demonstrated [8-10].

Despite the benefits of supervised CR programs, such interventions have been shown to be impractical in low- and middle-income countries (LMICs). Only 40% of them currently have a CR program, and in those, there is a grossly insufficient capacity [11]. In Brazil, it is estimated that more than 3.9 million people would benefit from a CR program; however, less than 20% of them have access to it [12]. The main obstacles for participation in CR programs in low-resource environments are the accessibility to programs provided by the public health system and the lack of time because of professional and family commitments and transport availability [10,12]. Therefore, alternative CR models are necessary to improve participation, considering the community diversities and the economic viability [13,14].

Therefore, the home CR model presents some advantages and improves patients' participation and compliance to a healthy lifestyle and drug treatment as well as facilitates the patient and health professional education process [15,16].

Home-based CR is a term used to refer to CR at home or in other nonclinical settings, such as community centers, health clubs, and parks. This term also encompasses the use of information and communication technologies and hybrid form rehabilitation (ie, some sessions held in person at the rehabilitation clinic in conjunction with rehabilitation sessions at home) [16]. The home-based CR approach has been shown to be more efficient compared with conventional rehabilitation programs [16-19]. Studies showed that CR programs performed at home can overcome the traditional participation barriers and

promote effects comparable with CR outpatients regarding the mortality, risk of recurrent coronary event, cardiovascular risk factors, and exercise capacity [17-19].

Different models of interventions and cardiac monitoring are used in home rehabilitation programs [5,6,15,17,19]. However, most models use equipment demanding a higher technological ability from the participants, such as manipulating digital equipment, downloading data from an exercise tracking equipment to a computer, using a chat software, and receiving information via email. Patients with a low education level living in a low-resource environment could have difficulties in making proper use of the required equipment. Thus, one of the challenges in designing a home-based CR program in LMICs is the use of a feasible, accessible, and viable technology for monitoring patients. Ideally, the technology should ensure an ideal heart rate range to allow for the expected training effects, without increasing the risk of adverse effects.

Objectives

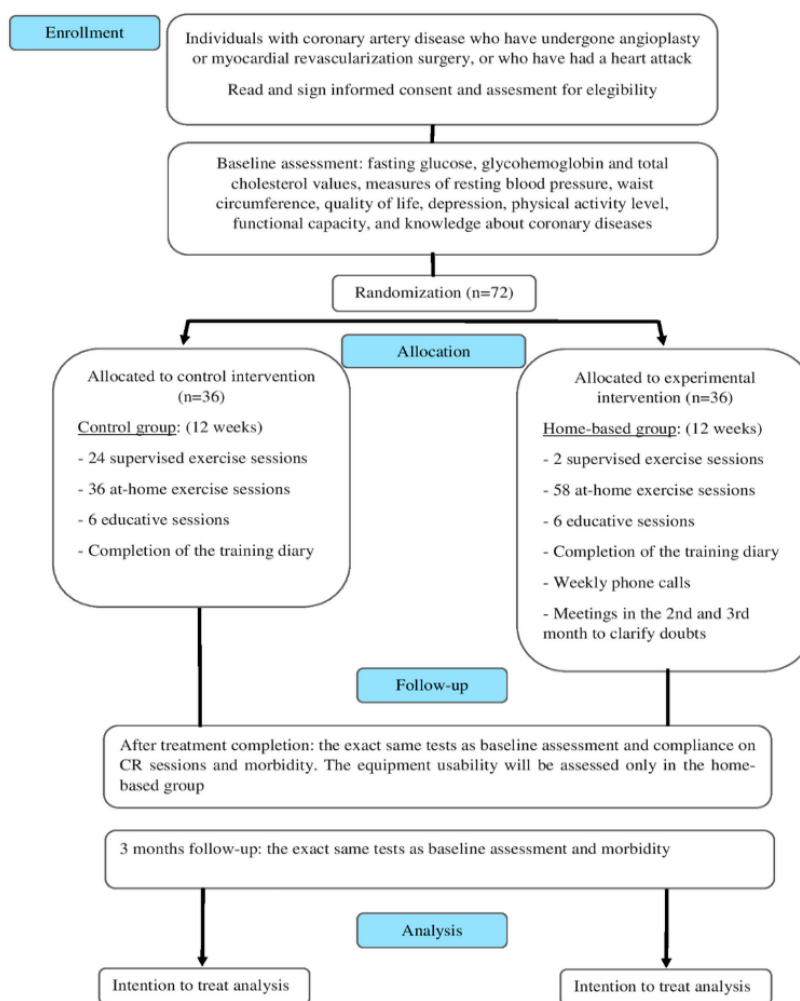
The aim of this trial is to verify the compliance and the effectiveness of a home-based CR program, which includes the health education and physical exercises components, mostly unsupervised and guided by telephone. We also compare this novel approach with the traditional, supervised CR program offered in most Brazilian hospital centers.

Methods

Study Design and Procedure

The study is a single-blind, randomized controlled trial. The researchers will be blinded for the treatment's allocation during the duration of the trial. Owing to the nature of the intervention, neither the participants nor the program staff can be blinded to the allocation type. Patients will be recruited at the outpatient University Hospital's CR Center. The study will conform to the Consolidated Standards of Reporting Trials (CONSORT) guidelines for nonpharmacological interventions [20]. After being invited to participate in the study, the volunteers will sign a consent form and will be randomized into 2 different groups: traditional CR (mostly supervised) and home-based CR (mostly unsupervised). The randomization will be made in blocks of 4 volunteers at a time [21]. A blinded researcher will evaluate the participants before and after the intervention and will collect the data into a database.

This study protocol is in accordance with the most recent version of the World Medical Association Declaration of Helsinki. This study was approved by the Ethics Committee in Research of the Universidade Federal de Minas Gerais, Brazil and was registered under the CAAE 51528615.3.0000.5149, on February 23, 2016. The CONSORT flowchart is reported in [Figure 1](#).

Figure 1. Consolidated Standards of Reporting Trials flow chart. CR: cardiac rehabilitation.

Patient and Public Involvement

Patients and the public were not directly involved in the study design. The intervention design was chosen based on previous studies, which reported that home-based CR programs promoted comparable effects with CR outpatient regarding the mortality, recurrent coronary event risk, cardiovascular risk factors, and exercise capacity [2,16-19,22]. The results of the study will be disseminated through institutional media, and educational activities will be conducted with CR patients and the study participants.

Participants

Patients will be eligible if they meet the following inclusion criteria: (1) if they have a CAD and have undergone angioplasty or myocardial revascularization surgery and (2) if they had a heart attack, provided that they were considered at low and moderate risk for the practice of physical exercise of moderate intensity, according to the stratification for the risk of events during a cardiovascular rehabilitation program [23]. Moreover, the inclusion criteria would require that patients have clinical stability (according to a medical evaluation) and be resident of the Belo Horizonte metropolitan region. Participants will be excluded if the history of recent cardiac events or clinical decompensation is more recent than 1 month and if at least one of the following limitations is present: peripheral arterial

occlusive disease, preventing the test of maximum exercise level (emergence of claudication before the maximal cardiorespiratory fatigue); chronic pulmonary disease (ie, chronic obstructive pulmonary disease, pulmonary fibrosis, and pulmonary arterial hypertension of precapillary etiology); history of ventricular fibrillation or sustained ventricular tachycardia in the last year; and physical, cognitive, and/or social limitations that prevent participation in a physical exercise program and the comprehension of monitoring the device usage.

Intervention

The parameters for monitoring the exercise prescription compliance will be the same for both groups. An exercise session will be constituted by 5 to 10 min of warm up, 40 min of aerobic activity with a heart rate between 60% and 80% of the heart's maximum rate, and 5 to 10 min of cool down [24]. The educational sessions will be given to both groups in 6 meetings of 40 min, using a systematized protocol [25]. In these meetings, topics regarding the control of risk factors and the treatment of CVDs will be taught. After the 12 weeks of intervention, all participants will be encouraged to continue practicing physical exercises either at home or at the community center and will be invited for a re-evaluation after 3 months.

Groups

Traditional and Face-to-Face Cardiac Rehabilitation as Control Group

The control group will receive, in person, the usual program consisting of supervised exercises and health educational activities at the CR center. This intervention will last for 12 weeks, with a total of 60 sessions: 24 supervised and 36 home sessions (5 exercise sessions per week). The participants of this group will be instructed to complete a training diary, with information regarding the frequency and intensity of exercises (using a scale of perceived exertion) as well as the presence of symptoms during or after exercises. The same information will be registered in their individual file while exercising at the CR center.

Home-Based Cardiac Rehabilitation

The participants of this program will perform their exercise mostly at home. Weekly phone calls will be programmed to check the correct execution of the previous stage of the program and also identify and register the presence of symptoms and undesirable effects. Monthly meetings will be programmed for educational activities to verify if the exercises and training diary are being both performed and compiled correctly and to address any kind of issue by the participants.

This intervention will have a duration of 12 weeks, with a total of 60 sessions: 2 supervised sessions and 58 home sessions (5 exercise sessions per week).

During the first week, all individuals of the home-based group will be receiving training regarding the utilization of the monitoring equipment. A heart rate monitor with the heart rate zone individually calculated will be given to each participant at the first supervised session. Furthermore, all participants of this group will be using a step counter (pedometer) to monitor the number of prescribed exercises as well as an aid to compile the training diary with information regarding the frequency of exercises, the presence of symptoms during the exercise, the perceived exertion, and the number of daily steps.

Measures

The participants will be invited to complete a sociodemographic questionnaire. The clinical characteristics will be extracted from the participant's medical records, including the risk factors, cardiac history, results of cardiac examinations, comorbidities, and medications in use.

Primary Outcome: Compliance of Cardiac Rehabilitation Sessions

The primary outcome of this trial was carefully chosen. A correct exercise compliance promotes positive changes in

behavior and lifestyle [18], besides reducing the risk for rehospitalization and improving quality of life [26].

The compliance on CR sessions will be analyzed by the percentage of participants who completed at least 75% (45/60) of the sessions. This parameter will be evaluated after 3 months.

Secondary Outcomes: Functional Capacity, Cost, Morbidity, Control of Risk Factors, Heart Health Behaviors, and Usability

Changes in the functional capacity will be analyzed using the incremental shuttle walk test (ISWT), a walking test that evaluates the functional capacity through the analysis of the walked distance [27].

The cost analysis and morbidity variables will be evaluated after 3 months and after 3 and 6 months, respectively, in both groups. The analysis of the programs' cost will be made by calculating the total sum of each procedure in the 2 groups, considering the hospital's payments table for procedures and services. Morbidity will be evaluated through a survey to identify the number of hospitalizations, complications, and the presence of adverse clinical events during the study period.

Resting blood pressure, measured in mm Hg, and waist circumference, measured in cm, will be analyzed. Waist circumference will be assessed at the superior border of the iliac crest, in accordance with the standardized guideline [28]. Alterations in fasting glucose (mg/dL), glycohemoglobin (%), and total cholesterol (mg/dL) values will be analyzed before the CR program and reanalyzed after 3 and 6 months.

Other behaviors will be assessed using psychometrically validated scales. Quality of life will be assessed using the Short Form 36 questionnaire [29], depression by the Patient Health Questionnaire-9 [30], the physical activity level using the Duke Activity Status Index Score [31], and the level of knowledge by the Coronary Artery Disease Education Questionnaire-Short Version [32].

Alterations in fasting glucose, glycohemoglobin, total cholesterol values, measures of resting blood pressure, waist circumference, quality of life, depression, physical activity level, functional capacity, and knowledge about coronary diseases will be evaluated at the beginning and after 3 and 6 months of the intervention in both groups. The assessment schedule is reported in Table 1.

The usability of the equipment used in the home-based group will be verified through the System Usability Scale after 3 months [33].

Table 1. Schedule of outcome assessments for control and home-based groups.

| Outcome measures | Control group | | | Home-based group | | |
|---|----------------|----------------|----------|------------------|----------|----------|
| | Baseline | 3 months | 6 months | Baseline | 3 months | 6 months |
| Primary outcome | | | | | | |
| Compliance on cardiac rehabilitation sessions | — ^a | X ^b | — | — | X | — |
| Secondary outcomes | | | | | | |
| Functional capacity | X | X | X | X | X | X |
| Cost analysis | — | X | — | — | X | — |
| Morbidity | — | X | X | — | X | X |
| Risk factors | | | | | | |
| Resting blood pressure | X | X | X | X | X | X |
| Waist circumference | X | X | X | X | X | X |
| Fasting glucose | X | X | X | X | X | X |
| Glycohemoglobin | X | X | X | X | X | X |
| Total cholesterol | X | X | X | X | X | X |
| Heart health behaviors | | | | | | |
| Quality of life | X | X | X | X | X | X |
| Depression | X | X | X | X | X | X |
| Physical activity level | X | X | X | X | X | X |
| Knowledge | X | X | X | X | X | X |
| Usability | — | — | — | — | X | — |

^aNo collection for the specified outcome measure on that date.

^bCollection for the specified outcome measure on that date.

Data Monitoring

An independent researcher, who will be blinded to the group allocation, will perform database management and the statistical analysis.

Sample Size

On the basis of previous CR studies [34] and on our 7-year experience in providing rehabilitation services in a university hospital, we estimated a compliance of 70% in the control group and of 96% in the home-based group. We calculated that for an alpha significance level of 5% and a power of 80% in the Fisher exact *t* test, the sample size of each group should be at least 36 volunteers. We also calculated the sample size for the secondary outcome, the functional capacity (ISWT), considering an arbitrary small size effect of 0.25. To detect a statistically significant difference within and between groups (2×2), at least 34 volunteers in each group are needed, keeping the same values of alpha and power. After a pilot study with 10 subjects in each group, the sample calculation will be performed again. All the calculations were made using the G Power 3.1.9.2. software (Franz, Universitat Kiel) [35].

Statistical Analyses

Data will be presented as a measure of the central tendency and dispersion. Data distribution will be analyzed using the Shapiro-Wilk test. All statistical analyses will be performed considering the intention-to-treat analysis and a per protocol

basis to mitigate bias. The comparison between groups of the primary outcome will be made using the Fisher exact test, considering that the expected frequency of noncompliance of the home-based group may assume a value lower than 5%. Differences between groups and at the follow-up 3 and 6 months after the intervention, in addition to the interaction effect, will be analyzed using the generalized estimation equations [36]. In all models, the endpoint variable will be analyzed as a dependent variable and the variable at baseline and after 3 months as independent variables. An alpha value of 5% will be considered for statistical significance. Post hoc tests will be performed where significant differences are observed between the groups.

Results

Recruitment started in February 2018 with an end date of October 2019. Between February 2018 and August 2019, 51 patients have consented to participate in this trial, and all of them were evaluated after 3 months. The recruitment was slower than estimated because of the reform of the CR sector during this period.

Discussion

Principal Findings

Various studies showed that home-based CR programs overcome the traditional participation barriers and promote effects comparable with CR outpatients regarding the mortality, risk

of recurrent coronary event, cardiovascular risk factors, and exercise capacity [16-34]. These studies were mostly performed in the middle- and high-income countries, where the use of technologies is viable without great difficulties.

In LMICs, the use of technologies for CR programs is oftentimes not feasible. Thus, our study is important because it is performed in a public hospital in a country with a prevalence of low-income, low-schooling population, which have difficulties in using new technologies.

To our knowledge, this is the first study performed in Brazil that contemplates a remote CR program using an accessible and low-cost technology. If positive results are obtained, this study will contribute to establish a new model of remote CR, where the participants will be able to perform the prescribed exercises near home, at convenient times, minimizing the barriers for

access to CR and reaching populations that frequently would not have accessibility to CR programs.

We believe that this study has a high potential to improve the care of patients affected by CAD in Brazil as well as in other countries from Latin America.

Strengths and Limitation of This Study

An important strength of this study is the first to examining the potential of assessing CR remotely in Brazil using an accessible and low-cost technology. There is currently insufficient evidence on the effectiveness of home-based CR programs in LMICs, so the results may be used to improve the care of patients with coronary diseases in Brazil as well as in other LMICs. The limitation of this study is that it enrolls participants with low and moderate risk. Therefore, the results of this study may be used in the practice of cardiovascular rehabilitation within certain limitations.

Acknowledgments

The authors would like to thank the Fundação de Amparo à Pesquisa do Estado de Minas Gerais, Conselho Nacional de Desenvolvimento Científico e Tecnológico, Coordenação de Aperfeiçoamento de Pessoal de Nível Superior, and Pró-Reitoria de Pesquisa da Universidade Federal de Minas Gerais for financial support.

Authors' Contributions

APL conceived and designed the study, drafted the first version of the manuscript, and approved the final version of the manuscript. ION, ACAO, and THSM participated in the design of the study, read and reviewed the manuscript, and approved the final version of the manuscript. DAGP participated in revising the study protocol, read and reviewed the manuscript, and approved the final version of the manuscript. RRB participated in and supervised the design of the study, read and reviewed the manuscript, and approved the final version of the manuscript.

Conflicts of Interest

None declared.

References

1. Ghisi GL, Santos RZ, Schweitzer V, Barros AL, Recchia TL, Oh P, et al. Development and validation of the Brazilian Portuguese version of the Cardiac Rehabilitation Barriers Scale. *Arq Bras Cardiol* 2012 Apr;98(4):344-351 [FREE Full text] [doi: [10.1590/s0066-782x2012005000025](https://doi.org/10.1590/s0066-782x2012005000025)] [Medline: [22426990](https://pubmed.ncbi.nlm.nih.gov/22426990/)]
2. Radtke MB, Wichmann FM, Couto AN. Diagnóstico primário dos fatores de risco coronariano em idosos vinculados à estratégia saúde da família no interior do Rio Grande do Sul. *Cinergis* 2016;17(4):350-357 [FREE Full text] [doi: [10.17058/cinergis.v17i0.8152](https://doi.org/10.17058/cinergis.v17i0.8152)]
3. DATASUS - Ministry of Health. SIM Mortality Information System URL: <http://datasus.saude.gov.br/sistemas-e-aplicativos/eventos-v/sim-sistema-de-informacoes-de-mortalidade> [accessed 2017-11-10]
4. Britto RR, Supervia M, Turk-Adawi K, Chaves GS, Pesah E, Lopez-Jimenez F, et al. Cardiac rehabilitation availability and delivery in Brazil: a comparison to other upper middle-income countries. *Braz J Phys Ther* 2019 Mar 05. [doi: [10.1016/j.bjpt.2019.02.011](https://doi.org/10.1016/j.bjpt.2019.02.011)] [Medline: [30862431](https://pubmed.ncbi.nlm.nih.gov/30862431/)]
5. Sankaran S, Dendale P, Coninx K. Evaluating the impact of the HeartHab app on motivation, physical activity, quality of life, and risk factors of coronary artery disease patients: multidisciplinary crossover study. *JMIR Mhealth Uhealth* 2019 Apr 4;7(4):e10874 [FREE Full text] [doi: [10.2196/10874](https://doi.org/10.2196/10874)] [Medline: [30946021](https://pubmed.ncbi.nlm.nih.gov/30946021/)]
6. Duan YP, Liang W, Guo L, Wienert J, Si GY, Lippke S. Evaluation of a web-based intervention for multiple health behavior changes in patients with coronary heart disease in home-based rehabilitation: pilot randomized controlled trial. *J Med Internet Res* 2018 Nov 19;20(11):e12052 [FREE Full text] [doi: [10.2196/12052](https://doi.org/10.2196/12052)] [Medline: [30455167](https://pubmed.ncbi.nlm.nih.gov/30455167/)]
7. Rehabilitation after cardiovascular diseases, with special emphasis on developing countries. Report of a WHO Expert Committee. *World Health Organ Tech Rep Ser* 1993;831:1-122. [Medline: [8351937](https://pubmed.ncbi.nlm.nih.gov/8351937/)]
8. Giannuzzi P, Saner H, Björnstad H, Fioretti P, Mendes M, Cohen-Solal A, Working Group on Cardiac Rehabilitation and Exercise Physiology of the European Society of Cardiology. Secondary prevention through cardiac rehabilitation: position

- paper of the Working Group on Cardiac Rehabilitation and Exercise Physiology of the European Society of Cardiology. *Eur Heart J* 2003 Jul;24(13):1273-1278. [doi: [10.1016/s0195-668x\(03\)00198-2](https://doi.org/10.1016/s0195-668x(03)00198-2)] [Medline: [12831822](https://pubmed.ncbi.nlm.nih.gov/12831822/)]
9. Leon AS, Franklin BA, Costa F, Balady GJ, Berra KA, Stewart KJ, American Heart Association, Council on Clinical Cardiology (Subcommittee on Exercise, Cardiac Rehabilitation, Prevention), Council on Nutrition, Physical Activity, Metabolism (Subcommittee on Physical Activity), American Association of Cardiovascular and Pulmonary Rehabilitation. Cardiac rehabilitation and secondary prevention of coronary heart disease: an American Heart Association scientific statement from the Council on Clinical Cardiology (Subcommittee on Exercise, Cardiac Rehabilitation, and Prevention) and the Council on Nutrition, Physical Activity, and Metabolism (Subcommittee on Physical Activity), in collaboration with the American Association of Cardiovascular and Pulmonary Rehabilitation. *Circulation* 2005 Jan 25;111(3):369-376. [doi: [10.1161/01.CIR.0000151788.08740.5C](https://doi.org/10.1161/01.CIR.0000151788.08740.5C)] [Medline: [15668354](https://pubmed.ncbi.nlm.nih.gov/15668354/)]
 10. Lavie CJ, Thomas RJ, Squires RW, Allison TG, Milani RV. Exercise training and cardiac rehabilitation in primary and secondary prevention of coronary heart disease. *Mayo Clin Proc* 2009 Apr;84(4):373-383 [FREE Full text] [doi: [10.1016/S0025-6196\(11\)60548-X](https://doi.org/10.1016/S0025-6196(11)60548-X)] [Medline: [19339657](https://pubmed.ncbi.nlm.nih.gov/19339657/)]
 11. Pesah E, Turk-Adawi K, Supervia M, Lopez-Jimenez F, Britto R, Ding R, et al. Cardiac rehabilitation delivery in low/middle-income countries. *Heart* 2019 Jun 28. [doi: [10.1136/heartjnl-2018-314486](https://doi.org/10.1136/heartjnl-2018-314486)] [Medline: [31253695](https://pubmed.ncbi.nlm.nih.gov/31253695/)]
 12. Cortes-Bergoderi M, Lopez-Jimenez F, Herdy AH, Zeballos C, Anchique C, Santibañez C, et al. Availability and characteristics of cardiovascular rehabilitation programs in South America. *J Cardiopulm Rehabil Prev* 2013;33(1):33-41. [doi: [10.1097/HCR.0b013e318272153e](https://doi.org/10.1097/HCR.0b013e318272153e)] [Medline: [23235320](https://pubmed.ncbi.nlm.nih.gov/23235320/)]
 13. Ghisi GL, dos Santos RZ, Aranha EE, Nunes AD, Oh P, Benetti M, et al. Perceptions of barriers to cardiac rehabilitation use in Brazil. *Vasc Health Risk Manag* 2013;9:485-491 [FREE Full text] [doi: [10.2147/VHRM.S48213](https://doi.org/10.2147/VHRM.S48213)] [Medline: [24039433](https://pubmed.ncbi.nlm.nih.gov/24039433/)]
 14. Grace SL, Turk-Adawi KI, Contractor A, Atrey A, Campbell N, Derman W, et al. Cardiac rehabilitation delivery model for low-resource settings. *Heart* 2016 Sep 15;102(18):1449-1455 [FREE Full text] [doi: [10.1136/heartjnl-2015-309209](https://doi.org/10.1136/heartjnl-2015-309209)] [Medline: [27181874](https://pubmed.ncbi.nlm.nih.gov/27181874/)]
 15. Neubeck L, Redfern J, Fernandez R, Briffa T, Bauman A, Freedman SB. Telehealth interventions for the secondary prevention of coronary heart disease: a systematic review. *Eur J Cardiovasc Prev Rehabil* 2009 Jun;16(3):281-289. [doi: [10.1097/HJR.0b013e32832a4e7a](https://doi.org/10.1097/HJR.0b013e32832a4e7a)] [Medline: [19407659](https://pubmed.ncbi.nlm.nih.gov/19407659/)]
 16. Thomas RJ, Beatty AL, Beckie TM, Brewer LC, Brown TM, Forman DE, et al. Home-based cardiac rehabilitation: a scientific statement from the American association of cardiovascular and pulmonary rehabilitation, the American heart association, and the American college of cardiology. *J Cardiopulm Rehabil Prev* 2019 Jul;39(4):208-225. [doi: [10.1097/HCR.0000000000000447](https://doi.org/10.1097/HCR.0000000000000447)] [Medline: [31082934](https://pubmed.ncbi.nlm.nih.gov/31082934/)]
 17. Oerkild B, Frederiksen M, Hansen JF, Simonsen L, Skovgaard LT, Prescott E. Home-based cardiac rehabilitation is as effective as centre-based cardiac rehabilitation among elderly with coronary heart disease: results from a randomised clinical trial. *Age Ageing* 2011 Jan;40(1):78-85. [doi: [10.1093/ageing/afq122](https://doi.org/10.1093/ageing/afq122)] [Medline: [20846961](https://pubmed.ncbi.nlm.nih.gov/20846961/)]
 18. Rawstorn JC, Gant N, Direito A, Beckmann C, Maddison R. Telehealth exercise-based cardiac rehabilitation: a systematic review and meta-analysis. *Heart* 2016 Aug 1;102(15):1183-1192. [doi: [10.1136/heartjnl-2015-308966](https://doi.org/10.1136/heartjnl-2015-308966)] [Medline: [26936337](https://pubmed.ncbi.nlm.nih.gov/26936337/)]
 19. Huang K, Liu W, He D, Huang B, Xiao D, Peng Y, et al. Telehealth interventions versus center-based cardiac rehabilitation of coronary artery disease: a systematic review and meta-analysis. *Eur J Prev Cardiol* 2015 Aug;22(8):959-971. [doi: [10.1177/2047487314561168](https://doi.org/10.1177/2047487314561168)] [Medline: [25488550](https://pubmed.ncbi.nlm.nih.gov/25488550/)]
 20. Boutron I, Altman DG, Moher D, Schulz KF, Ravaut P, CONSORT NPT Group. CONSORT statement for randomized trials of nonpharmacologic treatments: a 2017 update and a CONSORT extension for nonpharmacologic trial abstracts. *Ann Intern Med* 2017 Jul 4;167(1):40-47. [doi: [10.7326/M17-0046](https://doi.org/10.7326/M17-0046)] [Medline: [28630973](https://pubmed.ncbi.nlm.nih.gov/28630973/)]
 21. Dalal GE. Randomization. URL: <http://www.randomization.com> [accessed 2008-07-15]
 22. Clark RA, Conway A, Poulsen V, Keech W, Tirimacco R, Tideman P. Alternative models of cardiac rehabilitation: a systematic review. *Eur J Prev Cardiol* 2015 Jan;22(1):35-74. [doi: [10.1177/2047487313501093](https://doi.org/10.1177/2047487313501093)] [Medline: [23943649](https://pubmed.ncbi.nlm.nih.gov/23943649/)]
 23. American Association of Cardiovascular and Pulmonary Rehabilitation. Guidelines for Cardiac Rehabilitation and Secondary Prevention Programs. Champaign, IL: Human Kinetics c2004; 2004.
 24. Mezzani A, Hamm LF, Jones AM, McBride PE, Moholdt T, Stone JA, European Association for Cardiovascular Prevention and Rehabilitation, American Association of Cardiovascular and Pulmonary Rehabilitation, Canadian Association of Cardiac Rehabilitation. Aerobic exercise intensity assessment and prescription in cardiac rehabilitation: a joint position statement of the European Association for Cardiovascular Prevention and Rehabilitation, the American Association of Cardiovascular and Pulmonary Rehabilitation and the Canadian Association of Cardiac Rehabilitation. *Eur J Prev Cardiol* 2013 Jun;20(3):442-467. [doi: [10.1177/2047487312460484](https://doi.org/10.1177/2047487312460484)] [Medline: [23104970](https://pubmed.ncbi.nlm.nih.gov/23104970/)]
 25. Chaves GS, Ghisi GL, Grace SL, Oh P, Ribeiro AL, Britto RR. Effects of comprehensive cardiac rehabilitation on functional capacity in a middle-income country: a randomised controlled trial. *Heart* 2018 Oct 3. [doi: [10.1136/heartjnl-2018-313632](https://doi.org/10.1136/heartjnl-2018-313632)] [Medline: [30282639](https://pubmed.ncbi.nlm.nih.gov/30282639/)]
 26. Thomas RJ, Balady G, Banka G, Beckie TM, Chiu J, Gokak S, et al. 2018 ACC/AHA clinical performance and quality measures for cardiac rehabilitation: a report of the American College of Cardiology/American Heart Association task force on performance measures. *J Am Coll Cardiol* 2018 Apr 24;71(16):1814-1837 [FREE Full text] [doi: [10.1016/j.jacc.2018.01.004](https://doi.org/10.1016/j.jacc.2018.01.004)] [Medline: [29606402](https://pubmed.ncbi.nlm.nih.gov/29606402/)]

27. Singh SJ, Morgan MD, Scott S, Walters D, Hardman AE. Development of a shuttle walking test of disability in patients with chronic airways obstruction. *Thorax* 1992 Dec;47(12):1019-1024 [FREE Full text] [doi: [10.1136/thx.47.12.1019](https://doi.org/10.1136/thx.47.12.1019)] [Medline: [1494764](https://pubmed.ncbi.nlm.nih.gov/1494764/)]
28. Herdy AH, López-Jiménez F, Terzic CP, Milani M, Stein R, Carvalho T, et al. South American guidelines for cardiovascular disease prevention and rehabilitation. *Arq Bras Cardiol* 2014 Aug;103(2 Suppl 1):1-31 [FREE Full text] [doi: [10.5935/abc.2014s003](https://doi.org/10.5935/abc.2014s003)] [Medline: [25387466](https://pubmed.ncbi.nlm.nih.gov/25387466/)]
29. Ciconelli R, Ferraz M, Santos W, Meinão I, Quaresma M. Brazilian-Portuguese version of the SF-36 questionnaire: a reliable and valid quality of life outcome measure. *Rev Bras Reumatol* 1999;39(3):143-150 [FREE Full text]
30. Santos IS, Tavares BF, Munhoz TN, Almeida LS, Silva NT, Tams BD, et al. [Sensitivity and specificity of the Patient Health Questionnaire-9 (PHQ-9) among adults from the general population]. *Cad Saude Publica* 2013 Aug;29(8):1533-1543 [FREE Full text] [doi: [10.1590/0102-311x00144612](https://doi.org/10.1590/0102-311x00144612)] [Medline: [24005919](https://pubmed.ncbi.nlm.nih.gov/24005919/)]
31. Coutinho-Myrrha MA, Dias RC, Fernandes AA, Araújo CG, Hlatky MA, Pereira DG, et al. Duke Activity Status Index for cardiovascular diseases: validation of the Portuguese translation. *Arq Bras Cardiol* 2014 Apr;102(4):383-390 [FREE Full text] [doi: [10.5935/abc.20140031](https://doi.org/10.5935/abc.20140031)] [Medline: [24652056](https://pubmed.ncbi.nlm.nih.gov/24652056/)]
32. Ghisi GL, Sandison N, Oh P. Development, pilot testing and psychometric validation of a short version of the coronary artery disease education questionnaire: The CADE-Q SV. *Patient Educ Couns* 2016 Mar;99(3):443-447. [doi: [10.1016/j.pec.2015.11.002](https://doi.org/10.1016/j.pec.2015.11.002)] [Medline: [26610390](https://pubmed.ncbi.nlm.nih.gov/26610390/)]
33. Martins AI, Rosa AF, Queirós A, Silva A, Rocha NP. European Portuguese validation of the System Usability Scale (SUS). *Procedia Comput Sci* 2015;67:293-300. [doi: [10.1016/j.procs.2015.09.273](https://doi.org/10.1016/j.procs.2015.09.273)]
34. Varnfield M, Karunanithi M, Lee C, Honeyman E, Arnold D, Ding H, et al. Smartphone-based home care model improved use of cardiac rehabilitation in postmyocardial infarction patients: results from a randomised controlled trial. *Heart* 2014 Nov;100(22):1770-1779 [FREE Full text] [doi: [10.1136/heartjnl-2014-305783](https://doi.org/10.1136/heartjnl-2014-305783)] [Medline: [24973083](https://pubmed.ncbi.nlm.nih.gov/24973083/)]
35. 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](https://doi.org/10.3758/BRM.41.4.1149)] [Medline: [19897823](https://pubmed.ncbi.nlm.nih.gov/19897823/)]
36. Tu XM, Zhang J, Kowalski J, Shults J, Feng C, Sun W, et al. Power analyses for longitudinal study designs with missing data. *Stat Med* 2007 Jul 10;26(15):2958-2981. [doi: [10.1002/sim.2773](https://doi.org/10.1002/sim.2773)] [Medline: [17154250](https://pubmed.ncbi.nlm.nih.gov/17154250/)]

Abbreviations

- CAD:** coronary artery disease
CONSORT: Consolidated Standards of Reporting Trials
CR: cardiac rehabilitation
CVD: cardiovascular diseases
ISWT: incremental shuttle walk test
LMIC: low- and middle-income country

Edited by G Eysenbach; submitted 05.03.19; peer-reviewed by M Varnfield, W Glinkowski, M Gonzalez Garcia; comments to author 03.06.19; revised version received 02.08.19; accepted 16.09.19; published 07.11.19.

Please cite as:

Lima AP, Nascimento IO, Oliveira ACA, Martins THS, Pereira DAG, Britto RR

Home-Based Cardiac Rehabilitation in Brazil's Public Health Care: Protocol for a Randomized Controlled Trial

JMIR Res Protoc 2019;8(11):e13901

URL: <https://www.researchprotocols.org/2019/11/e13901>

doi: [10.2196/13901](https://doi.org/10.2196/13901)

PMID: [31697246](https://pubmed.ncbi.nlm.nih.gov/31697246/)

©Ana Paula Lima, Isabella Oliveira Nascimento, Anne Caroline A Oliveira, Thiago Henrique S Martins, Danielle A Gomes Pereira, Raquel Rodrigues Britto. Originally published in *JMIR Research Protocols* (<http://www.researchprotocols.org>), 07.11.2019. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in *JMIR Research Protocols*, is properly cited. The complete bibliographic information, a link to the original publication on <http://www.researchprotocols.org>, as well as this copyright and license information must be included.

Protocol

HIV Prevention Via Mobile Messaging for Men Who Have Sex With Men (M-Cubed): Protocol for a Randomized Controlled Trial

Patrick Sean Sullivan¹, DVM, PhD; Ryan J Zahn¹, MSPH; Sarah Wiatrek¹, MPH; Cristian J Chandler¹, PhD; Sabina Hirshfield², PhD; Rob Stephenson³, PhD; Jose A Bauermeister³, PhD; Mary Ann Chiasson^{4,5}, DrPH; Martin J Downing Jr⁶, PhD; Deborah J Gelaude⁷, MA; Aaron J Siegler⁸, PhD; Keith Horvath⁹, PhD; Erin Rogers³, MPH; Ana Alas³, MPH; Evelyn J Olansky¹⁰, MPH; Heather Saul¹⁰, MSc; Eli S Rosenberg¹¹, PhD; Gordon Mansergh⁷, PhD

¹Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, GA, United States

²Department of Medicine, SUNY Downstate Health Sciences University, Brooklyn, NY, United States

³Center for Sexuality and Health Disparities, School of Nursing, University of Michigan, Ann Arbor, MI, United States

⁴Mailman School of Public Health, Columbia University, New York, NY, United States

⁵Division of Infectious Diseases, Columbia University Medical School, New York, NY, United States

⁶Lehman College, City University of New York, Bronx, NY, United States

⁷Division of HIV/AIDS Prevention, Centers for Disease Control and Prevention, Atlanta, GA, United States

⁸Department of Behavioral Sciences and Health Education, Rollins School of Public Health, Emory University, Atlanta, GA, United States

⁹Department of Psychology, San Diego State University, San Diego, CA, United States

¹⁰Health, Science and Human Services Division, ICF, Atlanta, GA, United States

¹¹Department of Epidemiology and Biostatistics, University at Albany - SUNY, Albany, NY, United States

Corresponding Author:

Patrick Sean Sullivan, DVM, PhD

Department of Epidemiology

Rollins School of Public Health

Emory University

1518 Clifton Road NE

Atlanta, GA, 30322

United States

Phone: 1 404 727 2038

Email: pssulli@emory.edu

Abstract

Background: Men who have sex with men (MSM) continue to be the predominately impacted risk group in the United States HIV epidemic and are a priority group for risk reduction in national strategic goals for HIV prevention. Modeling studies have demonstrated that a comprehensive package of status-tailored HIV prevention and care interventions have the potential to substantially reduce new infections among MSM. However, uptake of basic prevention services, including HIV testing, sexually transmitted infection (STI) testing, condom distribution, condom-compatible lubricant distribution, and preexposure prophylaxis (PrEP), is suboptimal. Further, stronger public health strategies are needed to promote engagement in HIV care and viral load suppression among MSM living with HIV. Mobile health (mHealth) tools can help inform and encourage MSM regarding HIV prevention, care, and treatment, especially among men who lack access to conventional medical services. This protocol details the design and procedures of a randomized controlled trial (RCT) of a novel mHealth intervention that comprises a comprehensive HIV prevention app and brief, tailored text- and video-based messages that are systematically presented to participants based on the participants' HIV status and level of HIV acquisition risk.

Objective: The objective of the RCT was to test the efficacy of the Mobile Messaging for Men (M-Cubed, or M3) app among at least 1200 MSM in Atlanta, Detroit, and New York. The goal was to determine its ability to increase HIV testing (HIV-negative men), STI testing (all men), condom use for anal sex (all men), evaluation for PrEP eligibility, uptake of PrEP (higher risk HIV-negative men), engagement in HIV care (men living with HIV), and uptake of and adherence to antiretroviral medications (men living with HIV). A unique benefit of this approach is the HIV serostatus-inclusiveness of the intervention, which includes both HIV-negative and HIV-positive MSM.

Methods: MSM were recruited through online and venue-based approaches in Atlanta, Detroit, and New York City. Men who were eligible and consented were randomized to the intervention (immediate access to the M3 app for a period of three months) or to the waitlist-control (delayed access) group. Outcomes were evaluated immediately postintervention or control period, and again three and six months after the intervention period. Main outcomes will be reported as period prevalence ratios or hazards, depending on the outcome. Where appropriate, serostatus/risk-specific outcomes will be evaluated in relevant subgroups. Men randomized to the control condition were offered the opportunity to use (and evaluate) the M3 app for a three-month period after the final RCT outcome assessment.

Results: M3 enrollment began in January 2018 and concluded in November 2018. A total of 1229 MSM were enrolled. Data collection was completed in September 2019.

Conclusions: This RCT of the M3 mobile app seeks to determine the effects of an HIV serostatus-inclusive intervention on the use of multiple HIV prevention and care-related outcomes among MSM. A strength of the design is that it incorporates a large sample and broad range of MSM with differing prevention needs in three cities with high prevalence of HIV among MSM.

Trial Registration: ClinicalTrials.gov NCT03666247; <https://clinicaltrials.gov/ct2/show/NCT03666247>

International Registered Report Identifier (IRRID): DERR1-10.2196/16439

(*JMIR Res Protoc* 2019;8(11):e16439) doi:[10.2196/16439](https://doi.org/10.2196/16439)

KEYWORDS

men who have sex with men; HIV prevention; HIV care

Introduction

Background

Men who have sex with men (MSM) face the highest burden of HIV in the United States [1], and there is a paucity of efficacious or promising mobile health (mHealth), HIV-prevention interventions tailored specifically for MSM [2]. New HIV prevention tools are needed that can address the needs of MSM, especially young MSM aged 15-24 for whom yearly HIV incidence doubled from 2002 to 2014 [3], and for young MSM of color for whom these burdens are most severe [4-6]. Currently, HIV prevention services are underutilized by MSM, with just over half (56%) reporting being tested in the past 12 months, high proportions (76% of HIV-positive and 66% of HIV-negative MSM) reporting recent condomless, receptive anal intercourse, and few (<20%) reporting utilization of pre-exposure prophylaxis (PrEP) [7]. Statistical models of MSM epidemics parameterized to represent US epidemics demonstrate that high levels of prevention service coverage will be required to substantially reduce HIV incidence [8,9], and increased utilization of routine prevention activities, like frequent HIV testing, may enhance the uptake of biomedical interventions like PrEP [10]. At the same time, engaging MSM living with HIV in mHealth HIV-prevention efforts is critical and addresses the two most important factors that determine cost-effectiveness, namely the HIV prevalence of the target population and the cost per person reached [11].

Researchers in the past decade have been exploring the most effective ways to engage MSM in a package of HIV prevention services. A growing body of research has suggested that mobile phone apps provide a dynamic environment for intervention and can offer on-demand prevention services for MSM [12-17]. This research indicates that MSM are open to receiving prevention information and resources via apps [18]. Electronic messages communicated through apps, known as mobile messaging, are an appealing approach to enhance intervention uptake because they allow for messaging that can reach a wide

audience of MSM, including rural MSM [16]. Further, younger MSM might be especially interested in using mobile technology to receive health information [19]. This study builds on an existing HIV prevention app designed for MSM, HealthMindr, to add and evaluate tailored prevention messaging.

The HealthMindr App

The HealthMindr app is a comprehensive HIV prevention app for MSM [20]. Developed using social cognitive theory [20,21], HealthMindr features basic prevention services, including: screening for HIV and sexually transmitted infection (STI) risk; a scheduling and reminder system for routine HIV testing; a PrEP eligibility screener; a nonoccupational postexposure prophylaxis (nPEP) risk assessment tool; an ordering platform for delivery of at-home HIV and STI screening kits, condoms, and lubricant; and service locators for HIV and STI testing, and PrEP, nPEP, and HIV treatment and care. The app was built based on extensive input from MSM, public health leaders, and staff from community-based organizations [22,23]. The basic app (before the addition of messages and videos) was pilot tested with 121 MSM in Atlanta and Seattle, and the results indicated high levels of acceptability, use of tools to develop and maintain a consistent HIV testing routine, use of PrEP screening and referrals, and ordering of at-home HIV test kits and condoms [20].

Study Intervention: HealthMindr Plus Brief Messages

The current study utilized the HealthMindr platform with the addition of social cognitive theory-based, sexual health messaging components. For this randomized controlled trial (RCT), we developed a series of brief text-based (n=63) and sourced a series of video (n=12) messages designed to promote health-seeking behavior and further the adoption of sexual health services recommended by HealthMindr. The messages were delivered through the HealthMindr platform and aligned with the prevention tools offered in the app [20]. The purpose of this study was to evaluate the use and efficacy of the mobile-messaging platform as a public health strategy for

improving sexual health outcome measures among MSM by determining whether exposure to the message-delivery platform resulted in improvements in participants' self-reported sexual health and prevention behaviors, beliefs, and attitudes. Specific aims to accomplish this purpose included two phases: (1) formative research (focus groups and in-depth interviews) for app message development; and (2) an RCT for testing efficacy of the app. This paper describes the methods for this study in more detail.

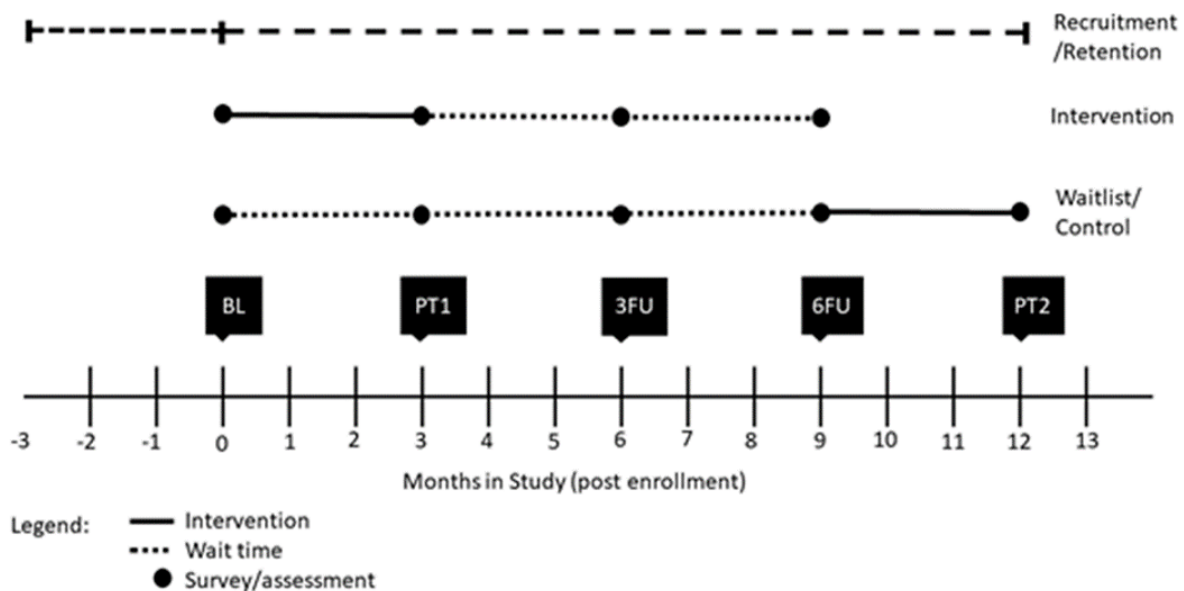
Methods

Overview

The Mobile Messaging for Men (M3) study was conducted in two phases. The first phase consisted of a series of focus groups and in-depth interviews to ensure that written messages, videos, and app features presented in the trial were appropriate for the audience. The second phase was an RCT, with MSM in three

serostatus/risk groups randomized to receive either the intervention condition (M3 app) for a three-month exposure period or a waitlist-control condition with the option to receive the app for three months at the end of the study. The serostatus/risk groups were defined by self-report as: (1) HIV seropositive; (2) HIV seronegative at higher risk (condomless anal sex and not taking PrEP as prescribed in the past 3 months); and (3) HIV seronegative at lower risk (no condomless anal sex in the past 3 months, or condomless anal sex while taking PrEP as prescribed in the past 3 months). Postintervention data collection occurred at three time points: 3 months (immediately postintervention), 6 months (three-months postintervention), and 9 months (six-months postintervention) (see [Figure 1](#)). Participant follow-up will be completed in September 2019, with primary outcome analyses to follow. The study was reviewed and approved by the Emory University Institutional Review Board (Protocol #87684) and registered at ClinicalTrials.gov (NCT03666247).

Figure 1. Timeline of participant activities and assessments. Only participants from the waitlist/control group who opt to participate in the intervention will be assessed in PT2. BL: baseline survey; PT: postintervention assessment; FU: follow-up survey.



Formative Research for Online Messages

Message Development Process

Message development for qualitative input from the target audience took two forms: brief written message and video message development. Two committees of subject matter experts (written messages: JB, GM, PS, KH, MD, EO, RZ; video messages: SH, MAC, EO, DG, BB, RZ, RS) were established to implement written and video message creation. First, the committees determined six domains of prevention messages and related study outcomes: (1) condom use; (2) HIV testing; (3) STI testing; (4) PrEP continuum outcomes; (5) antiretroviral therapy (ART) use; and (6) engagement in care.

The written message committee reviewed the literature on HIV prevention messages in the six domain areas, as well as messages used in their ongoing research, and developed 63 messages that were 2-3 sentences each and were organized into

the 6 prevention domains. Messages within each domain were mapped onto Social Cognitive Theory constructs (eg, information, relevance, norms, barriers, and self-efficacy). Through the mobile app, each participant received a common core of 36 messages (approximately 6 messages per domain) and another set of 9 secondary messages specific to each of the 3 serostatus/risk groups. For HIV-positive men, these secondary messages focused on ART uptake and adherence, for HIV-negative men who reported condomless anal sex in the past three months, additional messages pertained to PrEP, and for HIV-negative men who did not report recent condomless anal sex, additional messages were about condom use and HIV/STI testing. Participants were sent a written message every 1-2 days and a video message once per week.

The video messages were selected after identifying existing videos in the field of recent HIV and STI prevention related to the six domain areas, with the goal of identifying 12, approximately one-minute video clips for delivery on the mobile

app. About two videos per domain area were delivered to all study participants at a rate of one per week. Through online searches and common, prevention video-development funding agencies (eg, the Centers for Disease Control and Prevention and the Kaiser Family Foundation), an initial pool of several hundred videos was identified, and they were systematically and iteratively reduced in number by the subject matter expert committee through several rounds of reviews and ratings.

Phase 1: Formative Research

Qualitative Message Development Process

Two qualitative methods were used to elicit feedback from MSM who were potential participants in the RCT: focus group discussions and in-depth interviews. The goals of the qualitative phase were to: (1) develop knowledge around possible topics for HIV prevention messaging, preferred modes of receiving mobile prevention messages, and messaging frequency; and (2) develop HIV status/risk level-specific prevention messages intended for dissemination to MSM, cognitively test the messages, and finalize messages for inclusion in the RCT.

Nine focus group discussions, one per risk group per study city, were conducted. Focus group discussions focused on message delivery aspects, including mode, format, length, framing, delivery source, and other non-content related characteristics. Participants were prompted to describe notable HIV prevention messages they had encountered prior to their engagement with this study, describing both the content and format of the message as well as their thoughts on its efficacy and applicability. Participants were then asked to complete a pile-sorting activity [24], where participants were shown cards with HIV prevention messages and were asked to sort them into piles representing how they would like those messages to be received (eg, a card contained a message about regular condom use, and choices for delivery of message included video, scientific facts, or fun messaging). The aim was to understand which delivery and content factors were important for the delivery of each type of prevention message.

Two rounds of in-depth interviews were conducted: one round for text-based messages and one round for video messages. These in-depth interviews assessed the extent to which the

predeveloped text- or video-based messages were understood and believed, and how messages needed to be customized to address contextual differences and variations in prevention needs, such as local context, demographic contexts, risk group, or relationship contexts. For the written messages, 18 in-depth interviews were conducted, two per risk group per study city. Participants completed a ranking activity in which they were given cards on which predeveloped written messages were printed. Within each of the six domains listed above, participants ranked the messages from most effective to least effective. They were then asked about their reactions to each message, including their comprehension, willingness to read the message, appropriateness of the message and word choice, and their perception of their ability to enact behavioral change. For the video-based messages, 26 in-depth interviews were completed across the study sites. Participants were shown each video-based message and, after each, were asked about their reactions to the videos, including identification of intended messages, comprehension of the messages contained in each video, and willingness to view the message. Participants were also asked about specific elements of the video, such as length, style, language use, and how each video might be made more effective. Based on the feedback from participants in these focus group discussions and in-depth interviews, each written and video-based message was revised or edited by the subject matter experts to be made more suitable for inclusion in the RCT.

Intervention Messaging

The M3 intervention provided risk-customized written and video messages for participants, augmenting the core prevention services available in HealthMindr. Core messages were delivered to all participants regardless of HIV status and risk group. Secondary messages were delivered to participants based on their self-reported HIV status and risk group assignment at baseline; risk group status was dynamic during the trial and updated using data from monthly check-ins during the app exposure period or by participant self-initiation of check-in. Message domains for core and secondary messages are summarized in Table 1. Video messages were 60-80 second excerpts from existing videos related to HIV prevention and education. A total of 12 video messages were offered as part of the intervention for all participants regardless of risk group.

Table 1. M3 domains in the mobile app.

| Domain | Core messages | Secondary messages | | |
|--------------------------|-----------------|-------------------------|--------------------------|--------------|
| | All risk groups | Lower risk HIV-negative | Higher risk HIV-negative | HIV-positive |
| Condoms | ✓ | ✓ | ✓ | |
| STI ^a testing | ✓ | ✓ | ✓ | ✓ |
| HIV testing | ✓ | ✓ | ✓ | |
| PrEP ^b | ✓ | | ✓ | |
| ART ^c | ✓ | | | ✓ |
| Engagement in care | ✓ | | | ✓ |

^aSTI: sexually transmitted infection.

^bPrEP: pre-exposure prophylaxis.

^cART: antiretroviral therapy.

Messages were provided to participants according to a predetermined schedule and in a consistent sequence that started on their date of enrollment. Most messages provided a hyperlink to relevant services referenced in the message. For example, a message to promote routine HIV screening was paired with a link to the app function for scheduling routine HIV screening (Figure 2).

Commodity Ordering

Participants assigned to the intervention group also had the ability to order prevention commodities (HIV at-home self-test kits, home specimen collection kits for STI testing, condom variety packages, and condom-compatible lubricant) directly through the app for delivery to an address of their choosing. The kits were purchased or built by Emory University, and delivered through Amazon Fulfillment Services. At-home HIV self-test kits were fulfilled with OraQuick kits (Orasure Technologies, Bethlehem, Pennsylvania, United States). At-home specimen collection kits (CareKits) were provided through the Emory Center for AIDS Research, and included instructions and materials for participants to collect urine, a rectal swab, a pharyngeal swab, and microtainer blood specimens sufficient to support testing for urethral, rectal, and pharyngeal gonorrhea and chlamydia, and for syphilis. Specimens were returned to the study laboratory by mail, and STI testing was performed in a Clinical Laboratory Improvement Amendments–certified laboratory using methods previously reported [25]. Negative STI results were provided to participants through emails or text messages; positive STI results were provided to participants by phone call with referrals to treatment. Positive STI test results were reported to state and local health departments, as required by law and as disclosed to participants during the informed consent process; HIV self-tests are sent by participants directly to the vendor and thus HIV self-test results during the study were unknown to staff.

Phase 2: Randomized Controlled Trial

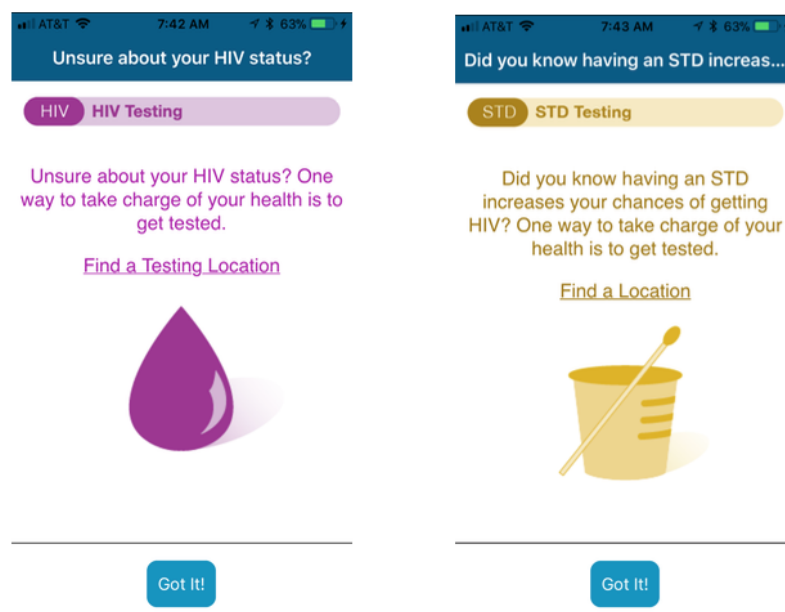
A total of 1229 MSM were recruited and enrolled into a randomized controlled trial in three US cities with substantial HIV incidence: Detroit, Michigan; New York City, New York; and Atlanta, Georgia [26]. The intervention of HIV prevention messages and HealthMindr services were delivered as a mobile phone app, available on both iOS and Android operating systems. At the time of randomization, all participants received standard of care referrals to HIV prevention and treatment services in the form of a paper list of local prevention resources.

Study Design and Procedures

Overview

Among the 1229 men enrolled, 478 were from Atlanta, 335 from Detroit, and 416 from New York City. Men were randomly assigned to either the immediate intervention group or the waitlist-control group at a 1:1 ratio. All participants received the same surveys at baseline and at three-month intervals thereafter. At baseline, participants assigned to the intervention group installed the M3 app and study staff gave them an orientation on its use. These participants received access to the full mobile app and messages based on their risk profiles over a period of three months, after which the app was deactivated. Wait-list control participants were not provided access to the intervention app at the baseline visit but continued to receive quarterly surveys. At nine months postenrollment, participants in the waitlist-control group were given the option of accessing the intervention app. Those who opted to do so were given the app for three months and were asked to complete one final study visit and survey at the 12-month point. Figure 2 provides an overview of the study timeline and includes study visits, procedures, and the participants involved at each time point.

Figure 2. Example text-based messages from the M3 app.



Recruitment

Recruitment activities were conducted over the course of 10 months in each study city from January-October 2018. To reflect the diversity of MSM, we used a multi-modal recruitment strategy with a goal of recruiting a sample of MSM who were diverse in terms of age, race/ethnicity, and HIV risk. Modes of recruitment included targeted banner advertisements (eg, Facebook), traditional print advertisements (eg, flyers, public transit), recruitment at venues, referrals from community service providers, and in-person outreach.

Eligibility

Men eligible to participate in this study were: (1) aged 18 years and older; (2) assigned a male sex at birth; (3) self-reported their current gender identity as male; (4) self-reported anal intercourse with a man in the past year; (5) were current residents of the study city metropolitan area (Atlanta, Detroit, or New York City); (6) planned to stay in the city area for the next nine months; (7) owned and used an Android or iOS smartphone; (8) were able to read and understand English without assistance; and (9) were included in one of the three groups of serostatus and risk groups described above. As of November 2018, all study participants provided written informed consent prior to participating in the study.

Enrollment

Men recruited in community venues were offered a brief interviewer-administered screening survey; men recruited through flyers or online venues were offered a brief online eligibility screener. Eligible men were invited to attend an in-person baseline enrollment visit. At the enrollment visit, research staff reviewed consent documentation with potential participants and reconfirmed eligibility criteria. Following consent and enrollment, all participants completed a baseline behavioral survey (see [Multimedia Appendix 1](#)) that collected information related to primary and secondary outcomes, including: (1) demographic characteristics; (2) HIV and STI status and testing history; (3) condom use; (4) PrEP use and adherence (for HIV-negative participants); (5) ART use and adherence (for HIV-positive participants); (6) knowledge, perceptions, beliefs, intents, and communication with sex partners about HIV status and risk reduction; (7) mobile phone and data usage; (8) access to Internet and information; and (9) psychosocial covariates. The initial visit took up to 90 minutes.

Randomization

Following completion of the behavioral survey, participants were randomized into either the intervention or the wait-list control group. Participants were successfully randomized within 18 strata based on the three serostatus/risk groups, three cities, and race/ethnicity (non-Hispanic white or not), ensuring balance in randomization for these three dimensions [27]. Within the strata of city, serostatus/risk group, and race/ethnicity, participants were randomly assigned to the next treatment allocation from a randomly permuted block sequence (block sizes were 2 and 4).

Follow-Up Assessments

To understand the effects of the intervention, follow-up surveys were administered to all participants in three-month intervals (a survey immediately postintervention, a three-month postintervention follow-up, and a six-month postintervention follow-up). The content of the postintervention surveys included study outcomes, which included sexual risk behaviors and use of prevention services. Participants took interim follow-up assessment remotely at 3 and 6 months and were given the option of taking the final 9-month outcome assessment remotely or in person as the baseline was done.

Incentives

Modest incentives were given to participants for completing assessments in the study. Participants in the intervention group could be compensated up to US \$140 when completing all assessments over the nine-month study period. Participants in the waitlist-control group were compensated up to US \$190 when opting to use the intervention app after nine months, and US \$140 if they chose not to use the intervention app. All consenting participants who completed in-person site visits, baseline visits, and nine-month follow-up were compensated US \$50, and an additional US \$20 for each remotely completed follow-up survey (immediately postintervention, after three months, and after six months). Waitlist-control participants who opted to use the intervention app were eligible for an additional US \$50 postintervention follow-up assessment incentive.

Measures

Serostatus-Specific Measures

HIV-Negative Participants

For HIV-negative participants, HIV testing was assessed at baseline using a series of questions about HIV screening in the previous 12-month and three-month intervals, including reasons for screening behavior. Follow-up surveys asked about HIV screening behaviors in the past three months. HIV-negative participants were also asked a series of questions related to PrEP, including if they were aware of PrEP, had ever used PrEP, were currently using PrEP, or had discontinued PrEP. Reasons for use or nonuse of PrEP were also included at baseline and in three-month follow-up intervals. HIV-negative participants were also asked about the likelihood of using possible PrEP agents in the future. Additionally, participants were asked to rank their prevention preferences when considering PrEP options that might be available as future PrEP formulations.

HIV-Positive Participants

Participants living with HIV were asked at baseline about their previous 12 months of engagement with HIV care, and at follow-up about their previous 3 months of engagement with HIV care. Questions included missed appointments, reasons for nonengagement, and measures of viral suppression. Participants living with HIV were also asked at baseline about their use of ART in the previous 12-month period and previous 30-day adherence. Postintervention surveys asked about previous three-month initiation of ART and past 30-day adherence to ART, if applicable. Questions also included reasons for missed doses as well as the HIV Self-Efficacy Adherence Scale [28].

Questions Asked of All Participants

STI testing was assessed at baseline by asking participants if they had been screened in the previous 12-month period for non-HIV STIs, reasons for screening behavior, and any STI-related vaccinations. STIs for analysis included chlamydia, gonorrhea, syphilis, herpes, genital warts, hepatitis A, B, and C, and any other STI. Follow-up surveys asked information about screening and diagnoses in the previous three months. All participants were asked at baseline and in follow-up surveys about their recent experiences in accessing health care. All participants were asked about their beliefs on the efficacy of various HIV prevention methods (eg, condoms, PrEP) as well as the likelihood they would engage in HIV prevention behaviors in the next three-month period. All participants were asked about sexual behaviors in the previous three-month period at baseline and during three-month follow up surveys. Questions delineated main from casual partners, enumerating casual partners, and determining patterns of behavior for ongoing risk group classification. Participants were asked at baseline and in all postintervention surveys about substance use and dependency. Alcohol misuse was assessed using the validated Alcohol Use Disorders Identification Test (AUDIT) [29]. Participants were also asked which, if any, substances other than alcohol they used. Substance dependency was assessed with the Drug Use Dependency Identification Test (DUDIT) [30].

Covariates

Factors that might be associated with intervention efficacy were assessed at baseline and at three-month intervals. These included the Centers for Epidemiological Studies on Depression 10-item (CESD-10) scale [31] for past-week depressive symptoms, a modified technology use scale from a 2015 Pew report [32], lifetime and previous three-month sex work, previous

three-month intimate partner violence (IPV), previous-month resilience, a subset of items from the HIV-related Stigma Scale, a modified HIV/AIDS Conspiracy Scale [33], Perceived HIV Severity Scale [34], and Health Care Mistrust Scale [35].

Data Analysis Plan

We will conduct bivariate analyses, stratified by intervention group, for characteristics related to demographic factors, educational history, social determinants of health, city of enrollment, risk group, and baseline behaviors, to assess for failure of randomization. Failure of randomization will be defined by a significant ($P < .05$) difference in the distribution of a characteristic between the intervention and control groups.

The primary outcomes of interest in this study (Table 2) will be associated with the following alternative hypotheses: assignment to the intervention group will be associated with increased HIV testing among HIV-negative men, increased engagement with HIV care and ART use/adherence among people living with HIV, increased uptake and adherence to PrEP among higher risk HIV-negative men, sustained lack of condomless anal sex among lower risk HIV-negative men, increased condom use for those who reported prior condomless sex, and increased STI testing for all sexually active men. Assuming that there are no failures of randomization, we will use descriptive analyses to calculate the ratios of rates or prevalence between participants assigned to the intervention group and participants assigned to the control group. For HIV testing, PrEP uptake, and STI testing, we will consider using descriptive methods for time-to-event analysis and describing unadjusted hazard ratios if randomization does not fail. If a failure of randomization occurs, we will conduct a stratified analysis for the association between outcomes and randomization assignment by variable where the failure occurred and will consider adjusting estimates for that factor if indicated.

Table 2. Primary outcomes.

| Outcome | Participant HIV risk group | |
|-------------------------------------|---|--------------|
| | Lower risk and higher risk HIV-negative | HIV-positive |
| HIV testing | ✓ | |
| Engagement in HIV preventative care | ✓ | |
| PrEP ^a uptake | ✓ | |
| PrEP adherence | ✓ | |
| Engagement in HIV care | | ✓ |
| ART ^b uptake | | ✓ |
| ART adherence | | ✓ |
| Condom use | ✓ | ✓ |
| Condom use compliance | ✓ | ✓ |
| STI ^c testing | ✓ | ✓ |

^aPrEP: pre-exposure prophylaxis.

^bART: antiretroviral therapy.

^cSTI: sexually transmitted infection.

Secondary outcomes will focus on participants' self-reported intentions, such as increasing the frequency of preventive

behaviors, decreasing risk behavior, seeking information and treatment, and partner communication, particularly around risk

and prevention behaviors such as ART and PrEP. Secondary outcome analysis will include intervention and control group comparisons, similar to primary outcome analysis.

Human Subjects

Study procedures and documents, including consent forms, eligibility screeners, assessments, recruitment advertisements, and sexual health messages, were submitted and approved by Emory University's Institutional Review Board. All study staff were required to complete training in human subjects research ethics and data security before they were permitted to engage in research procedures and view participant identification information. Any third parties contracted in the data collection and management process have established Business Associates Agreements with Emory University, to ensure their adherence to the scientific and ethical standards of the university. A data safety monitoring board was not required for this study, as it poses no greater than minimal risk due to the limited safety concerns to the study population.

Results

M3 enrollment began in January 2018 and concluded in November 2018. A total of 1229 MSM were enrolled. Data collection was completed in September 2019.

Discussion

Eisinger and Fauci have recently written that we have the tools to end the HIV/AIDS pandemic, and that the remaining challenge is to aggressively implement the effective strategies that we have [36]. We agree and believe that the same premise applies to HIV prevention: that prevention tools, including HIV testing, condoms, STI testing, PrEP, and postexposure prophylaxis, offer significant promise to curb new infections among MSM if deployed at scale and aligned with the needs of MSM. Here, we describe an RCT to test the effects of a mobile phone app to help MSM select, coordinate, and manage their use of prevention tools. The design incorporates both the previously described HealthMindr app and a set of text and video messages that are tailored to the HIV status and the risk level of participants.

The resulting M3 mobile app provides tailored electronic messages along with service offerings in a unified platform, potentially increasing the uptake of primary prevention interventions. It features several characteristics of best practice in the development of mHealth tools: it is theoretically grounded, was developed through an iterative process with input from likely end users and current prevention providers, and uses tailoring of content based on the specific needs and circumstances of users. If assignment to the intervention is associated with higher use of prevention services, the M3 app could be used by public health agencies to reach MSM with a consistent, epidemiologically tailored package of HIV prevention interventions, and could provide an opportunity to reach men who might be geographically less accessible for

existing, in-person prevention services. The inclusion of mail-out condoms and STI and HIV testing commodities also facilitates the provision of a full package of basic services to rural MSM, who are a group that are consistently less served with basic sexual health services and commodities than urban MSM [37]. A further potential benefit of this approach is the HIV serostatus-inclusiveness of the intervention: all men can potentially benefit from the M3 app, regardless of HIV serostatus.

Our study is subject to a number of possible limitations, typical of the potential biases associated with randomized prevention trials [38]. It is possible that we might have selection bias, manifested as a failure of randomization. We have taken steps to mitigate this possibility by implementing stratified randomization by site and risk group; stratified randomization minimizes the risk for failure of randomization across a domain that might be associated with efficacy. We will assess failure of randomization by comparing the distribution of key participant characteristics by randomization arm, using chi-square or Fisher exact tests as appropriate. We anticipate that there could be measurement bias because we are relying on self-reported outcomes, as is common in behavioral studies. We have attempted to minimize this bias by allowing options for completing assessments privately or remotely, by using previously established or validated items, and by measuring key outcomes with multiple measures (for example, adherence is assessed in both 7-day and 30-day recall periods, and assesses condom use in the past 3 months and at last sexual encounter). We could be subject to exclusion bias if there is differential loss to follow-up between the intervention and control arms. We mitigated this risk by using proven approaches to increase retention in both arms, including multiple modes of contact (phone, email, text message) and offering flexible options for completing surveys at home or in the research clinic. Because we set quotas to ensure adequate representation of men of color and high- and low-risk HIV-negative men, our sample may not have high external generalizability; however, we have designed the study to have power to analyze within specific, high-priority groups of participants, given their importance in HIV epidemics among MSM living in the United States. Because of the recruitment structure, cross-sectional analyses of the levels of prevention and risk behaviors from the baseline data should be interpreted in light of the sampling strategy.

Future study activities include completion of data collection for the RCT, analysis of RCT data, and identification of possible areas of improvement of the app for usability, including the assessment of use patterns of waitlist-control participants. In parallel, it is important that conversations with possible implementers of electronic health interventions (eg, local and state health departments and community-based prevention organizations) continue to anticipate possible implementation strategies and opportunities based on the principles of implementation science, in case the results of the RCT indicate improved outcomes for men randomized to the intervention group [39].

Acknowledgments

This study was funded through the CDC Cooperative Agreement #U01PS004977 to Emory University.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Baseline survey for the M3 (M-Cubed) study.

[[PDF File \(Adobe PDF File\), 1047 KB - resprot_v8i11e16439_app1.pdf](#)]

References

- Centers for Disease Control and Prevention. 2015. Diagnoses of HIV Infection in the United States and Dependent Areas, 2014 URL: <http://www.cdc.gov/hiv/library/reports/surveillance/index.html> [accessed 2019-11-04]
- Centers for Disease Control and Prevention. 2017. Compendium of Evidence-Based Interventions and Best Practices for HIV Prevention (online index of proven effective interventions) URL: <https://www.cdc.gov/hiv/research/interventionresearch/compendium/rr/complete.html> [accessed 2019-11-04]
- Mayer KH, Wang L, Koblin B, Mannheimer S, Magnus M, del Rio C, HPTN061 Protocol Team. Concomitant socioeconomic, behavioral, and biological factors associated with the disproportionate HIV infection burden among Black men who have sex with men in 6 U.S. cities. *PLoS One* 2014;9(1):e87298 [FREE Full text] [doi: [10.1371/journal.pone.0087298](https://doi.org/10.1371/journal.pone.0087298)] [Medline: [24498067](https://pubmed.ncbi.nlm.nih.gov/24498067/)]
- Hightow-Weidman LB, Magnus M, Beauchamp G, Hurt CB, Shoptaw S, Emel L, et al. Incidence and Correlates of Sexually Transmitted Infections Among Black Men Who Have Sex With Men Participating in the HIV Prevention Trials Network 073 Preexposure Prophylaxis Study. *Clin Infect Dis* 2019 Oct 15;69(9):1597-1604. [doi: [10.1093/cid/ciy1141](https://doi.org/10.1093/cid/ciy1141)] [Medline: [30615169](https://pubmed.ncbi.nlm.nih.gov/30615169/)]
- Sullivan PS, Peterson J, Rosenberg ES, Kelley CF, Cooper H, Vaughan A, et al. Understanding racial HIV/STI disparities in black and white men who have sex with men: a multilevel approach. *PLoS One* 2014;9(3):e90514 [FREE Full text] [doi: [10.1371/journal.pone.0090514](https://doi.org/10.1371/journal.pone.0090514)] [Medline: [24608176](https://pubmed.ncbi.nlm.nih.gov/24608176/)]
- Sullivan PS, Rosenberg ES, Sanchez TH, Kelley CF, Luisi N, Cooper HL, et al. Explaining racial disparities in HIV incidence in black and white men who have sex with men in Atlanta, GA: a prospective observational cohort study. *Ann Epidemiol* 2015 Jun;25(6):445-454 [FREE Full text] [doi: [10.1016/j.annepidem.2015.03.006](https://doi.org/10.1016/j.annepidem.2015.03.006)] [Medline: [25911980](https://pubmed.ncbi.nlm.nih.gov/25911980/)]
- Zlotorzynska M, Sullivan P, Sanchez T. The Annual American Men's Internet Survey of Behaviors of Men Who Have Sex With Men in the United States: 2016 Key Indicators Report. *JMIR Public Health Surveill* 2019 Feb 20;5(1):e11313 [FREE Full text] [doi: [10.2196/11313](https://doi.org/10.2196/11313)] [Medline: [30785405](https://pubmed.ncbi.nlm.nih.gov/30785405/)]
- Sullivan PS, Carballo-Diéguez A, Coates T, Goodreau SM, McGowan I, Sanders EJ, et al. Successes and challenges of HIV prevention in men who have sex with men. *Lancet* 2012 Jul 28;380(9839):388-399 [FREE Full text] [doi: [10.1016/S0140-6736\(12\)60955-6](https://doi.org/10.1016/S0140-6736(12)60955-6)] [Medline: [22819659](https://pubmed.ncbi.nlm.nih.gov/22819659/)]
- Jenness SM, Goodreau SM, Rosenberg E, Beylerian EN, Hoover KW, Smith DK, et al. Impact of the Centers for Disease Control's HIV Preexposure Prophylaxis Guidelines for Men Who Have Sex With Men in the United States. *J Infect Dis* 2016 Dec 15;214(12):1800-1807 [FREE Full text] [doi: [10.1093/infdis/jiw223](https://doi.org/10.1093/infdis/jiw223)] [Medline: [27418048](https://pubmed.ncbi.nlm.nih.gov/27418048/)]
- Brookmeyer R, Boren D, Baral SD, Bekker L, Phaswana-Mafuya N, Beyrer C, et al. Combination HIV prevention among MSM in South Africa: results from agent-based modeling. *PLoS One* 2014;9(11):e112668 [FREE Full text] [doi: [10.1371/journal.pone.0112668](https://doi.org/10.1371/journal.pone.0112668)] [Medline: [25398143](https://pubmed.ncbi.nlm.nih.gov/25398143/)]
- Cohen DA, Wu S, Farley TA. Comparing the cost-effectiveness of HIV prevention interventions. *J Acquir Immune Defic Syndr* 2004 Nov 01;37(3):1404-1414. [doi: [10.1097/01.qai.0000123271.76723.96](https://doi.org/10.1097/01.qai.0000123271.76723.96)] [Medline: [15483470](https://pubmed.ncbi.nlm.nih.gov/15483470/)]
- Hightow-Weidman LB, Muessig KE, Bauermeister J, Zhang C, LeGrand S. Youth, Technology, and HIV: Recent Advances and Future Directions. *Curr HIV/AIDS Rep* 2015 Dec;12(4):500-515 [FREE Full text] [doi: [10.1007/s11904-015-0280-x](https://doi.org/10.1007/s11904-015-0280-x)] [Medline: [26385582](https://pubmed.ncbi.nlm.nih.gov/26385582/)]
- Muessig K, Nekkanti M, Bauermeister J, Bull S, Hightow-Weidman L. A systematic review of recent smartphone, Internet and Web 2.0 interventions to address the HIV continuum of care. *Curr HIV/AIDS Rep* 2015 Mar;12(1):173-190 [FREE Full text] [doi: [10.1007/s11904-014-0239-3](https://doi.org/10.1007/s11904-014-0239-3)] [Medline: [25626718](https://pubmed.ncbi.nlm.nih.gov/25626718/)]
- Muessig KE, Pike EC, Legrand S, Hightow-Weidman LB. Mobile phone applications for the care and prevention of HIV and other sexually transmitted diseases: a review. *J Med Internet Res* 2013 Jan 04;15(1):e1 [FREE Full text] [doi: [10.2196/jmir.2301](https://doi.org/10.2196/jmir.2301)] [Medline: [23291245](https://pubmed.ncbi.nlm.nih.gov/23291245/)]
- Hightow-Weidman L, Muessig K, Rosenberg E, Sanchez T, LeGrand S, Gravens L, et al. University of North Carolina/Emory Center for Innovative Technology (iTech) for Addressing the HIV Epidemic Among Adolescents and Young Adults in the United States: Protocol and Rationale for Center Development. *JMIR Res Protoc* 2018 Aug 03;7(8):e10365 [FREE Full text] [doi: [10.2196/10365](https://doi.org/10.2196/10365)] [Medline: [30076126](https://pubmed.ncbi.nlm.nih.gov/30076126/)]

16. Sullivan PS, Grey JA, Simon Rosser BR. Emerging technologies for HIV prevention for MSM: what we have learned, and ways forward. *J Acquir Immune Defic Syndr* 2013 Jun 01;63 Suppl 1:S102-S107 [FREE Full text] [doi: [10.1097/QAI.0b013e3182949e85](https://doi.org/10.1097/QAI.0b013e3182949e85)] [Medline: [23673879](https://pubmed.ncbi.nlm.nih.gov/23673879/)]
17. Sullivan PS, Jones J, Kishore N, Stephenson R. The Roles of Technology in Primary HIV Prevention for Men Who Have Sex with Men. *Curr HIV/AIDS Rep* 2015 Dec;12(4):481-488. [doi: [10.1007/s11904-015-0293-5](https://doi.org/10.1007/s11904-015-0293-5)] [Medline: [26519083](https://pubmed.ncbi.nlm.nih.gov/26519083/)]
18. Muessig K, Pike E, Fowler B, LeGrand S, Parsons J, Bull S, et al. Putting prevention in their pockets: developing mobile phone-based HIV interventions for black men who have sex with men. *AIDS Patient Care STDS* 2013 Apr;27(4):211-222 [FREE Full text] [doi: [10.1089/apc.2012.0404](https://doi.org/10.1089/apc.2012.0404)] [Medline: [23565925](https://pubmed.ncbi.nlm.nih.gov/23565925/)]
19. Khosropour CM, Lake JG, Sullivan PS. Are MSM willing to SMS for HIV prevention? *J Health Commun* 2014;19(1):57-66. [doi: [10.1080/10810730.2013.798373](https://doi.org/10.1080/10810730.2013.798373)] [Medline: [23905653](https://pubmed.ncbi.nlm.nih.gov/23905653/)]
20. Sullivan PS, Driggers R, Stekler JD, Siegler A, Goldenberg T, McDougal SJ, et al. Usability and Acceptability of a Mobile Comprehensive HIV Prevention App for Men Who Have Sex With Men: A Pilot Study. *JMIR Mhealth Uhealth* 2017 Mar 09;5(3):e26 [FREE Full text] [doi: [10.2196/mhealth.7199](https://doi.org/10.2196/mhealth.7199)] [Medline: [28279949](https://pubmed.ncbi.nlm.nih.gov/28279949/)]
21. Bandure A. *Social Foundations Of Thought And Action: A Social Cognitive Theory*. Englewood Cliffs, NJ: Prentice-Hall; 1986.
22. Goldenberg T, McDougal SJ, Sullivan PS, Stekler JD, Stephenson R. Preferences for a Mobile HIV Prevention App for Men Who Have Sex With Men. *JMIR Mhealth Uhealth* 2014 Oct 29;2(4):e47 [FREE Full text] [doi: [10.2196/mhealth.3745](https://doi.org/10.2196/mhealth.3745)] [Medline: [25355249](https://pubmed.ncbi.nlm.nih.gov/25355249/)]
23. Goldenberg T, McDougal SJ, Sullivan PS, Stekler JD, Stephenson R. Building a Mobile HIV Prevention App for Men Who Have Sex With Men: An Iterative and Community-Driven Process. *JMIR Public Health Surveill* 2015;1(2):e18 [FREE Full text] [doi: [10.2196/publichealth.4449](https://doi.org/10.2196/publichealth.4449)] [Medline: [27227136](https://pubmed.ncbi.nlm.nih.gov/27227136/)]
24. Weller S, Romney A. *Qualitative Research Methods: Systematic data collection*. Newbury Park, CA: SAGE Publications, Inc; 1988.
25. Mustanski B, Parsons J, Sullivan P, Madkins K, Rosenberg E, Swann G. Biomedical and Behavioral Outcomes of Keep It Up!: An eHealth HIV Prevention Program RCT. *Am J Prev Med* 2018 Aug;55(2):151-158 [FREE Full text] [doi: [10.1016/j.amepre.2018.04.026](https://doi.org/10.1016/j.amepre.2018.04.026)] [Medline: [29937115](https://pubmed.ncbi.nlm.nih.gov/29937115/)]
26. Centers for Disease Control and Prevention. CDC Surveillance Report: Diagnoses of HIV Infection in the United States and Dependent Areas, 2017 URL: <http://www.cdc.gov/hiv/library/reports/surveillance/index.html> [accessed 2019-11-04]
27. Kernan W, Viscoli C, Makuch R, Brass L, Horwitz R. Stratified randomization for clinical trials. *J Clin Epidemiol* 1999 Jan;52(1):19-26. [doi: [10.1016/s0895-4356\(98\)00138-3](https://doi.org/10.1016/s0895-4356(98)00138-3)] [Medline: [9973070](https://pubmed.ncbi.nlm.nih.gov/9973070/)]
28. Johnson M, Neilands T, Dilworth S, Morin S, Remien R, Chesney M. The role of self-efficacy in HIV treatment adherence: validation of the HIV Treatment Adherence Self-Efficacy Scale (HIV-ASES). *J Behav Med* 2007 Oct;30(5):359-370 [FREE Full text] [doi: [10.1007/s10865-007-9118-3](https://doi.org/10.1007/s10865-007-9118-3)] [Medline: [17588200](https://pubmed.ncbi.nlm.nih.gov/17588200/)]
29. Babor T, Higgins-Biddle J, Saunders J, Monteiro, MG. AUDIT: the alcohol use disorders identification test. 2001. URL: http://apps.who.int/iris/bitstream/handle/10665/67205/WHO_MSD_?sequence=1 [accessed 2019-07-08]
30. Berman A, Bergman H, Palmstierna T, Schlyter F. Evaluation of the Drug Use Disorders Identification Test (DUDIT) in criminal justice and detoxification settings and in a Swedish population sample. *Eur Addict Res* 2005;11(1):22-31. [doi: [10.1159/000081413](https://doi.org/10.1159/000081413)] [Medline: [15608468](https://pubmed.ncbi.nlm.nih.gov/15608468/)]
31. Andresen E, Malmgren J, Carter W, Patrick D. Screening for depression in well older adults: evaluation of a short form of the CES-D (Center for Epidemiologic Studies Depression Scale). *Am J Prev Med* 1994;10(2):77-84. [Medline: [8037935](https://pubmed.ncbi.nlm.nih.gov/8037935/)]
32. Lenhart A. *Teen, Social Media and Technology Overview 2015*. 2015. URL: http://www.pewresearch.org/wp-content/uploads/sites/9/2015/04/PI_TeensandTech_Update2015_0409151.pdf [accessed 2019-11-04]
33. Bogart L, Thorburn S. Are HIV/AIDS conspiracy beliefs a barrier to HIV prevention among African Americans? *J Acquir Immune Defic Syndr* 2005 Feb 01;38(2):213-218. [doi: [10.1097/00126334-200502010-00014](https://doi.org/10.1097/00126334-200502010-00014)] [Medline: [15671808](https://pubmed.ncbi.nlm.nih.gov/15671808/)]
34. Stephenson R, Freeland R, Sullivan SP, Riley E, Johnson BA, Mitchell J, et al. Home-Based HIV Testing and Counseling for Male Couples (Project Nexus): A Protocol for a Randomized Controlled Trial. *JMIR Res Protoc* 2017 May 30;6(5):e101 [FREE Full text] [doi: [10.2196/resprot.7341](https://doi.org/10.2196/resprot.7341)] [Medline: [28559225](https://pubmed.ncbi.nlm.nih.gov/28559225/)]
35. Thompson HS, Valdimarsdottir HB, Winkel G, Jandorf L, Redd W. The Group-Based Medical Mistrust Scale: psychometric properties and association with breast cancer screening. *Prev Med* 2004 Feb;38(2):209-218. [doi: [10.1016/j.ympmed.2003.09.041](https://doi.org/10.1016/j.ympmed.2003.09.041)] [Medline: [14715214](https://pubmed.ncbi.nlm.nih.gov/14715214/)]
36. Eisinger RW, Fauci AS. Ending the HIV/AIDS Pandemic. *Emerg Infect Dis* 2018 Mar;24(3):413-416 [FREE Full text] [doi: [10.3201/eid2403.171797](https://doi.org/10.3201/eid2403.171797)] [Medline: [29460740](https://pubmed.ncbi.nlm.nih.gov/29460740/)]
37. McKenney J, Sullivan PS, Bowles KE, Oraka E, Sanchez TH, DiNenno E. HIV Risk Behaviors and Utilization of Prevention Services, Urban and Rural Men Who Have Sex with Men in the United States: Results from a National Online Survey. *AIDS Behav* 2018 Jul;22(7):2127-2136. [doi: [10.1007/s10461-017-1912-5](https://doi.org/10.1007/s10461-017-1912-5)] [Medline: [28986669](https://pubmed.ncbi.nlm.nih.gov/28986669/)]
38. Greenhalgh T. Assessing the methodological quality of published papers. *BMJ* 1997 Aug 02;315(7103):305-308 [FREE Full text] [doi: [10.1136/bmj.315.7103.305](https://doi.org/10.1136/bmj.315.7103.305)] [Medline: [9274555](https://pubmed.ncbi.nlm.nih.gov/9274555/)]

39. Li D, Brown C, Gallo C, Morgan E, Sullivan P, Young S, et al. Design Considerations for Implementing eHealth Behavioral Interventions for HIV Prevention in Evolving Sociotechnical Landscapes. *Curr HIV/AIDS Rep* 2019 Aug;16(4):335-348. [doi: [10.1007/s11904-019-00455-4](https://doi.org/10.1007/s11904-019-00455-4)] [Medline: [31250195](https://pubmed.ncbi.nlm.nih.gov/31250195/)]

Abbreviations

ART: antiretroviral therapy

AUDIT: Alcohol Use Disorders Identification Test

CESD-10: Centers for Epidemiological Studies on Depression 10-item scale

DUDIT: Drug Use Dependency Identification Test

IPV: intimate partner violence

M-Cubed/M3: Mobile Messaging for Men

mHealth: mobile health

MSM: men who have sex with men

nPEP: nonoccupational postexposure prophylaxis

PrEP: pre-exposure prophylaxis

RCT: randomized controlled trial

STI: sexually transmitted infection

Edited by G Eysenbach; submitted 30.09.19; peer-reviewed by T Winder, D Levine; accepted 23.10.19; published 15.11.19.

Please cite as:

Sullivan PS, Zahn RJ, Wiatrek S, Chandler CJ, Hirshfield S, Stephenson R, Bauermeister JA, Chiasson MA, Downing Jr MJ, Gelaude DJ, Siegler AJ, Horvath K, Rogers E, Alas A, Olansky EJ, Saul H, Rosenberg ES, Mansergh G

HIV Prevention Via Mobile Messaging for Men Who Have Sex With Men (M-Cubed): Protocol for a Randomized Controlled Trial

JMIR Res Protoc 2019;8(11):e16439

URL: <http://www.researchprotocols.org/2019/11/e16439/>

doi: [10.2196/16439](https://doi.org/10.2196/16439)

PMID: [31730043](https://pubmed.ncbi.nlm.nih.gov/31730043/)

©Patrick Sean Sean Sullivan, Ryan J Zahn, Sarah Wiatrek, Cristian J Chandler, Sabina Hirshfield, Rob Stephenson, Jose A Bauermeister, Mary Ann Chiasson, Martin J Downing Jr, Deborah J Gelaude, Aaron J Siegler, Keith Horvath, Erin Rogers, Ana Alas, Evelyn J Olansky, Heather Saul, Eli S Rosenberg, Gordon Mansergh. Originally published in *JMIR Research Protocols* (<http://www.researchprotocols.org>), 15.11.2019. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in *JMIR Research Protocols*, is properly cited. The complete bibliographic information, a link to the original publication on <http://www.researchprotocols.org>, as well as this copyright and license information must be included.

Protocol

Remotely Monitored Gamification and Social Incentives to Improve Glycemic Control Among Adults With Uncontrolled Type 2 Diabetes (iDiabetes): Protocol for a Randomized Controlled Trial

Michael Fortunato^{1,2}, BA; Joseph Harrison^{1,2}, BS; Ai Leen Oon^{1,2}, BA; Dylan Small^{1,2}, PhD; Victoria Hilbert^{1,2}, MPH; Charles Rareshide^{1,2}, MS; Mitesh Patel^{1,2,3}, MD, MBA, MS

¹University of Pennsylvania, Philadelphia, PA, United States

²Penn Medicine Nudge Unit, Philadelphia, PA, United States

³Crescenz Veteran Affairs Medical Center, Philadelphia, PA, United States

Corresponding Author:

Mitesh Patel, MD, MBA, MS

University of Pennsylvania

3400 Civic Center Blvd

Philadelphia, PA, 19103

United States

Phone: 1 12158983367

Email: mpatel@pennteam.upenn.edu

Abstract

Background: Type 2 diabetes is a significant cause of morbidity and mortality in the United States. Lifestyle modifications including increasing physical activity and losing weight have been demonstrated to improve glycemic control. However, most patients struggle to make these changes. Many stakeholders are interested in using gamification and social incentives to increase engagement in healthy behaviors. However, these approaches often do not appropriately leverage insights from behavioral economics that could be used to address predictable barriers to behavior change.

Objective: This study aimed to describe the protocol for the *Influencing Diabetics to Adapt Behaviors related to Exercise and weight by Enhancing Social incentives* (iDiabetes) trial, which aimed to evaluate the effectiveness of gamification interventions that leverage insights from behavioral economics to enhance supportive, competitive, or collaborative social incentives to improve glycemic control, promote weight loss, and increase physical activity among overweight and obese adults with type 2 diabetes.

Methods: We are conducting a one-year four-arm randomized controlled trial of 361 overweight and obese patients with type 2 diabetes and a glycated hemoglobin (HbA_{1c}) level ≥ 8.0 . Wireless weight scales and wearable devices are provided to remotely monitor weight and physical activity and transmit data to the study team. Patients are recruited by email, following which they establish a baseline measure of weight, daily step count, HbA_{1c} level, and low-density lipoprotein cholesterol level and then repeat these measures at 6 and 12 months. The control arm receives no other interventions. Patients randomized to one of the three intervention arms are entered into a game designed using insights from behavioral economics to enhance supportive, competitive, or collaborative social incentives. To examine predictors of strong or poor performance, participants completed validated questionnaires on a range of areas including their personality, risk preferences, and social network.

Results: Enrollment of 361 patients was completed in January 2019. Results are expected in 2020.

Conclusions: The iDiabetes trial represents a scalable model to remotely monitor the daily health behaviors of adults with type 2 diabetes. Results from this trial will help provide insights into how to improve management of patients with type 2 diabetes.

Trial Registration: ClinicalTrials.gov NCT02961192; <https://clinicaltrials.gov/ct2/show/NCT02961192>

International Registered Report Identifier (IRRID): DERR1-10.2196/14180

(*JMIR Res Protoc* 2019;8(11):e14180) doi:[10.2196/14180](https://doi.org/10.2196/14180)

KEYWORDS

behavioral economics; gamification; social incentives; diabetes; glycemic control weight; physical activity; remote monitoring; wearable devices

Introduction

Background

Type 2 diabetes is a significant cause of morbidity and mortality in the United States [1,2]. Lifestyle modifications including increasing physical activity and losing weight have been demonstrated to improve glycemic control [3,4]. However, changing daily health behaviors can be challenging for many patients, especially those who start with lower levels of motivation. Recently, many stakeholders have become interested in using mobile technologies to passively monitor these daily behaviors and to deploy interventions at a broader scale [5,6].

Gamification is the use of game design elements in nongame settings and is increasingly being used in interventions to promote healthy behaviors [7]. Although gamification is used widely, it is often not designed to incorporate theories from health behavior [8-11]. Behavioral economics is a field that incorporates principles from psychology and economics to help us understand why individuals make decisions that are predictably irrational [12,13]. For example, individuals tend to be more motivated to avoid losses than gain an equivalent reward [14-16], by immediate rather than delayed gratification [17], and they tend to avoid the feeling of regret [18]. In a randomized trial, members of our group found that insights from behavioral economics could be embedded within gamification design to enhance social incentives such as accountability, peer support, and collaboration to significantly increase physical activity among families in the community [19]. We have also conducted a pilot study to demonstrate how these approaches could be used to promote weight loss [20].

Objective

The objective of this article was to describe the protocol for the *Influencing Diabetics to Adapt Behaviors related to Exercise and weightT by Enhancing Social incentives* (iDiabetes) trial, which aimed to evaluate the effectiveness of gamification interventions that leverage insights from behavioral economics to enhance either supportive, competitive, or collaborative social incentives to improve glycemic control, promote weight loss, and increase physical activity among overweight and obese adults with type 2 diabetes. This builds upon our previous work by testing more types of social incentives and implementing them with a more high-risk population. The trial recruited patients from Penn Medicine, an academic health system in Philadelphia, and used a Web-based platform at the University of Pennsylvania, called Way to Health [21], which facilitated virtual recruitment, Web-based informed consent, automated study communication, and remote monitoring of behavior.

Methods

Study Design

iDiabetes is a 4-arm randomized controlled trial with a 1-year intervention period. The trial was conducted using Way to Health [21], an automated information technology platform at the University of Pennsylvania that integrates wireless devices, conducts clinical trial randomization and enrollment processes,

delivers messaging (via text or email), delivers self-administered surveys, automates payment transfers, and securely captures data for research purposes. This platform has been used to run over 100 clinical trials including several by our group focusing on physical activity and weight loss [8,15,16,19,20,22-25]. All participants received US \$25 for completing laboratory testing to assess baseline hemoglobin A1c (HbA_{1c}) and low-density lipoprotein cholesterol (LDL-C) during the enrollment process. Participants who were eligible and completed enrollment into the study received an additional US \$25. Participants received US \$50 to obtain laboratory tests (HbA_{1c} and LDL-C) and conduct a virtual weigh-in at home via FaceTime (Apple Inc.) or Skype (Microsoft Inc) after 6 months and 12 months, similar to prior work [20]. Participants were randomly assigned to the control arm or 1 of 3 gamification intervention arms designed to enhance supportive, competitive, or collaborative social incentives. Data on participant characteristics were collected through validated questionnaires. The University of Pennsylvania Institutional Review Board approved the study.

Participant Recruitment

Potential participants were identified from EPIC, the electronic health record at Penn Medicine, by using Penn Data Store (the health system's clinical data warehouse) and Clarity, an EPIC reporting database. The study team sent email invitations, letters, and made phone calls introducing the study and its eligibility criteria with instructions on how to learn more and begin the enrollment process online. Recruitment occurred from January 23, 2017, to January 7, 2019.

Participants were eligible for the program if they were aged between 18 and 70 years, they were able to read and provide informed consent to participate, they had a diagnosis of type 2 diabetes with an HbA_{1c} level of 8.0 or greater within the last 90 days, they had a self-reported body mass index of 25 or greater, and they owned a smartphone or tablet compatible with the wearable device and wireless weight scale. Participants were excluded if there was a condition that made their participation unfeasible (eg, inability to provide informed consent and illiteracy or inability to speak, read, and write English), if there was a condition that made participation unsafe (eg, pregnancy, previous diagnosis of an eating disorder, or history of unsafe weight loss practices), or if he or she was already enrolled in another study targeting physical activity, weight loss, or glycemic control or any other medical conditions or reasons because of which the participant would be unable to complete the 1-year program.

Participant Enrollment

Interested participants were instructed to visit the study website to create an account, review and complete informed consent, and complete the eligibility survey. Eligible participants who had not recently had blood tests were then instructed to obtain baseline HbA_{1c} and LDL-C laboratory tests that were conducted at either a qualifying Penn Medicine facility or a Quest Diagnostics laboratory. Participants were also instructed to complete a series of assessments including surveys and validated questionnaires described in Table 1. These included a baseline survey assessing sociodemographic and health characteristics,

the domain-specific risk-tasking survey collecting data related to risk preferences [26], personality type (Big Five Inventory) [27], and the Medical Outcomes Study Social Support survey [28]. The qualitative assessment at the end of the study is conducted through an online survey and participants are asked to rate their satisfaction with the devices, interventions, and study overall by using Likert scales (strongly agree, agree, neutral, disagree, and strongly disagree). Participants are also asked to respond to open-ended prompts to describe ways in which their experience helped or did not help them to lose weight, increase physical activity, and manage their diabetes.

After baseline assessments were completed, participants were mailed a wearable device (Withings Steel) and were given instructions on how to authorize the device to send data to the Way to Health technology platform (Figure 1). This wearable device tracked physical activity (daily step count) and sleep (minutes of total sleep, light sleep, and deep sleep). These types of devices have been demonstrated by our previous study to be accurate for tracking step counts [29]. The wearable device was waterproof and had a battery that lasted about 6 months. Participants were provided with a replacement battery at the beginning of the study and, if necessary, were mailed a new battery later. The study team was available on phone to help participants set up the wearable device.

Table 1. Participant survey assessments.

| Domain | Questionnaire | Questions (n) | Baseline | 6 months | 12 months |
|--------------------|---------------------------------------|---------------|----------|----------|-----------|
| Baseline | — ^a | — | ✓ | — | — |
| Social support | Medical outcomes study social support | 19 | ✓ | — | — |
| Risk preferences | Domain-specific risk-tasking survey | 30 | ✓ | — | — |
| Personality | Big Five | 44 | ✓ | — | — |
| Qualitative survey | — | — | — | — | ✓ |

^aNot applicable.

Figure 1. Depiction of the wireless devices used by participants.



Baseline Step Count

Once the participants' wearable device was setup and connected to the study, they were asked to get used to wearing the device for several weeks. During this period, a baseline step count was estimated using the second week of data—a method used in previous work [16,19]. The first week of data was ignored to diminish the potential upward bias of the estimate from higher activity during initial device use. To prevent potential mismeasurement, we ignored any daily values less than 1000 steps because evidence indicates that these values are unlikely to represent capture of the actual activity [30,31]. If less than 4 days of data were available during the second week, the patient was contacted to inquire about any device issues, and the run-in period was expanded until at least four days of data were captured.

In-Person Visit and Randomization

After a baseline step count had been established, the participant was scheduled for an in-person visit with the study team to complete the enrollment process. During this visit, all participants received education on the importance of diet and physical activity for weight loss and glycemic control. The participants were provided with a wireless weight scale and had a baseline weight measured (Figure 1). As weight can fluctuate based on time of day and clothing, we monitored for weights taken at home that were >5 lbs different. In those cases, the study team reached out to participants to clarify the most accurate weight to use as his or her baseline. At the in-person visit, participants were then randomized to one of the study arms. A participant was considered ready to be randomized once he or she had completed all surveys, established a baseline step count, completed baseline laboratory work for HbA_{1c} and

LDL-C, and had come in for an in-person study visit to establish a baseline weight measurement. Randomization was conducted electronically using block sizes of 4 groups with 3 participants per group. The first participant in the group was randomly assigned to an arm, and the next 2 participants were assigned to fill that group. In most cases, the participants in a group did not previously know each other. However, if 2 participants did know each other and wanted to join together, then they were randomized together as either groups of 2 or 3 persons. Participants were informed of their arm assignment during the in-person visit with the opportunity to ask any questions related to the intervention design.

All investigators, statisticians, and data analysts were blinded to arm assignments until the study and analysis were completed.


Interventions

Participants in the control arm used the devices but received no other interventions and were not asked to conduct goal setting. Participants randomized to 1 of the 3 gamification arms conducted goal setting during the in-person visit. This included selecting a HbA_{1c} reduction goal (1.5%, 2%, or 2.5%), a weight loss goal (6%, 7%, or 8% of their baseline weight), or an increase in daily step counts (33%, 40%, or 50% greater than baseline, or any step goal that is at least 1500 steps above their baseline). A number of design considerations were incorporated to help participants achieve their goals while minimizing risks. First, the weight loss goal was set for a gradual decline over the first 26 weeks and then to maintain that level during the next 26 weeks. Participants were given a weight target each week, and if not achieved, the target remained the same for the following week. Second, participants had a 4-week ramp up toward their daily step goal. For example, a participant with a baseline of 6000 steps per day and goal of 8000 steps per day was asked to achieve goals of 6500, 7000, 7500, and 8000 for each of the first 4 weeks of the study. Then, they were asked to maintain the 8000 steps per day goal for the remainder of the study. Finally, the HbA_{1c} goal was set for the 6-month time point and was expected to be maintained through 1 year.

Participants in the gamification arms were entered into an intervention approach based on prior work that used points and levels designed to incorporate insights from behavioral economics [19,20]. First, participants were asked to sign a precommitment pledge to strive to achieve their goals during the study. Precommitment has been demonstrated to motivate behavior change [32,33]. Second, at the beginning of each week, the participant received 70 points (10 for each day that week). If the participant did not weigh-in, they lost 10 points from their balance. This leverages loss aversion, which has demonstrated that loss framing is more effective at motivating behavior change than gain framing [14-16]. Third, at the end of each week, if participants had at least 40 points, achieved their weekly weight target, and averaged at or above their daily step goal, they were moved up a level (levels from lowest to highest: blue, bronze,

silver, gold, and platinum). If not, participants were dropped a level. This design creates achievable goal gradients—the notion that the next highest level was attainable—and a sense of social status and progression through the game. All participants begin at the silver level, so that they will feel the loss of dropping to bronze if they do not achieve enough points in the first week. Participants who finished in the platinum level received a trophy, and participants who finished in the gold level received a medal. Fourth, participants got a new set of 70 points every Monday. This design leverages the *fresh start effect* that is the tendency for aspirational behavior around temporal landmarks such as the beginning of the year, month, or week [34]. Fifth, to help re-engage participants who are struggling to meet their goals at months 3, 6, and 9 (defined as being in the blue or bronze levels of the game), the study coordinators called them to inquire about their progress in the study, reset them to the silver level, and offered them the opportunity to readjust their goals based on their initial options. Sixth, the participants' primary care physician was mailed a monthly report with data on their change in weight, step goals, HbA_{1c}, and LDL-C (Figure 2). A copy of this letter was also mailed to the participant. Finally, the game varied based on the social incentive arm described as follows:

1. In the supportive social incentive arm, participants were asked to identify a family member or friend to be their support sponsor. This sponsor is encouraged to support the participant in their progress during the study. A weekly report is sent by email to the sponsors with the participants' performance including their points and level (Figure 3).
2. In the competitive social incentive arm, participants are placed into a group of 3 participants. These participants typically did not know each other before the study but were introduced to each other by email at the beginning of the intervention. At the end of each week, the participants receive an email with a leaderboard that ranks them on their cumulative points in the study thus far and also displays their level. In the event of a tie in total cumulative points, the participants will be secondarily ranked on level. This feedback may help to induce participants to compete for the top spot among the group.
3. In the collaborative social incentive arm, participants are placed into a group of 3 participants as a team. These participants typically did not know each other before the study but were introduced to each other by email at the beginning of the intervention. Each day, one of the members of the group is randomly selected to represent his or her team for that day, and that information is shared with the entire group. If the participant selected weighed in on the previous day, the team keeps their points. If he or she did not, then the team is told that they lost 10 points. In this design, each person is accountable to the others in the team, and this may induce a collaborative effort to meet their daily goals. The entire team moves up a level only if the team has at least 40 points by the end of the week.

Figure 2. Example of a physician letter.


July 24, 2019

Dear Dr. Smith,

Your patient, Jane Doe (DOB 1/1/1980), is participating in the iDiabetes Study at the University of Pennsylvania. Below is an update on their progress. If you have any questions you can contact us by email at iDiabetes@waytohealth.org or by telephone at (484)-243-0599.

| Baseline | Weight | Daily Step Count | HbA1c | LDL |
|--------------------------------------|--------|------------------|-------|-----|
| 12/3/2018 | 257 | 1595 | 8 | 143 |
| Past Month | | | | |
| 6/24/2019 - 6/30/2019 11:59:00 PM | 216.9 | 5313 | NA | NA |
| 6/17/2019 - 6/23/2019 11:59:00 PM | 220.5 | 6246 | NA | NA |
| 6/10/2019 - 6/16/2019 11:59:00 PM | 220.6 | 5883 | NA | NA |
| 6/3/2019 - 6/9/2019 11:59:00 PM | 220 | 5656 | NA | NA |

Thank you for your help,

James Smith
Project Manager, iDiabetes Study
Perelman School of Medicine, University of Pennsylvania

Figure 3. Example of support partner messages.

Supper Partner Weekly Message

If Participant moved up a level this week

Last week John D. met all their goals, averaged 6000 steps and is now at the Silver level in the iDiabetes study. Thank you for helping support them as they work on improving their diabetes control. John D's goals for this week are to weigh less than 206 lbs., average more than 5500 steps, and have at least 40 points by the end of the week.

If Participant did not move up a level this week

Last week John D. did NOT meet all of their goals and is now at the Blue level in the iDiabetes study. John D. averaged 4800 steps last week and finished with 20 points. Thank you for helping support them as they work on improving their diabetes control. John D.'s goals for this week are to weigh less than 206 lbs., average more than 5500 steps, and have at least 40 points by the end of the week. Please feel free to reach out to John D. or find any other way to support them toward these goals.

Outcome Measures

The primary outcomes were change in HbA_{1c}, change in weight in pounds, and change in mean daily steps from baseline to the

end of the 1-year study. Secondary outcomes include the change in LDL-C levels from baseline to end of the 1-year study, and change in mean daily steps, weight in pounds, and HbA_{1c} from baseline to the 6-month time point of the study.

Power

We estimated that a sample size of 360 participants (90 per arm) will provide at least 80% power using a conservative Bonferroni adjustment of the type I error rate with a 2-sided alpha of .017 and accounting for a dropout rate of 10% to detect (1) an 1100-step change in physical activity with a standard deviation of 2000 steps; (2) a 6-lb change in weight with a standard deviation of 10 lbs; and (3) a 0.8% change in HbA_{1c} with a standard deviation of 1.5%. These values are based on prior work [19,20,35,36]. This trial has been powered for 2 phases of hypothesis testing. In the first phase, we will compare each of the 3 intervention arms with control. In the second phase, we will compare successful intervention arms with each other. We expect that the magnitude of difference between intervention arms will be less than that of successful intervention arms compared with control. For this second phase of analyses, we will use a conservative Bonferroni adjustment of the type I error rate with a 2-sided alpha of .017 to adjust for up to 3 comparisons. As only intervention arms that demonstrated a significant difference with the control are compared with each other in the second phase, the overall family-wise error rate of this 2-phase procedure is controlled at 0.05 [37].

Statistical Analysis

All analyses will be performed using intention-to-treat. For the main analysis, we will use multiple imputation for missing data. Similar to prior work [16,19], for missing step data, including values less than 1000 steps per day, we will perform 5 sets of imputations, and results will be combined using Rubin's standard rules [38]. We will perform sensitivity analyses using

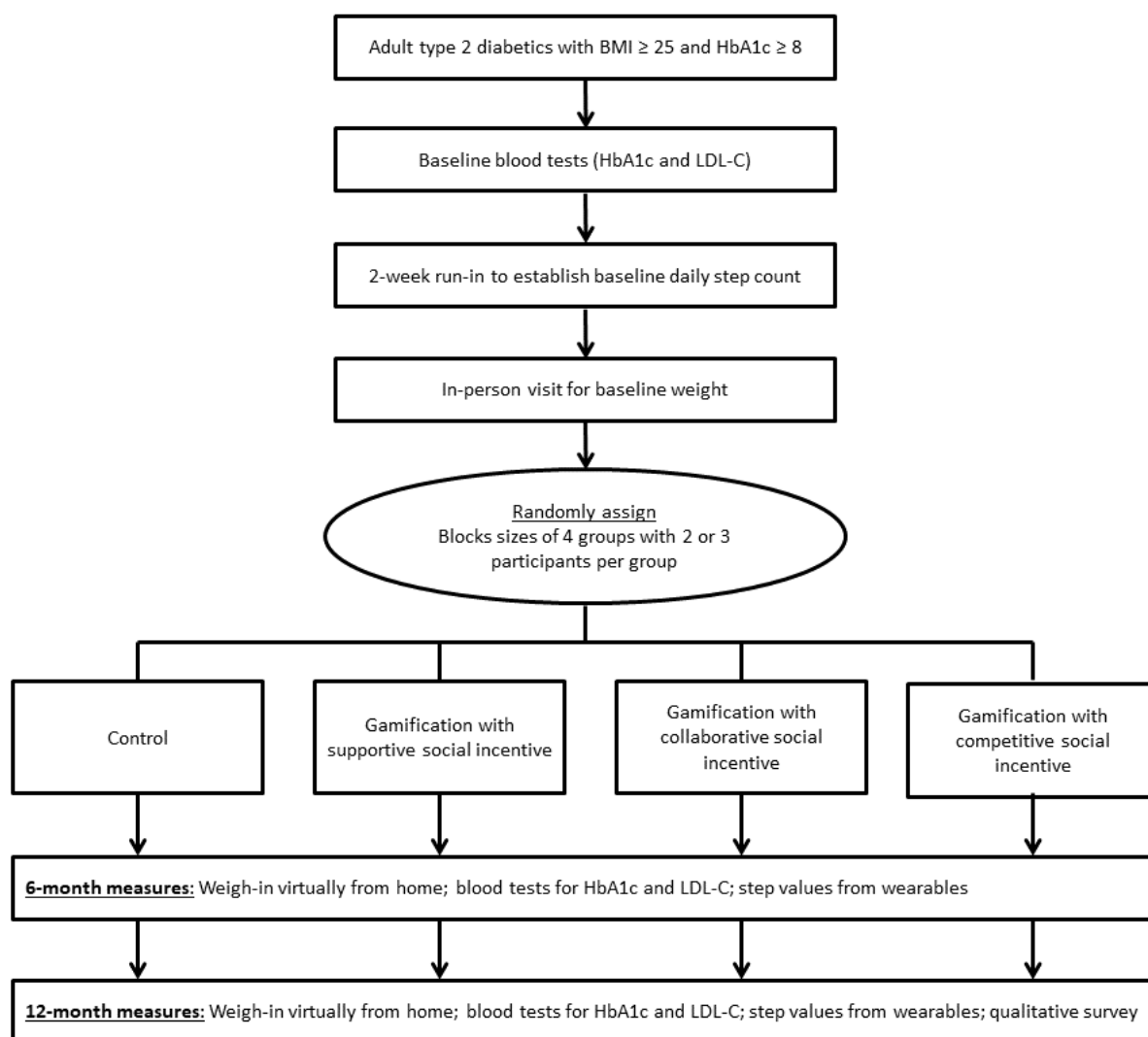
available data without imputation. The primary analysis will fit a mixed effect regression model to evaluate changes in outcome measures adjusted for each participant baseline measure, time at the observation level using calendar month fixed effects, and participant random effects. Secondary analyses will fit mixed effects regression models adjusted for other variables of interest such as participant characteristics.

To understand predictors of response to the interventions, exploratory analyses will fit mixed effects regression models to evaluate associations of participant characteristics or behaviors with strong or poor performance in the outcome measures. In addition, we will use latent class analysis of the baseline variables to identify classes of participants and compare differences in their performance across the arms. We will also conduct an exploratory qualitative evaluation of the survey's free text responses by using grounded theory to identify themes reported by the participants.

Results

The study flow diagram is depicted in [Figure 4](#). Over a 2-year period, 361 participants were randomized into the trial. Among the approximately 10,000 individuals identified in the electronic health record and invited to participate, 1420 created an account on Way to Health and were assessed for eligibility. Reasons for exclusion included ineligibility (168), declining informed consent (61), and not completing all enrollment steps before recruitment closed (651). The trial will conclude in January 2020, and analyses will be reported separately.

Figure 4. Study flow diagram of participants randomized into the *Influencing Diabetics to Adapt Behaviors related to Exercise and weight by Enhancing Social incentives* trial. BMI: body mass index; HbA_{1c}: glycated hemoglobin; LDL-C: low-density lipoprotein cholesterol.



Discussion

Overview

Daily behaviors related to management of type 2 diabetes have typically been challenging to address because they occur within the everyday lives of patients and not during in-person visits with a clinician. The iDiabetes trial uses remotely monitored devices to test a scalable approach to monitor these behaviors and deploy interventions. Insights from behavioral economics are incorporated within the gamification interventions to address predictable barriers to behavior change. Social incentives, which are the influencers that motivate individuals to adjust their behaviors based on social ties and connections [39-41], are compared across different designs including supportive, competitive, and collaborative types. We will also explore whether data from validated assessments completed by participants can identify predictors of response to interventions.

Strengths and Limitations

This study has several limitations. First, only a small portion of the individuals invited enrolled into the trial, and this may limit generalizability. Second, the control arm did not receive daily messaging; therefore, we cannot disentangle the impact of the gamification interventions with daily messaging. Third, we are evaluating physical activity using step counts and do not have other measures of physical activity or exercise. Finally, we are unable to measure variations in the amount of support, competition, or collaboration for each participant in those respective arms.

This study also has several strengths. First, although gamification is used widely by insurance and workplace wellness programs, these designs often do not incorporate principles from theories of health behavior. Lessons from this study could help to inform the design of those programs to increase effectiveness. Second, insights from interventions among diabetics could be applied to patients with other chronic conditions that may benefit from changes in physical activity

or weight. Third, this trial was conducted through a remote-monitoring approach that could be scaled more broadly at a lower cost than a more personnel-intensive approach. Finally, our exploratory analysis will enable us to design more targeted interventions in the future by understanding which participants respond best to each of the interventions.

Conclusions

The iDiabetes study is one of the first evaluations of behaviorally designed gamification in a high-risk patient population. This trial has demonstrated that it is feasible to conduct a remotely monitored intervention, and the findings could help us to understand how to improve the management of adults with type 2 diabetes.

Acknowledgments

This study was supported by grant 2016101 from the Doris Duke Charitable Foundation and the University of Pennsylvania Health System through the Penn Medicine Nudge Unit. The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the paper; and decision to submit the paper for publication.

Conflicts of Interest

MP is supported by career development awards from the Department of Veterans Affairs HSR&D and the Doris Duke Charitable Foundation. MP is the founder of Catalyst Health, a technology and behavior change consulting firm. MP also has received research funding from Deloitte, which is not related to the work described in this paper. No other disclosures were reported.

References

1. Menke A, Casagrande S, Geiss L, Cowie CC. Prevalence of and trends in diabetes among adults in the United States, 1988-2012. *J Am Med Assoc* 2015 Sep 8;314(10):1021-1029. [doi: [10.1001/jama.2015.10029](https://doi.org/10.1001/jama.2015.10029)] [Medline: [26348752](https://pubmed.ncbi.nlm.nih.gov/26348752/)]
2. Gregg EW, Li Y, Wang J, Burrows NR, Ali MK, Rolka D, et al. Changes in diabetes-related complications in the United States, 1990-2010. *N Engl J Med* 2014 Apr 17;370(16):1514-1523. [doi: [10.1056/NEJMoa1310799](https://doi.org/10.1056/NEJMoa1310799)] [Medline: [24738668](https://pubmed.ncbi.nlm.nih.gov/24738668/)]
3. Balk EM, Earley A, Raman G, Avendano EA, Pittas AG, Remington PL. Combined diet and physical activity promotion programs to prevent type 2 diabetes among persons at increased risk: a systematic review for the community preventive services task force. *Ann Intern Med* 2015 Sep 15;163(6):437-451 [FREE Full text] [doi: [10.7326/M15-0452](https://doi.org/10.7326/M15-0452)] [Medline: [26167912](https://pubmed.ncbi.nlm.nih.gov/26167912/)]
4. Jeon CY, Lokken RP, Hu FB, van Dam RM. Physical activity of moderate intensity and risk of type 2 diabetes: a systematic review. *Diabetes Care* 2007 Mar;30(3):744-752. [doi: [10.2337/dc06-1842](https://doi.org/10.2337/dc06-1842)] [Medline: [17327354](https://pubmed.ncbi.nlm.nih.gov/17327354/)]
5. Patel MS, Asch DA, Volpp KG. Wearable devices as facilitators, not drivers, of health behavior change. *J Am Med Assoc* 2015 Mar 3;313(5):459-460. [doi: [10.1001/jama.2014.14781](https://doi.org/10.1001/jama.2014.14781)] [Medline: [25569175](https://pubmed.ncbi.nlm.nih.gov/25569175/)]
6. Patel MS, Foschini L, Kurtzman GW, Zhu J, Wang W, Rareshide CAL, et al. Using wearable devices and smartphones to track physical activity: initial activation, sustained use, and step counts across sociodemographic characteristics in a national sample. *Ann Intern Med* 2017 Nov 21;167(10):755-757. [doi: [10.7326/M17-1495](https://doi.org/10.7326/M17-1495)] [Medline: [28973116](https://pubmed.ncbi.nlm.nih.gov/28973116/)]
7. Kawachi I. It's all in the game-the uses of gamification to motivate behavior change. *JAMA Intern Med* 2017 Nov 1;177(11):1593-1594. [doi: [10.1001/jamainternmed.2017.4798](https://doi.org/10.1001/jamainternmed.2017.4798)] [Medline: [28973152](https://pubmed.ncbi.nlm.nih.gov/28973152/)]
8. Cotton V, Patel MS. Gamification use and design in popular health and fitness mobile applications. *Am J Health Promot* 2019 Mar;33(3):448-451 [FREE Full text] [doi: [10.1177/0890117118790394](https://doi.org/10.1177/0890117118790394)] [Medline: [30049225](https://pubmed.ncbi.nlm.nih.gov/30049225/)]
9. Edwards EA, Lumsden J, Rivas C, Steed L, Edwards LA, Thiyagarajan A, et al. Gamification for health promotion: systematic review of behaviour change techniques in smartphone apps. *BMJ Open* 2016 Oct 4;6(10):e012447 [FREE Full text] [doi: [10.1136/bmjopen-2016-012447](https://doi.org/10.1136/bmjopen-2016-012447)] [Medline: [27707829](https://pubmed.ncbi.nlm.nih.gov/27707829/)]
10. Hamari J, Sarsa H, Koivisto J. Does Gamification Work? -- A Literature Review of Empirical Studies on Gamification. In: Proceedings of the 2014 47th Hawaii International Conference on System Sciences. 2014 Presented at: HICSS'14; January 6-9, 2014; Hawaii, USA. [doi: [10.1109/hicss.2014.377](https://doi.org/10.1109/hicss.2014.377)]
11. Sardi L, Idri A, Fernández-Alemán JL. A systematic review of gamification in e-Health. *J Biomed Inform* 2017 Jul;71:31-48 [FREE Full text] [doi: [10.1016/j.jbi.2017.05.011](https://doi.org/10.1016/j.jbi.2017.05.011)] [Medline: [28536062](https://pubmed.ncbi.nlm.nih.gov/28536062/)]
12. Loewenstein G, Asch DA, Volpp KG. Behavioral economics holds potential to deliver better results for patients, insurers, and employers. *Health Aff (Millwood)* 2013 Jul;32(7):1244-1250. [doi: [10.1377/hlthaff.2012.1163](https://doi.org/10.1377/hlthaff.2012.1163)] [Medline: [23836740](https://pubmed.ncbi.nlm.nih.gov/23836740/)]
13. Loewenstein G, Brennan T, Volpp KG. Asymmetric paternalism to improve health behaviors. *J Am Med Assoc* 2007 Nov 28;298(20):2415-2417. [doi: [10.1001/jama.298.20.2415](https://doi.org/10.1001/jama.298.20.2415)] [Medline: [18042920](https://pubmed.ncbi.nlm.nih.gov/18042920/)]
14. Kahneman D, Tversky A. Prospect theory: an analysis of decision under risk. *Econometrica* 1979 Mar;47(2):263. [doi: [10.2307/1914185](https://doi.org/10.2307/1914185)]
15. Patel MS, Asch DA, Rosin R, Small DS, Bellamy SL, Heuer J, et al. Framing financial incentives to increase physical activity among overweight and obese adults: a randomized, controlled trial. *Ann Intern Med* 2016 Mar 15;164(6):385-394 [FREE Full text] [doi: [10.7326/M15-1635](https://doi.org/10.7326/M15-1635)] [Medline: [26881417](https://pubmed.ncbi.nlm.nih.gov/26881417/)]

16. Chokshi NP, Adusumalli S, Small DS, Morris A, Feingold J, Ha YP, et al. Loss-framed financial incentives and personalized goal-setting to increase physical activity among ischemic heart disease patients using wearable devices: the active reward randomized trial. *J Am Heart Assoc* 2018 Jun 13;7(12):pii: e009173 [FREE Full text] [doi: [10.1161/JAHA.118.009173](https://doi.org/10.1161/JAHA.118.009173)] [Medline: [29899015](https://pubmed.ncbi.nlm.nih.gov/29899015/)]
17. O'Donoghue T, Rabin M. Doing it now or later. *Am Econ Rev* 1999 Mar;89(1):103-124. [doi: [10.1257/aer.89.1.103](https://doi.org/10.1257/aer.89.1.103)]
18. Zeelenberg M, Pieters R. Consequences of regret aversion in real life: the case of the Dutch postcode lottery. *Organ Behav Hum Decis Process* 2004;93(2):155-168. [doi: [10.1016/j.obhdp.2003.10.001](https://doi.org/10.1016/j.obhdp.2003.10.001)]
19. Patel MS, Benjamin EJ, Volpp KG, Fox CS, Small DS, Massaro JM, et al. Effect of a game-based intervention designed to enhance social incentives to increase physical activity among families: the be fit randomized clinical trial. *JAMA Intern Med* 2017 Nov 1;177(11):1586-1593 [FREE Full text] [doi: [10.1001/jamainternmed.2017.3458](https://doi.org/10.1001/jamainternmed.2017.3458)] [Medline: [28973115](https://pubmed.ncbi.nlm.nih.gov/28973115/)]
20. Kurtzman GW, Day SC, Small DS, Lynch M, Zhu J, Wang W, et al. Social incentives and gamification to promote weight loss: the LOSE IT randomized, controlled trial. *J Gen Intern Med* 2018 Oct;33(10):1669-1675. [doi: [10.1007/s11606-018-4552-1](https://doi.org/10.1007/s11606-018-4552-1)] [Medline: [30003481](https://pubmed.ncbi.nlm.nih.gov/30003481/)]
21. Asch DA, Volpp KG. On the way to health. *LDI Issue Brief* 2012;17(9):1-4. [Medline: [22934330](https://pubmed.ncbi.nlm.nih.gov/22934330/)]
22. Patel MS, Asch DA, Rosin R, Small DS, Bellamy SL, Eberbach K, et al. Individual versus team-based financial incentives to increase physical activity: a randomized, controlled trial. *J Gen Intern Med* 2016 Jul;31(7):746-754 [FREE Full text] [doi: [10.1007/s11606-016-3627-0](https://doi.org/10.1007/s11606-016-3627-0)] [Medline: [26976287](https://pubmed.ncbi.nlm.nih.gov/26976287/)]
23. Patel MS, Volpp KG, Rosin R, Bellamy SL, Small DS, Fletcher MA, et al. A randomized trial of social comparison feedback and financial incentives to increase physical activity. *Am J Health Promot* 2016 Jul;30(6):416-424 [FREE Full text] [doi: [10.1177/0890117116658195](https://doi.org/10.1177/0890117116658195)] [Medline: [27422252](https://pubmed.ncbi.nlm.nih.gov/27422252/)]
24. Patel MS, Volpp KG, Rosin R, Bellamy SL, Small DS, Heuer J, et al. A randomized, controlled trial of lottery-based financial incentives to increase physical activity among overweight and obese adults. *Am J Health Promot* 2018 Sep;32(7):1568-1575. [doi: [10.1177/0890117118758932](https://doi.org/10.1177/0890117118758932)] [Medline: [29534597](https://pubmed.ncbi.nlm.nih.gov/29534597/)]
25. Patel MS, Asch DA, Troxel AB, Fletcher M, Osman-Koss R, Brady J, et al. Premium-based financial incentives did not promote workplace weight loss in a 2013-15 study. *Health Aff (Millwood)* 2016 Jan;35(1):71-79. [doi: [10.1377/hlthaff.2015.0945](https://doi.org/10.1377/hlthaff.2015.0945)] [Medline: [26733703](https://pubmed.ncbi.nlm.nih.gov/26733703/)]
26. Blais AW. A Domain-Specific Risk-Taking (DOSPERT) scale for adult populations. *Judgm Decis Mak* 2006;1(1):33-47 [FREE Full text]
27. McCrae RR, Costa PT. Validation of the five-factor model of personality across instruments and observers. *J Pers Soc Psychol* 1987 Jan;52(1):81-90. [doi: [10.1037//0022-3514.52.1.81](https://doi.org/10.1037//0022-3514.52.1.81)] [Medline: [3820081](https://pubmed.ncbi.nlm.nih.gov/3820081/)]
28. 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](https://doi.org/10.1016/0277-9536(91)90150-b)] [Medline: [2035047](https://pubmed.ncbi.nlm.nih.gov/2035047/)]
29. Case MA, Burwick HA, Volpp KG, Patel MS. Accuracy of smartphone applications and wearable devices for tracking physical activity data. *J Am Med Assoc* 2015;313(6):625-626. [doi: [10.1001/jama.2014.17841](https://doi.org/10.1001/jama.2014.17841)] [Medline: [25668268](https://pubmed.ncbi.nlm.nih.gov/25668268/)]
30. Bassett DR, Wyatt HR, Thompson H, Peters JC, Hill JO. Pedometer-measured physical activity and health behaviors in US adults. *Med Sci Sports Exerc* 2010 Oct;42(10):1819-1825 [FREE Full text] [doi: [10.1249/MSS.0b013e3181dc2e54](https://doi.org/10.1249/MSS.0b013e3181dc2e54)] [Medline: [20305579](https://pubmed.ncbi.nlm.nih.gov/20305579/)]
31. Kang M, Rowe DA, Barreira TV, Robinson TS, Mahar MT. Individual information-centered approach for handling physical activity missing data. *Res Q Exerc Sport* 2009 Jun;80(2):131-137. [doi: [10.1080/02701367.2009.10599546](https://doi.org/10.1080/02701367.2009.10599546)] [Medline: [19650377](https://pubmed.ncbi.nlm.nih.gov/19650377/)]
32. Rogers T, Milkman KL, Volpp KG. Commitment devices: using initiatives to change behavior. *J Am Med Assoc* 2014 May;311(20):2065-2066. [doi: [10.1001/jama.2014.3485](https://doi.org/10.1001/jama.2014.3485)] [Medline: [24777472](https://pubmed.ncbi.nlm.nih.gov/24777472/)]
33. Ariely D, Wertenbroch K. Procrastination, deadlines, and performance: self-control by precommitment. *Psychol Sci* 2002 May;13(3):219-224. [doi: [10.1111/1467-9280.00441](https://doi.org/10.1111/1467-9280.00441)] [Medline: [12009041](https://pubmed.ncbi.nlm.nih.gov/12009041/)]
34. Dai H, Milkman KL, Riis J. The fresh start effect: temporal landmarks motivate aspirational behavior. *Manag Sci* 2014;60(10):2563-2582. [doi: [10.1287/mnsc.2014.1901](https://doi.org/10.1287/mnsc.2014.1901)]
35. Sen AP, Sewell TB, Riley EB, Stearman B, Bellamy SL, Hu MF, et al. Financial incentives for home-based health monitoring: a randomized controlled trial. *J Gen Intern Med* 2014 May;29(5):770-777 [FREE Full text] [doi: [10.1007/s11606-014-2778-0](https://doi.org/10.1007/s11606-014-2778-0)] [Medline: [24522623](https://pubmed.ncbi.nlm.nih.gov/24522623/)]
36. Long JA, Jahnle EC, Richardson DM, Loewenstein G, Volpp KG. Peer mentoring and financial incentives to improve glucose control in African American veterans: a randomized trial. *Ann Intern Med* 2012 Mar 20;156(6):416-424 [FREE Full text] [doi: [10.7326/0003-4819-156-6-201203200-00004](https://doi.org/10.7326/0003-4819-156-6-201203200-00004)] [Medline: [22431674](https://pubmed.ncbi.nlm.nih.gov/22431674/)]
37. Burman C, Sonesson C, Guilbaud O. A recycling framework for the construction of Bonferroni-based multiple tests. *Stat Med* 2009 Mar 28;28(5):739-761. [doi: [10.1002/sim.3513](https://doi.org/10.1002/sim.3513)] [Medline: [19142850](https://pubmed.ncbi.nlm.nih.gov/19142850/)]
38. Rubin DB. *Multiple Imputation for Nonresponse in Surveys*. New York, NY: Wiley; 1987.
39. Asch DA, Rosin R. Engineering social incentives for health. *N Engl J Med* 2016 Dec 29;375(26):2511-2513. [doi: [10.1056/NEJMp1603978](https://doi.org/10.1056/NEJMp1603978)] [Medline: [28029924](https://pubmed.ncbi.nlm.nih.gov/28029924/)]
40. Christakis NA, Fowler JH. The collective dynamics of smoking in a large social network. *N Engl J Med* 2008 May 22;358(21):2249-2258 [FREE Full text] [doi: [10.1056/NEJMs0706154](https://doi.org/10.1056/NEJMs0706154)] [Medline: [18499567](https://pubmed.ncbi.nlm.nih.gov/18499567/)]

41. Christakis NA, Fowler JH. The spread of obesity in a large social network over 32 years. *N Engl J Med* 2007 Jul 26;357(4):370-379. [doi: [10.1056/NEJMsa066082](https://doi.org/10.1056/NEJMsa066082)] [Medline: [17652652](https://pubmed.ncbi.nlm.nih.gov/17652652/)]

Abbreviations

HbA_{1c}: glycated hemoglobin

iDiabetes: Influencing Diabetics to Adapt Behaviors related to Exercise and weightT by Enhancing Social incentives

LDL-C: low-density lipoprotein cholesterol

Edited by C Hoving; submitted 08.04.19; peer-reviewed by K Bul, P Timpel; comments to author 09.05.19; revised version received 26.06.19; accepted 26.07.19; published 20.11.19.

Please cite as:

Fortunato M, Harrison J, Oon AL, Small D, Hilbert V, Raeshide C, Patel M

Remotely Monitored Gamification and Social Incentives to Improve Glycemic Control Among Adults With Uncontrolled Type 2 Diabetes (iDiabetes): Protocol for a Randomized Controlled Trial

JMIR Res Protoc 2019;8(11):e14180

URL: <http://www.researchprotocols.org/2019/11/e14180/>

doi: [10.2196/14180](https://doi.org/10.2196/14180)

PMID: [31746765](https://pubmed.ncbi.nlm.nih.gov/31746765/)

©Michael Fortunato, Joseph Harrison, Ai Leen Oon, Dylan Small, Victoria Hilbert, Charles Raeshide, Mitesh Patel. Originally published in JMIR Research Protocols (<http://www.researchprotocols.org>), 20.11.2019. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in JMIR Research Protocols, is properly cited. The complete bibliographic information, a link to the original publication on <http://www.researchprotocols.org>, as well as this copyright and license information must be included.

Protocol

Social Media Intervention to Promote Smoking Treatment Utilization and Cessation Among Alaska Native People Who Smoke: Protocol for the Connecting Alaska Native People to Quit Smoking (CAN Quit) Pilot Study

Pamela S Sinicrope¹, DrPH; Kathryn R Koller², PhD; Judith J Prochaska³, PhD, MPH; Christine A Hughes¹, BS; Martha J Bock¹, BS; Paul A Decker⁴, MS; Christie A Flanagan², MPH; Zoe T Merritt², MBA; Crystal D Meade², BS; Abbie L Willetto², MA; Ken Resnicow⁵, PhD; Timothy K Thomas², MD; Christi A Patten¹, PhD

¹Department of Psychiatry and Psychology and Behavioral Health Research Program, Mayo Clinic, Rochester, MN, United States

²Clinical and Research Services, Division of Community Health Services, Alaska Native Tribal Health Consortium, Anchorage, AK, United States

³Stanford Prevention Research Center, Department of Medicine, Stanford University, Stanford, CA, United States

⁴Division of Biomedical Statistics and Informatics, Department of Health Sciences Research, Mayo Clinic, Rochester, MN, United States

⁵School of Public Health, University of Michigan, Ann Arbor, MI, United States

Corresponding Author:

Pamela S Sinicrope, DrPH

Department of Psychiatry and Psychology and Behavioral Health Research Program

Mayo Clinic

200 1st St SW

Rochester, MN, 55905

United States

Phone: 1 507 266 1238

Email: Sinicrope.Pamela@mayo.edu

Abstract

Background: Despite the high prevalence of tobacco use among Alaska Native (AN) people, tobacco cessation interventions developed specifically for this group are lacking. Social media hold promise as a scalable intervention strategy to promote smoking treatment utilization and cessation, given the barriers to treatment delivery (ie, geographic remoteness, limited funding, climate, and travel costs) in the state of Alaska (AK). Building on a longstanding tobacco control research partnership with the AK Tribal Health System, in this study, we are developing and pilot-testing a culturally relevant, Facebook (FB)-delivered intervention that incorporates a digital storytelling approach adapted from the effective Centers for Disease Control Tips from Former Smokers campaign.

Objective: This study aims to promote evidence-based smoking treatment (eg, state quitline and Tribal cessation programs) uptake and cessation among AN people.

Methods: This study fulfills the objectives for stage 1 of the National Institute on Drug Abuse behavioral integrative treatment development program. In stage 1a, we will use a mixed method approach to develop the FB intervention. Cultural variance and surface/deep structure frameworks will address the influence of culture in designing health messages. These developmental activities will include qualitative and quantitative assessments, followed by beta testing of proposed intervention content. In stage 1b, we will conduct a randomized pilot trial enrolling 60 AN adults who smoke. We will evaluate the feasibility, uptake, consumer response, and potential efficacy of the FB intervention compared with a control condition (quitline/treatment referral only). Primary outcome measures include feasibility and biochemically verified smoking abstinence at 1-, 3-, and 6-month follow-ups. Secondary outcomes will include self-reported smoking cessation treatment utilization and abstinence from tobacco/nicotine products. We will also explore interdependence (relationship orientation and collaborative efforts in lifestyle change) as a culturally relevant mediator of intervention efficacy.

Results: The study enrolled 40 participants for phase 1, with data saturation being achieved at 30 AN people who smoke and 10 stakeholders. For phase 2, we enrolled 40 participants. Qualitative assessment of proposed intervention content was completed with 30 AN smokers and 10 stakeholders. We are currently analyzing data from the quantitative assessment with 40 participants in preparation for the beta testing, followed by the randomized pilot trial.

Conclusions: The project is innovative for its use of social media communication tools that are culturally relevant in a behavioral intervention designed to reach AN people statewide to promote smoking treatment utilization and cessation. The study will further advance tobacco cessation research in an underserved disparity group. If the pilot intervention is successful, we will have a blueprint to conduct a large randomized controlled efficacy trial. Our approach could be considered for other remote AN communities to enhance the reach of evidence-based tobacco cessation treatments.

International Registered Report Identifier (IRRID): DERR1-10.2196/15155

(*JMIR Res Protoc* 2019;8(11):e15155) doi:[10.2196/15155](https://doi.org/10.2196/15155)

KEYWORDS

smoking; tobacco cessation; Alaska; Alaska Natives; tobacco smoking; internet; social media; clinical trial randomized; smoking cessation; intervention

Introduction

Background and Significance

Cigarette smoking, the most preventable cause of morbidity, mortality, and excess health cost in the United States, accounts for 480,000 premature deaths yearly [1]. At 22%, American Indian (AI)/Alaska Native (AN) persons have the highest US smoking prevalence; and within this group, AN residents of Alaska (AK) have a prevalence of smoking more than double that of Alaskan whites (42% vs 17%) [2]. Accordingly, AN people who smoke experience more tobacco-related diseases and mortality compared with non-Native people living in AK or US whites [3-6]. A national public health objective is to reduce tobacco-caused health disparities [7,8]. The state of AK developed its own health improvement plan, Healthy Alaskans 2020, that identifies priority health indicators. Decreasing smoking prevalence among AN adults to 17% is one of the priorities [9]. We will address both objectives by developing effective strategies to decrease tobacco use within AN communities across the state of AK and among AN people as a whole. With approximately 20% of the state's population self-identifying as AN race [10], substantial reductions in tobacco use will greatly contribute to reducing statewide tobacco use rates.

Quitlines have proven efficacy [11] but remain underutilized by AN people [12,13]. In addition, only 4% to 7% of unaided quit attempts are successful among AN smokers compared with 10% among non-Native smokers. Evidence-based counseling and medication treatments could boost quit rates to as high as 30% to 40% [14,15]. Therefore, a need exists to increase utilization of available, low/no cost, and evidence-based smoking cessation resources such as AK's Tobacco Quitline or Tribal tobacco cessation resources.

The Alaska Native Tribal Health Consortium (ANTHC), a consortium of regional Tribal health leaders, represents diverse AN people in AK. ANTHC co-owns and comanages the Alaska Native Medical Center (ANMC) in Anchorage. ANMC provides specialty care to AN people statewide, serving as the AK Tribal Health System's only tertiary care facility. ANTHC's Community Health Services Tobacco Prevention and Control Program provides tobacco cessation counseling and nicotine replacement therapy (NRT) to inpatients at ANMC. Upon discharge, patients are referred to cessation services at their regional Tribal health organization, which vary widely, or to

AK's Tobacco Quitline. AK's Tobacco Quitline, operated by the state, is available to all Alaskans but provides free NRT for only 1 month. Given these barriers, the ANTHC Tobacco Prevention and Control Program appealed to ANTHC's Clinical and Research Services to explore ways to expand capacity for support of AN Tribal members' cessation efforts statewide.

Although our study with AN pregnant women and youth demonstrated that face-to-face interventions had limited reach and efficacy [16,17], Web-based social networks, such as Facebook (FB), are potentially powerful tools for reaching, engaging, and connecting AN people who smoke in cessation efforts [18] because of their large reach, relatively low cost, and potential for greater adoption and sustainability. The following section reviews the literature on the topic of social media use for health promotion with ANs and, generally, in the area of tobacco cessation. Utilization of the internet to access health information and social media use have increased among AN people, even in remote regions. In a representative survey of 340 households in rural southwest AK (73% AN adults), 87% had at least 1 cell phone, 60% had a smartphone, and 81% used FB, Twitter, or other social media sites [19,20]. A survey of 362 AN females from a rural census area reported that 80% used internet, 78% had smartphones, and 90% used FB [21]. Although the potential of social media to enhance smoking cessation is understudied, it remains a priority research area [18,22,23], with some trials using social media platforms for smoking cessation reporting effectiveness [24-27].

An intervention with both a website and an FB group evaluated quasi-experimentally among 238 young adult smokers resulted in greater self-reported 7- and 30-day smoking abstinence rates and quit attempts, compared with an unmatched comparison group of quitline users at a 3-month follow-up [24]. Participants interacted significantly more with FB than the website; of FB users, 56% were men and 44% were women, with women more actively posting and engaging than men. An analysis of sex differences in communication styles revealed that women emphasized support and connecting, whereas men expressed strong assertions about quitting smoking [25].

Another study evaluated a 100-day Twitter intervention [26]. Among 160 smokers aged 18 to 59 years, Tweet2Quit doubled the rate of self-reported sustained abstinence at 2 months post quit date compared with a control condition (smokefree.gov cessation website referral plus nicotine patches), 40% versus 20%. Sex, but not age, was related to treatment outcome, with

women less likely to quit smoking than men in both study conditions.

An uncontrolled FB study for young adult smokers tested whether monetary incentives enhanced FB intervention engagement [27]. FB engagement was high, did not differ by incentive, and self-reported smoking abstinence at 6 months was 18%. Another observational study evaluated social media to support smoking cessation efforts among participants enrolled in a state-run cessation program in Saudi Arabia. Investigators found that WhatsApp- and Twitter-based social media support groups were more likely to report a decrease in smoking frequency compared with those not using social media [27].

A total of 3 other feasibility studies examined FB use among smokers. Haines-Saah et al [28] found more postings to the *Picture Me Smokefree* FB page among women than men (ie, 189 total photos posted among women, mean 9.5, vs 94 posted by men, mean 4.2). Content analysis revealed that postings were of similar quality for both sexes; sharing of photos and captions about experiences with tobacco use and struggles with quitting in the context of family life and relationships were the main themes. Evaluation of the FB page smokefreewomen.gov [29] found that increased frequency of moderator postings to facilitate dialogue and provide support engaged existing and new users, resulting in a marked increase in user postings and reach. Finally, an FB intervention using health communication messaging and supportive moderator postings was associated with a decrease in cigarettes smoked per day from baseline to 2-week follow-up; increased engagement was associated with greater smoking reduction [30].

Objective

To overcome barriers of geography, climate, and scalability, we proposed to create and pilot-test a culturally salient social media (ie, FB) intervention to promote evidence-based smoking treatment utilization and cessation for AN people that will eventually be maintained by ANTHC's Tobacco Prevention and Control Program. The project builds on ANTHC and Mayo Clinic's longstanding tobacco control research partnership with the AN community and is informed by our understanding of cultural factors that can both impede (eg, stress and adverse childhood experiences) and encourage (eg, close family ties and community values) cessation in this population. The goal of

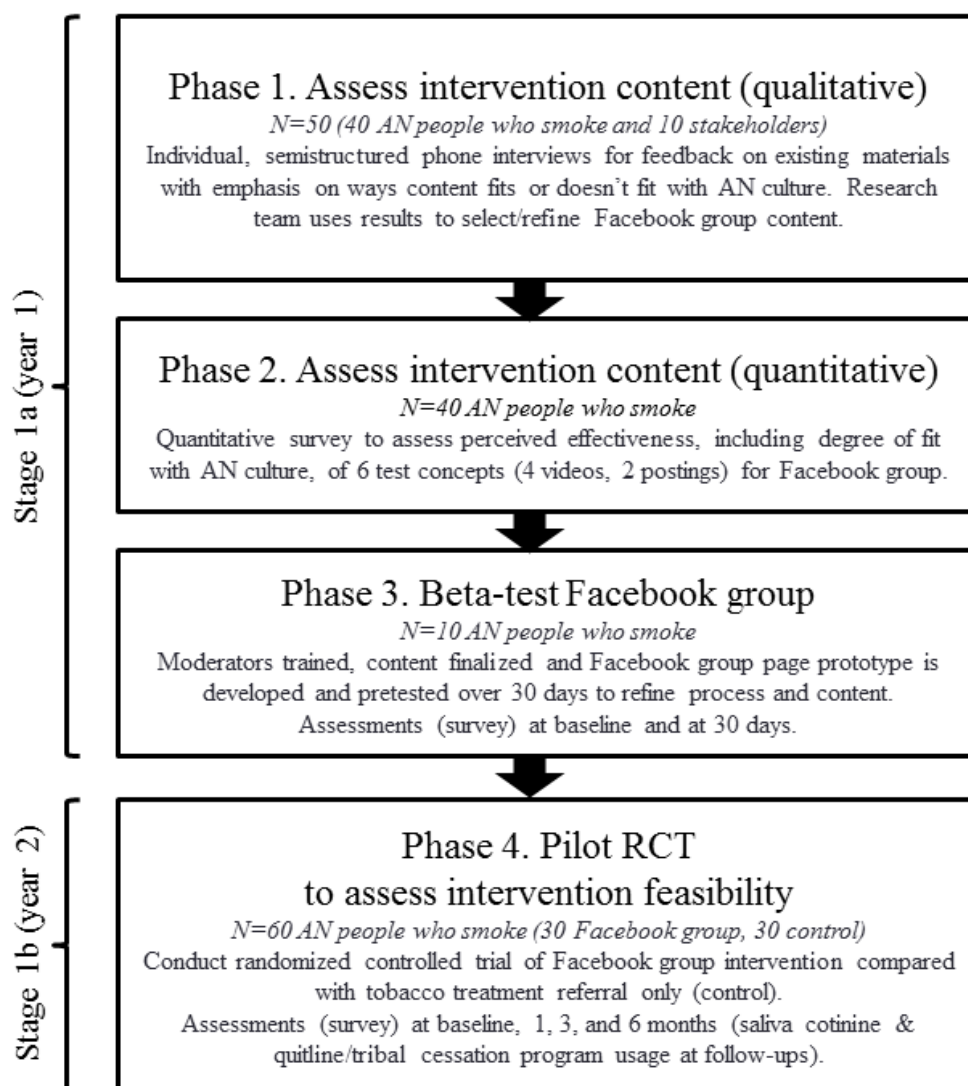
this formative study is to develop an FB intervention that will be a hidden and closed FB group. The goal of the randomized pilot trial is to obtain effect size estimates to adequately power a larger scale efficacy trial. For this phase of the research, the main outcome measures will be intervention feasibility (treatment acceptability and program satisfaction) and verified smoking abstinence. Secondary outcome measures will be self-reported other tobacco abstinence, smoking treatment utilization, and interdependence as a culturally relevant mediator of intervention effectiveness. Additional feasibility measures such as social media engagement, usability, and satisfaction will also be addressed.

The goal of the pilot trial is to obtain effect size estimates to adequately power a larger scale stage 2 efficacy trial.

Theoretical Framework

We used cultural variance and surface/deep structure frameworks [31,32] to address the influence of culture in designing health messages. Cultural variance framework considers AN cultural influences on health behaviors, including beliefs and norms (ie, communication styles and social acceptance of tobacco use), values (eg, interdependence), and AN knowledge systems/ways of knowing [33-38]. Surface and deep structure inform content and format of messages. Surface structure matches materials/messages to observable social and behavioral characteristics (eg, AN people, music, and clothing), and deep structure incorporates cultural beliefs and values. Surface structure generally enhances receptivity, comprehension, and acceptance of messages, whereas deep structure conveys salience. We will also use a planning framework based on the National Cancer Institute [39] and Centers for Disease Control (CDC) [40] recommendations for developing social media and other digital health communication tools, addressing key components of message construction [41,42] that are also consistent with stage 1 of the 3-stage model of behavioral therapies development [43] that includes intervention development, refinement, modification/adaptation, and pilot testing. In summary, we will conduct the research in 4 phases. In phase 1, we will use qualitative in-depth interviews and then in phase 2, quantitative methods to develop/refine message concepts. Next, in phase 3, we will develop and beta-test the intervention prototype; and finally, in phase 4, we will conduct a randomized pilot trial of the intervention (Figure 1).

Figure 1. Overview of process to develop CAN Quit Facebook intervention. AN: Alaska Native; RCT: randomized controlled trial. CAN Quit: Connecting Alaska Native people to quit smoking (CAN Quit).



Intervention Content

Content for our FB intervention is culturally relevant, adapting the storytelling approach used in both the ANTHC digital stories about smoking cessation from AN people and the CDC Tips mass media campaign [44]. On the basis of factual health communication messaging, Tips features graphic, emotional, true stories from former smokers to increase awareness of smoking harms and encourage quitting. It includes the call to use free, evidence-based statewide quitline numbers and smoking cessation website resources (smokefree.gov). The campaign increased quitline utilization and quit attempts on a population level [44,45].

Tips stories promote salience and reduce tendency for smokers to discount adverse health outcomes as uncommon because stories feature real people [46]. Numerous studies, including a previous study by our team [33], suggest that storytelling is congruent with AN culture (strong oral storytelling tradition) [47-49], making the Tips format ideal for social media content development. Digital storytelling and other narrative forms of communication (eg, photonovela and photovoice) have emerged

as important tools for health behavior change [50-52]. The communication forms reinforce traditional knowledge systems and cross-generational learning and build social connections [36,38]. Also relevant to the Tips campaign is the study conducted by our team indicating that AN adults preferred graphic, factual messages on tobacco use harms compared with other appeals, although this research was limited to interventions communicating risks during pregnancy [53,54].

The intervention will comprise an FB group moderated by a facilitator. To address potential concerns about FB privacy [55], we will utilize a closed and hidden FB group and a group policy/guideline that emphasizes confidentiality of all content. A hidden group is defined as invitation only, with the group and content not visible to anyone on FB except participants. Thus, anyone searching on FB would not find the group nor be able to request to join. Also, group membership or postings through news feeds will not be visible on the participants' personal FB page.

We chose to use a moderated group based on research indicating that moderators play a critical role in directing and tailoring

content to the group and enhancing overall social media engagement [25,56]. Also, the frequency of moderator FB postings is associated with increased participant engagement [29].

Methods

Overview

This study was reviewed and approved by the Institutional Review Boards for the AK area and Mayo Clinic. Tribal approval for the study was received from ANTHC. Our study fulfills objectives for stage 1 of the National Institute on Drug Abuse (NIDA) behavioral integrative treatment development program, where the intervention is developed in stage 1a and then evaluated for feasibility in 1b (Figure 1) [43].

Participants and Recruitment

For all study phases, we will recruit AN men and women who smoke, statewide, using targeted and paid FB ads (ie, digital targeting) based on the following: (1) aged >19 years, (2)

self-reported AN race/ethnicity, and (3) keywords related to tobacco use. FB ads are a successful method of recruiting for research studies, especially among hard-to-reach populations [57,58]. We developed ads that include an image and short text consistent with FB's advertising guidelines. We will partner with organizations that have a large FB following, such as the Alaska Federation of Natives, along with community-specific FB pages to advertise the study. We will also advertise in Tribal newsletters, newspapers, and websites and hand out flyers.

Eligibility criteria for participation are as follows: (1) AN person (male or female); (2) aged >19 years; (3) smoked at least 1 cigarette per day over the past 7-day period; (4) person with cigarettes as main tobacco product used; (5) considering or willing to make a quit attempt; (6) has access to broadband (high speed) internet on a mobile phone, at home, work, or other location; (7) has an FB account or willing to set one up before study enrollment; and (8) has not been enrolled in a program or using pharmacotherapy to stop smoking over the last 3 months. Participants will participate in the study only once, not in multiple phases (Table 1).

Table 1. Participant eligibility and rationale for both the formative study and pilot trial.

| Study inclusion criteria | Rationale |
|---|---|
| AN ^a person (based on self-reported race/ethnicity) and resides in AK ^b | Study targets a population with the highest prevalence of tobacco use in the United States. We chose to conduct this initial study in AK to reduce sample and intervention design heterogeneity. Across the nation, there is immense cultural and geographic variability among ANs, for example, urban versus reservation dwelling and ceremonial versus nonceremonial tobacco use. ANs do not commonly use tobacco for ceremonial purposes. Also, AK has the highest percentage of AN residents versus all other states (19% vs 2%) [59,60]. If effective, the intervention could be adapted for and disseminated to AN adults nationwide. |
| Aged ≥19 years | Legal smoking age in AK is 19 years. Different social media venues and content may be warranted to address developmental issues among those <18 years. A Twitter-based intervention for adult smokers aged 20 to 59 years found that age was not related to engagement or cessation [61]; thus, we chose not to restrict the upper age limit. |
| Both men and women will be included | There are no preliminary data to indicate that sex-specific interventions are warranted at this stage of the research. We will explore sex differences on feasibility and efficacy as a research question. |
| Smoked at least 1 cigarette per day over the past 7-day period | This allows for participation of AN smokers who report fewer cigarettes per day and are considered <i>light</i> smokers but have cotinine concentrations equivalent to <i>heavy</i> white smokers, indicating differences in nicotine metabolism [15,62]. |
| If other tobacco products are used, cigarettes are the main tobacco product used | Cigarette smoking in combination with other tobacco product use is highly prevalent in some AK rural regions [2]; thus, results are more generalizable if other tobacco use is allowed. |
| Considering or willing to make a quit attempt | Intervention promotes treatment utilization and quitting. We will explore readiness to quit as a potential moderator of FB engagement and efficacy. |
| Has access to broadband (high-speed) internet on mobile phone, at home, work, or other location | FB can be accessed on a variety of technology devices, such as computers, iPads, and mobile phones. Broadband internet access is needed to access social media and upload and download videos and other links. |
| Has an existing FB account or willing to set up an account before study enrollment | There is already good adoption of FB in rural regions of AK. Including participants familiar with regular social media interaction enhances participation, whereas nonusers or those unfamiliar with FB are less likely to engage in the intervention [61,63]. To provide study access to a broader group, we will offer a Web- or paper-based tutorial for those without an FB account. |
| For past 3 months, not enrolled in a program or using pharmacotherapy to stop smoking | Study promotes treatment uptake, utilization, and quitting. |

^aAN: Alaska Native.

^bAK: Alaska.

Enrollment will occur online and by phone. All advertisements will contain the study toll-free phone number, email address, and a website link to Qualtrics, where interested participants

can verify eligibility and enroll. Individuals emailing or calling will receive a brief description of the study and a link to the study website. The website will contain a short description of

the study and eligibility criteria. Participants will receive a US \$25 Visa gift card as appreciation for their participation for each assessment they complete.

Measures

For all phases, we will ask the same sociodemographic and tobacco use questions: sex, age, Tribal affiliation, cultural identity (eg, language and traditionalism) [34], region of residence, marital status, education, employment, and current frequency of use of FB and other social media platforms. Tobacco use measures will include cigarettes per day, readiness to quit (Contemplation Ladder) [64], use of other tobacco and nicotine products, time to first cigarette after waking (<30 min vs >30 min) [65-67].

Analyses

Sample characteristics will be summarized using descriptive statistics including means, percentages, and frequencies. Further analyses are described later by phase.

Quality Assurance

For all phases, we use the same coordination and communication procedures successfully utilized in our previous study that include regular study team meetings held via teleconference and a systematic plan for following up with participants to ensure as high a follow-up rate as possible is achieved with regard to key outcomes. First, to track follow-up (number and type) and reasons for attrition, the study coordinator keeps a database of all contacted and consented participants. Generally, subjects are contacted up to about 3 times (with actual contact) before being considered lost to follow-up. This same process is followed for mailed saliva collection kits that include a self-addressed, stamped return envelope with every mailing. For survey data, missing data will be minimized through Web-based assessments using Qualtrics. An email link will be sent automatically by the Mayo Clinic Survey Research Center to complete the assessment. If a participant does not complete Web-based assessments, he/she will be contacted through email or by phone by the project coordinator and prompted to complete the assessment. The baseline and follow-up surveys will be done on the Web or by phone, or the survey will be mailed with a postage-paid return envelope depending on participant preference. These surveys will take about 15 to 30 min each to complete. Participants will be mailed a US \$25 Visa gift card as remuneration for completing each assessment, including returned saliva cotinine kits (Mayo Clinic Laboratories).

Stage 1a, Phases 1 to 3

We evaluated existing content using a mixed method approach, beginning with qualitative work to refine intervention content and a quantitative survey to evaluate the perceived effectiveness (PE) of selected content (phases 1-2). Once content was evaluated both qualitatively and quantitatively, a content library and moderator guide were developed, group moderators were trained, and the FB group prototype was developed. The complete FB group is now being beta-tested for final refinement (phase 3) using quantitative measures.

Stage 1a, Phase 1

Sample

We used a stratified purposeful sample [68] of AN adults who smoke with divisions based on audience segment (sex; age group 19-29, 30-49, and ≥50 years; and region—urban and rural). Krueger [69] recommends conducting at least 10 to 15 interviews per major subset before reaching data saturation, whereby no new information is being learned [69]. We estimate about 50 interviews, 40 with AN smokers (20 men, 20 women; 20 urban, 20 rural; 12-13 within each age group) and 10 with stakeholders (eg, AK's Tobacco Quitline coaches and Tribal cessation program counselors) before reaching data saturation. An interview and moderator guide were developed to qualitatively assess potential intervention content. All participants being interviewed received a US \$25 gift card for remuneration.

Procedures

Moderator Guide and Training

In all, 2 ANTHC research associates conducted interviews. They are experienced in phone interviewing and completed Tobacco Treatment Specialist training and training on qualitative research methods.

Analysis

Recordings were transcribed and content analysis [70] was performed using QSR NVivo software [71] to generate response themes. Codes and categories were developed based on moderator guide topics and themes emerging from the data. A total of 2 study team members coded responses for each topic area. During this open-coding process, themes were extracted for analysis when there was code endorsement or elaboration by several interviews. *In addition to open coding, planned comparisons within and across sex, age, and region strata were conducted and connections were made between identified categories.* Coding discrepancies were resolved through discussion with a third study team member until consensus was reached.

Stage 1a, Phase 2

From qualitative results, the research team selected 6 test concepts: 4 videos and 2 image/text moderator postings representing different types of appeals and message sources to evaluate for PE [72] via a quantitative Web-based survey.

Sample

We tested these concepts using a Web-based survey with a new sample of 40 AN adults who smoke (eligibility criteria Table 1) via a stratified purposeful sample [68], with divisions based on audience segment (eg, sex, age group, and urban/rural region) [69].

Procedures

Respondents viewed test concepts (eg, video, pictures, and text) embedded in a Web-based survey via Qualtrics survey software, or by phone if preferred, with the option to be mailed or emailed the concepts for review in advance of the survey.

Measures

Measures included a validated measure of PE to pretest each concept. PE is useful for assessing the likelihood of success of potential messages when large-scale efficacy pretesting for behavioral impact is impractical [72]. We used a 6-item validated measure of PE used to evaluate Tips stories [72], similar to PE measures used in other research [73]. After viewing each concept, respondents rated their level of agreement on a scale from 1 (strongly disagree) to 5 (strongly agree) with the following statements: (1) this was worth remembering; (2) this grabbed my attention; (3) this was powerful; (4) this was informative; (5) this was meaningful; and (6) this was convincing. Participants also rated each concept for *this fits with my culture*.

Analysis

PE items were summarized using descriptive statistics including means, percentages, and frequencies. The Chi-square goodness of fit test was used to summarize concepts most and least preferred by the participants. The associations of participant sex, age, and region with message concept preferences were examined using linear regression. Following the analysis of PE data, the research team reviewed and synthesized results from the previous phases to develop the prototype intervention for beta testing. Postings that were consistent with the content had high scores for PE, and those that qualitatively generated a positive reaction as being culturally salient and emotional and included images specific to AN culture as expressed by the interview participants were included.

Stage 1a, Phase 3

Prototype

The Mayo Clinic Social Media Department created the FB group page, and members of the research team developed the content library of moderator postings and set up the software to capture participant use data. Existing Tips and ANTHC digital stories deemed culturally acceptable in the formative phases were utilized for moderator postings. Additional content was added from an ANTHC photo library based on participant feedback and the expertise on AN culture provided by our ANTHC partners [47-49]. We created a content library of 66 postings that included 8 videos and 58 image/text postings. For each piece of content, a sample of accompanying text is provided for moderators to use, as well as a probe for generating further discussion or ways to respond to users' questions. All sample text ends in a question to spark discussion among group members. All content includes the phone number of the AK state Quitline as well as a study-specific link that connects participants to the Quitline and AN Tribal cessation resources. Although the content library is crucial for generating discussion among participants, a central aspect of the intervention is the way that the moderators interact with group members. Therefore, in addition to rigorously refining our content, we also engaged our moderators in a structured training process where they were taught principles of group moderation, best practices for moderating and engaging participants, how to promote appropriate conversations and redirect engagement, and how to respond to difficult situations that often arise in a Web-based group among other topics. Moderators also participated in

didactic training to learn about basic communication principles consistent with active listening and motivational interviewing. Finally, moderators were given the opportunity to practice their moderating skills with a social media expert/consultant using a role-playing format. This reinforced the content of the structured training and developed the moderators' skills in writing posts to promote engagement, promoting participation and support of group members, and pulling in and welcoming new members. Moderators were encouraged to help generate daily participation in the FB group until group members became the main drivers of communication, but not to post new content daily, to avoid the risk of participants simply reading content rather than engaging with it.

The FB group is currently being beta-tested over a 30-day period. Results will be used to evaluate our processes and make any final refinements to our content (Figure 1).

Beta Test

Sample

We will beta-test the FB group with 10 AN adult smokers (Table 1) via a stratified purposeful sample [68], with divisions based on audience segment (eg, sex, age group, and urban/rural region) [69]. An FB group size of 10 was the minimum number for optimal engagement in previous studies [74,75]. The purpose of this phase will be to expose participants to the 30 days of moderator postings and obtain feedback to ensure that the system works as intended, note any technical issues that need to be remedied, and facilitate any refinements of the program.

Measures

We will utilize a Web-based survey that includes the 3-item Social Media Usability Measure: perceived ease of use, usefulness, and satisfaction rated on 5-point scales (1-strongly disagree and 5-strongly agree) [76] as well as open-ended questions. Refinements will be made based on user feedback.

Analysis

Sample characteristics, Social Media Usability measures, and concepts most and least preferred will be summarized using descriptive statistics including means, percentages, and frequencies. Open-ended questions will be summarized, and themes will be generated using content analysis [70]. Results from this phase are for beta testing purposes, only for purposes of refining the content for the pilot randomized trial.

Stage 1b, Phase 4

We will use rigorous design and methodology to evaluate the FB intervention's feasibility and potential efficacy via a pilot randomized controlled trial.

Participants

Although not able to detect statistically significant study group differences on smoking abstinence, the study can obtain estimates of the intervention effect toward planning a definitive stage 2 efficacy trial. For the dichotomous variable of point prevalence abstinence, 30 subjects per condition should provide relatively stable group proportions for effect size estimates. Effect size estimates will include odds ratios for smoking abstinence. In addition to demonstrating feasibility, a doubling

of the abstinence rate for the intervention versus control condition at 6 months will be considered to be of clinical significance and warrant proceeding to an efficacy trial [77]. This approach is consistent with recommendations for stage 1 study in behavioral addictions treatment development [43] and conducting small-scale trials to advance electronic health interventions [65]. Given the small sample size, proposed mediational analyses are exploratory.

Both recruitment and eligibility will be similar to the previous 3 phases of the research, whereby flyers and targeted FB ads of AN people who smoke will be used (Table 1).

Procedure

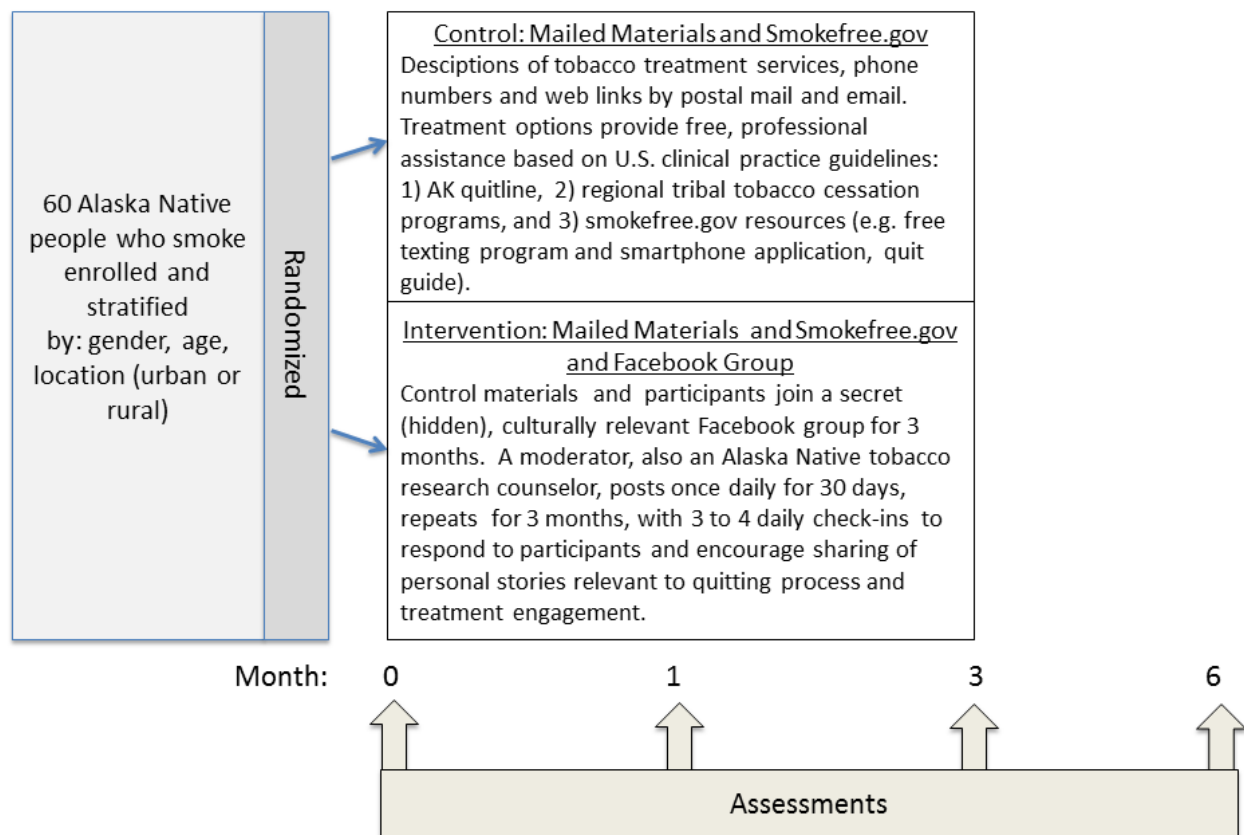
We will utilize a 2-arm, parallel-group, randomized controlled design with 60 participants randomized with 1:1 allocation to the intervention or control condition. Participants will be randomized within stratified blocks based on sex (ie, male or female), age group (eg, 19-29, 30-49, and ≥ 50 years), and region (ie, urban or rural)—potential variables related to outcomes [78,79]. Assessments will be conducted for both study groups at baseline and at 1-, 3-, and 6-month follow-ups. The primary outcomes are feasibility indicators and the 7-day biochemically confirmed smoking abstinence rate at the 6-month follow-up. Secondary end points are self-reported engagement in smoking cessation treatment and quit attempts (Figure 1).

Study Conditions

All participants will receive evidence-based [14] tobacco treatment referral information by postal mail (printed materials) and/or email, including information on their regional Tribal tobacco treatment program, state quitline and information on access to NRT, and smokefree.gov quit smoking resources. The control condition will receive no additional intervention provided by research staff. The intervention condition will, additionally, receive the FB intervention developed in stage 1a.

The FB intervention, comprising 30 days of prewritten and evaluated postings, will be moderated daily by an ANTHC tobacco research counselor. When participants enter the study, they will be informed about the policies for posting content and that any inappropriate postings will be removed. As engagement may be optimal in the first 4 weeks, we will have 30 days of moderator postings available. However, we opted to have the FB group active for 3 months because participants might continue to engage in the intervention for continued social support; thus, the 30 postings will be repeated for each month the group is active. We will, therefore, measure engagement over time to empirically inform decisions about treatment duration in future trials. Accordingly, our assessments are timed to capture smoking behavior changes within the first 30 days (ie, 1 month), at the end of treatment (3 months), and at 6-month follow-up (Figure 2).

Figure 2. Study design. AK: Alaska; AN: Alaska Native.



Feasibility

We will collect data on the number of potential participants screened, number eligible based on the inclusion/exclusion criteria, number of eligible participants enrolled, and reasons for exclusion or nonparticipation. The proportion of 60 participants completing the 6-month follow-up assessment (ie, retention) and the proportion providing a saliva cotinine specimen at each assessment will also be summarized. Treatment acceptability will be assessed with brief intervention satisfaction rating scales [16].

For each week of the study, we will extract for each intervention participant the following engagement metrics: number of logins;

Table 2. Pilot trial measures.

| Measures | Baseline | 1, 3, and 6 months |
|--|----------|--------------------|
| Sociodemographics and tobacco use | X | — ^a |
| Feasibility measures (eg, retention, Facebook use, and engagement) | — | X |
| Self-reported smoking abstinence | — | X |
| Self-reported tobacco/nicotine product use | X | X |
| Saliva cotinine to verify smoking abstinence | — | X |
| Self-reported smoking treatment utilization | — | X |
| Communal Orientation Scale (mediator) | X | X |

^aNot applicable.

Smoking Abstinence

At each follow-up, we will obtain self-reported cigarette use in the past 7 and 30 days, number of cigarettes smoked per day, and quit attempts. We will also assess current use of smokeless tobacco/*iqmik*, electronic cigarettes, and other tobacco/nicotine products. All participants will be mailed a saliva kit with a collection tube and postage-paid return envelope. Participants returning a saliva specimen will receive an additional US \$25 Visa gift card. The specimen will be shipped to and assayed by Mayo Clinic laboratories, a standard approach for randomized trials, especially those with sample sizes <500 [30,79].

Smoking Treatment Utilization

As a secondary aim, we will document the self-reported use of any evidence-based cessation aid during the 6-month study period. For this pilot study, it is not practical to objectively verify self-reported treatment use given heterogeneity of potential services/medications used.

Communal Orientation Scale

The 14-item validated Communal Orientation Scale (COS) [80,81] will be administered at baseline and follow-up to examine interdependence as a culturally relevant mediator of intervention efficacy. In the intervention condition, we will also explore association of COS baseline scores with the degree of FB engagement, whereby a higher COS score would most likely be associated with a higher degree of engagement. This measure assesses the extent to which individuals are relationship- versus self-oriented.

number of digital story downloads; number of user-generated posts, comments, questions, and responses to the moderator or other users; number of likes, shares, and reactions; and time and date of each. In addition, a transcript of all participant postings will be generated for content analysis.

Measures

Assessments will be completed at baseline and 1-, 3-, and 6-month follow-ups. With the exception of obtaining a saliva specimen from all participants for cotinine analysis, all measures will be administered on the Web using Qualtrics (Table 2).

Analysis

Recruitment data will be summarized, including the number of potential participants screened, number excluded for each inclusion/exclusion criteria, and number of eligible individuals agreeing to participate. To assess program reach, we will calculate proportion of subjects enrolled to total eligible subjects and compare enrollment rates by region (rural or urban) using the Chi-square test. Baseline demographics will be summarized and compared between study groups using the Chi-square test for categorical variables and the 2-sample *t* test/rank sum test for continuous variables. Percentage of enrolled participants completing each follow-up assessment (ie, study retention) and ratings of treatment acceptability will be compared between study groups using the Chi-square test (Fisher exact test). FB use and engagement will be summarized using descriptive statistics and time effects over the 3-month treatment period and assessed via mixed effects models as appropriate to explore sex, age group, and region effects, respectively. The association of COS baseline scores and FB engagement will be evaluated using linear regression. Qualitative (content) analysis [70] will be utilized to generate themes in FB postings and comments.

Biochemically confirmed 7-day point prevalence tobacco use rate at 1-, 3-, and 6-month follow-ups will be compared between conditions using logistic regression (with odds ratio and 95% confidence interval estimates). Using an intent-to-treat approach, we will classify participants eligible but lost to follow-up or not providing biochemical verification of smoking abstinence as smoking. We will also explore multiple imputation methods [82-84] to classify lost to follow-up as cigarette smokers or nonsmokers and conduct sensitivity analyses as appropriate. For these analyses, we will adjust for stratification factors (eg,

sex, age group, and urban/rural region) and any baseline differences observed between treatment conditions if data allow (ie, adequate numbers of subjects verified as abstinent). Secondary analyses using logistic regression will explore intervention effects on self-reported abstinence from all tobacco/nicotine products, quit attempts, and self-reported tobacco treatment utilization. We will follow procedures suggested by MacKinnon [85,86] to assess mediation, fitting logistic/linear regression models to the data.

Results

The study enrolled 40 participants for phase 1, with data saturation being achieved at 30 AN people who smoke and 10 stakeholders. For phase 2, we enrolled 40 participants. Qualitative assessment of proposed intervention content was completed with 30 AN smokers and 10 stakeholders. We are currently analyzing data from the quantitative assessment with 40 participants in preparation for the beta testing, followed by the randomized pilot trial.

Discussion

Principal Findings

This multistage pilot project will develop a social media intervention to promote smoking cessation among AN people through utilization of existing evidence-based approaches, such as AK's Tobacco Quitline.

The proposed study, focusing on AN smokers, advances the methods of published social media intervention studies through the use of biochemical verification of smoking abstinence and extended duration of follow-up. Previously, most studies have targeted only young adults, whereas we plan to include a wide age range. We will also explore potential sex, age, and regional (urban/rural) effects on FB engagement and quitting, as there is limited research exploring these variables within the context of social media platforms for smoking cessation [24,26]. Within smoking cessation intervention efficacy and effectiveness trials generally, a recent literature review on sex/gender differences found that of 126 tests conducted, only 2 observed that women were significantly more likely to quit smoking than men, compared with 59 that found women were significantly less likely to quit smoking than men; the remaining 65 studies reported no difference by gender [87].

Acknowledgments

This study was supported by the NIDA, grant number R34 DA046008 (CAP). The funding source had no role in the design and conduct of this study or the drafting of this paper (CAP, PI; KRK, PI).

The authors wish to thank the ANTHC Research Consultation Committee for providing feedback on the development of this study and Selma Oskolkoff-Simon, Program Administrator for ANTHC Marketing and Communication, who provided them with pictures for the flyers.

Conflicts of Interest

JJP has consulted to technology and pharmaceutical companies focused on smoking cessation and served as an expert in litigation against the tobacco companies. All other authors have no conflicts of interest to disclose.

Strengths

This pilot project is innovative for using social media communication tools that are culturally relevant and have already been adopted and that create statewide intervention access, thus promoting a scalable and sustainable approach that is tailored to the culture of AN people. The study is significant because it will advance research on population-specific treatments for ANs, an underserved, tobacco-use disparity group. If the pilot intervention is successful, we will have a blueprint to conduct a large randomized controlled efficacy trial.

Limitations

Despite our strong mixed method experimental design, there are some limitations to our approach. First of all, although FB adoption is high among AN people overall, those not using social media will not be reached by this intervention. It is possible that some age groups will be more represented in this study than others because of possible gender-based differences in FB use and engagement. Finally, from the study design, we will not be able to assess the relative contribution of each component to intervention efficacy. Furthermore, FB utilizes certain algorithms to notify their users about topics that may be of interest to them based on their usage. However, as this is a hidden and closed group, none of the page posts will be added to a user's news feed. Despite this, it is possible that exposure to Quitline-related ads or posts may be increased among those who participate in the group—an aspect to an FB intervention that the authors will have no control over. To explore these possible exposures, we will query intervention participants at the close of the FB group, a question about the perceptions about whether or not they received more than normal notifications, posts, or ads related to smoking, smoking cessation, or quitlines.

Conclusions

The described intervention has potential for promoting engagement with evidence-based smoking cessation treatment including AK's Tobacco Quitline and Tribal cessation programs statewide and holds promise for AN people because it is scalable and sustainable. It utilizes a popular channel of communication and an existing, evidence-based treatment that could be considered for other remote AN communities to enhance the reach of evidence-based tobacco cessation treatments.

Multimedia Appendix 1

Peer-review reports.

[\[PDF File \(Adobe PDF File\), 170 KB - resprot_v8i11e15155_app1.pdf\]](#)**References**

1. Jamal A, King BA, Neff LJ, Whitmill J, Babb SD, Graffunder CM. Current cigarette smoking among adults - United States, 2005-2015. *MMWR Morb Mortal Wkly Rep* 2016 Nov 11;65(44):1205-1211 [[FREE Full text](#)] [doi: [10.15585/mmwr.mm6544a2](https://doi.org/10.15585/mmwr.mm6544a2)] [Medline: [27832052](https://pubmed.ncbi.nlm.nih.gov/27832052/)]
2. Alaska DOHS(. Alaska Tobacco Facts. 2016. 2016. URL: http://dhss.alaska.gov/dph/Chronic/Documents/Tobacco/PDF/2016_AKTobaccoFacts.pdf [accessed 2017-04-30]
3. Espey DK, Jim MA, Cobb N, Bartholomew M, Becker T, Haverkamp D, et al. Leading causes of death and all-cause mortality in American Indians and Alaska Natives. *Am J Public Health* 2014 Jun;104(Suppl 3):S303-S311. [doi: [10.2105/AJPH.2013.301798](https://doi.org/10.2105/AJPH.2013.301798)] [Medline: [24754554](https://pubmed.ncbi.nlm.nih.gov/24754554/)]
4. Heron M. Deaths: leading causes for 2016. *Natl Vital Stat Rep* 2018 Jul;67(6):1-77 [[FREE Full text](#)] [Medline: [30248017](https://pubmed.ncbi.nlm.nih.gov/30248017/)]
5. Galloway JM. Cardiovascular health among American Indians and Alaska Natives: successes, challenges, and potentials. *Am J Prev Med* 2005 Dec;29(5):11-17. [doi: [10.1016/j.amepre.2005.07.023](https://doi.org/10.1016/j.amepre.2005.07.023)] [Medline: [16389120](https://pubmed.ncbi.nlm.nih.gov/16389120/)]
6. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health. Tobacco use among US racial/ethnic minority groups--African Americans, American Indians and Alaska natives, Asian Americans and Pacific islanders, Hispanics. A report of the surgeon general. Executive summary. *MMWR Recomm Rep* 1998 Oct 9;47(RR-18):v-xv, 1 [[FREE Full text](#)] [Medline: [9784089](https://pubmed.ncbi.nlm.nih.gov/9784089/)]
7. Passey M, Bonevski B. The importance of tobacco research focusing on marginalized groups. *Addiction* 2014 Jul;109(7):1049-1051. [doi: [10.1111/add.12548](https://doi.org/10.1111/add.12548)] [Medline: [24758261](https://pubmed.ncbi.nlm.nih.gov/24758261/)]
8. Healthy People. URL: <https://www.healthypeople.gov/> [accessed 2017-03-01]
9. Healthy Alaskans 2020. 2016. URL: <http://hss.state.ak.us/ha2020/> [accessed 2019-10-09]
10. Alaska DOL. Alaska's native population. *Alaska Economic Trends* 2013 Apr;33(4):1-19.
11. Lichtenstein E, Zhu S, Tedeschi GJ. Smoking cessation quitlines: an underrecognized intervention success story. *Am Psychol* 2010;65(4):252-261 [[FREE Full text](#)] [doi: [10.1037/a0018598](https://doi.org/10.1037/a0018598)] [Medline: [20455619](https://pubmed.ncbi.nlm.nih.gov/20455619/)]
12. Kaufman A, Augustson E, Davis K, Finney Rutten LJ. Awareness and use of tobacco quitlines: evidence from the Health Information National Trends Survey. *J Health Commun* 2010;15(Suppl 3):264-278 [[FREE Full text](#)] [doi: [10.1080/10810730.2010.526172](https://doi.org/10.1080/10810730.2010.526172)] [Medline: [21154098](https://pubmed.ncbi.nlm.nih.gov/21154098/)]
13. Ossip-Klein DJ, McIntosh S. Quitlines in North America: evidence base and applications. *Am J Med Sci* 2003 Oct;326(4):201-205. [doi: [10.1097/00000441-200310000-00010](https://doi.org/10.1097/00000441-200310000-00010)] [Medline: [14557735](https://pubmed.ncbi.nlm.nih.gov/14557735/)]
14. Fiore M, Jaen C, Baker T, Human Services, US Department of Health, Public Health Service. Treating Tobacco Use and Dependence - Quick Reference Guide for Clinicians: 2008 Update. Rockville, MD: U.S. Department of Health and Human Services. Public Health Service; 2008.
15. Zhu AZX, Binnington MJ, Renner CC, Lanier AP, Hatsukami DK, Stepanov I, et al. Alaska Native smokers and smokeless tobacco users with slower CYP2A6 activity have lower tobacco consumption, lower tobacco-specific nitrosamine exposure and lower tobacco-specific nitrosamine bioactivation. *Carcinogenesis* 2013 Jan;34(1):93-101 [[FREE Full text](#)] [doi: [10.1093/carcin/bgs306](https://doi.org/10.1093/carcin/bgs306)] [Medline: [23027621](https://pubmed.ncbi.nlm.nih.gov/23027621/)]
16. Patten CA, Windsor RA, Renner CC, Enoch C, Hochreiter A, Nevak C, et al. Feasibility of a tobacco cessation intervention for pregnant Alaska Native women. *Nicotine Tob Res* 2010 Feb;12(2):79-87 [[FREE Full text](#)] [doi: [10.1093/ntr/ntp180](https://doi.org/10.1093/ntr/ntp180)] [Medline: [20018946](https://pubmed.ncbi.nlm.nih.gov/20018946/)]
17. Patten CA, Fadahunsi O, Hanza MM, Smith CA, Decker PA, Boyer R, et al. Tobacco cessation treatment for Alaska native adolescents: group randomized pilot trial. *Nicotine Tob Res* 2014 Jun;16(6):836-845 [[FREE Full text](#)] [doi: [10.1093/ntr/ntu004](https://doi.org/10.1093/ntr/ntu004)] [Medline: [24532352](https://pubmed.ncbi.nlm.nih.gov/24532352/)]
18. Cobb NK, Graham AL, Byron MJ, Niaura RS, Abrams DB, Workshop Participants. Online social networks and smoking cessation: a scientific research agenda. *J Med Internet Res* 2011 Dec 19;13(4):e119 [[FREE Full text](#)] [doi: [10.2196/jmir.1911](https://doi.org/10.2196/jmir.1911)] [Medline: [22182518](https://pubmed.ncbi.nlm.nih.gov/22182518/)]
19. Hudson HE. Digital diversity: broadband and indigenous populations in Alaska. *J Inf Policy* 2011;1:378-393. [doi: [10.5325/jinfopoli.1.2011.0378](https://doi.org/10.5325/jinfopoli.1.2011.0378)]
20. Hudson HE. Institute of Social and Economic Research. 2012. Toward Universal Broadband in Rural Alaska - Part 1: An Analysis of Internet Use in Southwest Alaska Part 2: Literature Review. URL: http://www.iser.uaa.alaska.edu/Publications/2012_11-TERRA.pdf [accessed 2017-05-08]
21. Power JM, Bersamin A. The FASEB Journal. 2016. Exploring the potential for technology-based nutrition education for Alaska Native WIC recipients in rural southwest Alaska. URL: https://www.fasebj.org/doi/10.1096/fasebj.30.1_supplement.lb430 [accessed 2019-10-09]
22. Papale G, Caponnetto P. Social media: potential tool for smoking cessation. In: Palosa R, Caponnetto P, editors. *Advances in smoking cessation*. London, UK: Future Medicine Ltd; 2013:152-163.

23. Division of Cancer Control and Population Sciences. 2016. Tobacco Control Research Priorities for the Next Decade: Working Group Recommendations for 2016 - 2025. URL: <https://cancercontrol.cancer.gov/pdf/nci-tobacco-control-research-priorities-rpt-feb-2016.pdf> [accessed 2017-06-10]
24. Baskerville NB, Struik LL, Hammond D, Guindon GE, Norman CD, Whittaker R, et al. Effect of a mobile phone intervention on quitting smoking in a young adult population of smokers: randomized controlled trial study protocol. *JMIR Res Protoc* 2015 Jan 19;4(1):e10 [FREE Full text] [doi: [10.2196/resprot.3823](https://doi.org/10.2196/resprot.3823)] [Medline: [25599695](https://pubmed.ncbi.nlm.nih.gov/25599695/)]
25. Struik LL, Baskerville NB. The role of Facebook in Crush the Crave, a mobile- and social media-based smoking cessation intervention: qualitative framework analysis of posts. *J Med Internet Res* 2014 Jul 11;16(7):e170 [FREE Full text] [doi: [10.2196/jmir.3189](https://doi.org/10.2196/jmir.3189)] [Medline: [25016998](https://pubmed.ncbi.nlm.nih.gov/25016998/)]
26. Pechmann C, Pan L, Delucchi K, Lakon CM, Prochaska JJ. Development of a Twitter-based intervention for smoking cessation that encourages high-quality social media interactions via automessages. *J Med Internet Res* 2015 Feb 23;17(2):e50 [FREE Full text] [doi: [10.2196/jmir.3772](https://doi.org/10.2196/jmir.3772)] [Medline: [25707037](https://pubmed.ncbi.nlm.nih.gov/25707037/)]
27. Onezi HA, Khalifa M, El-Metwally A, Househ M. The impact of social media-based support groups on smoking relapse prevention in Saudi Arabia. *Comput Methods Programs Biomed* 2018 Jun;159:135-143. [doi: [10.1016/j.cmpb.2018.03.005](https://doi.org/10.1016/j.cmpb.2018.03.005)] [Medline: [29650308](https://pubmed.ncbi.nlm.nih.gov/29650308/)]
28. Haines-Saah RJ, Kelly MT, Oliffe JL, Bottorff JL. Picture Me Smokefree: a qualitative study using social media and digital photography to engage young adults in tobacco reduction and cessation. *J Med Internet Res* 2015 Jan 26;17(1):e27 [FREE Full text] [doi: [10.2196/jmir.4061](https://doi.org/10.2196/jmir.4061)] [Medline: [25624064](https://pubmed.ncbi.nlm.nih.gov/25624064/)]
29. Post SD, Taylor SC, Sanders AE, Goldfarb JM, Hunt YM, Augustson EM. If you build (and moderate) it, they will come: the Smokefree Women Facebook page. *J Natl Cancer Inst Monogr* 2013 Dec;2013(47):206-208 [FREE Full text] [doi: [10.1093/jncimonographs/igt019](https://doi.org/10.1093/jncimonographs/igt019)] [Medline: [24395993](https://pubmed.ncbi.nlm.nih.gov/24395993/)]
30. Kim SJ, Marsch LA, Brunette MF, Dallery J. Harnessing Facebook for smoking reduction and cessation interventions: Facebook user engagement and social support predict smoking reduction. *J Med Internet Res* 2017 May 23;19(5):e168 [FREE Full text] [doi: [10.2196/jmir.6681](https://doi.org/10.2196/jmir.6681)] [Medline: [28536096](https://pubmed.ncbi.nlm.nih.gov/28536096/)]
31. Davis RE, Resnicow K. The cultural variance framework for tailoring health messages. In: Cho H, editor. *Health Communication Message Design: Theory and Practice*. Thousand Oaks, CA: Sage Publications Inc; 2012:115-136.
32. Resnicow K, Braithwaite RL. Cultural sensitivity in public health. In: Braithwaite RL, Taylor SE, editors. *Health Issues in the Black Community*. Second Edition. San Francisco, CA: Jossey-Bass; 2001:516-542.
33. Renner CC, Patten CA, Enoch C, Petraitis J, Offord KP, Angstman S, et al. Focus groups of Y-K Delta Alaska Natives: attitudes toward tobacco use and tobacco dependence interventions. *Prev Med* 2004 Apr;38(4):421-431. [doi: [10.1016/j.ypmed.2003.11.005](https://doi.org/10.1016/j.ypmed.2003.11.005)] [Medline: [15020175](https://pubmed.ncbi.nlm.nih.gov/15020175/)]
34. Mohatt G, McDiarmid G, Montoya V. Societies, families, and change: the Alaskan example. In: Manson SM, Dinges NG, editors. *Behavioral Health Issues Among American Indians and Alaska Natives: Explorations on the Frontiers of the Biobehavioral Sciences*. American Indian and Alaska Native Mental Health Research, Monograph no. 1. CA: University of Colorado Health Sciences Center; 1988:325-365.
35. Wolsko C, Lardon C, Hopkins S, Ruppert E. Conceptions of wellness among the Yup'ik of the Yukon-Kuskokwim Delta: the vitality of social and natural connection. *Ethn Health* 2006 Nov;11(4):345-363. [doi: [10.1080/13557850600824005](https://doi.org/10.1080/13557850600824005)] [Medline: [17060033](https://pubmed.ncbi.nlm.nih.gov/17060033/)]
36. Barnhardt R, Oscar Kawagley A. Indigenous knowledge systems and Alaska native ways of knowing. *Anthropol Edu Quart* 2005;36(1):8-23 [FREE Full text] [doi: [10.1525/aeq.2005.36.1.008](https://doi.org/10.1525/aeq.2005.36.1.008)]
37. Carmack E, Macdonald R. Water and ice-related phenomena in the Coastal Region of the Beaufort Sea: some parallels between Native experience and western science. *Arctic* 2008;61(3):265-280 [FREE Full text] [doi: [10.14430/arctic24](https://doi.org/10.14430/arctic24)]
38. Cochran PA, Marshall CA, Garcia-Downing C, Kendall E, Cook D, McCubbin L, et al. Indigenous ways of knowing: implications for participatory research and community. *Am J Public Health* 2008 Jan;98(1):22-27. [doi: [10.2105/AJPH.2006.093641](https://doi.org/10.2105/AJPH.2006.093641)] [Medline: [18048800](https://pubmed.ncbi.nlm.nih.gov/18048800/)]
39. National Cancer Institute. 2004. Making Health Communication Programs Work. URL: <https://www.cancer.gov/publications/health-communication/pink-book.pdf> [accessed 2017-06-01]
40. Centers for Disease Control and Prevention. 2016. CDC's Guide to Writing for Social Media. URL: <https://www.cdc.gov/socialmedia/tools/guidelines/pdf/GuidetoWritingforSocialMedia.pdf> [accessed 2017-05-08]
41. Mummah SA, Robinson TN, King AC, Gardner CD, Sutton S. IDEAS (Integrate, Design, Assess, and Share): a framework and toolkit of strategies for the development of more effective digital interventions to change health behavior. *J Med Internet Res* 2016 Dec 16;18(12):e317 [FREE Full text] [doi: [10.2196/jmir.5927](https://doi.org/10.2196/jmir.5927)] [Medline: [27986647](https://pubmed.ncbi.nlm.nih.gov/27986647/)]
42. Pagoto S, Bennett GG. How behavioral science can advance digital health. *Transl Behav Med* 2013 Sep;3(3):271-276 [FREE Full text] [doi: [10.1007/s13142-013-0234-z](https://doi.org/10.1007/s13142-013-0234-z)] [Medline: [24073178](https://pubmed.ncbi.nlm.nih.gov/24073178/)]
43. Rounsaville BJ, Carroll KM, Onken LS. A stage model of behavioral therapies research: getting started and moving on from stage I. *Clin Psychol-Sci and Pr* 2001;8(2):133-142 [FREE Full text] [doi: [10.1093/clipsy.8.2.133](https://doi.org/10.1093/clipsy.8.2.133)]
44. McAfee T, Davis KC, Alexander RL, Pechacek TF, Bunnell R. Effect of the first federally funded US antismoking national media campaign. *Lancet* 2013 Dec 14;382(9909):2003-2011. [doi: [10.1016/S0140-6736\(13\)61686-4](https://doi.org/10.1016/S0140-6736(13)61686-4)] [Medline: [24029166](https://pubmed.ncbi.nlm.nih.gov/24029166/)]

45. Centers for Disease Control and Prevention (CDC). Impact of a national tobacco education campaign on weekly numbers of quitline calls and website visitors--United States, March 4-June 23, 2013. *MMWR Morb Mortal Wkly Rep* 2013 Sep 20;62(37):763-767 [FREE Full text] [Medline: 24048152]
46. Rigotti NA, Wakefield M. Real people, real stories: a new mass media campaign that could help smokers quit. *Ann Intern Med* 2012 Dec 18;157(12):907-909. [doi: 10.7326/0003-4819-156-1-201201010-00541] [Medline: 23007853]
47. Cueva M, Kuhnley R, Revels L, Schoenberg NE, Dignan M. Digital storytelling: a tool for health promotion and cancer awareness in rural Alaskan communities. *Int J Circumpolar Health* 2015;74:28781 [FREE Full text] [doi: 10.3402/ijch.v74.28781] [Medline: 26343881]
48. Cueva M, Kuhnley R, Revels L, Schoenberg NE, Lanier A, Dignan M. Engaging elements of cancer-related digital stories in Alaska. *J Cancer Educ* 2016 Sep;31(3):500-505 [FREE Full text] [doi: 10.1007/s13187-015-0826-z] [Medline: 25865400]
49. Cueva M, Kuhnley R, Revels LJ, Cueva K, Dignan M, Lanier AP. Bridging storytelling traditions with digital technology. *Int J Circumpolar Health* 2013;72 [FREE Full text] [doi: 10.3402/ijch.v72i0.20717] [Medline: 23984267]
50. Gubrium A. Digital storytelling: an emergent method for health promotion research and practice. *Health Promot Pract* 2009 Apr;10(2):186-191. [doi: 10.1177/1524839909332600] [Medline: 19372280]
51. Kreuter MW, Green MC, Cappella JN, Slater MD, Wise ME, Storey D, et al. Narrative communication in cancer prevention and control: a framework to guide research and application. *Ann Behav Med* 2007 Jun;33(3):221-235. [doi: 10.1007/bf02879904] [Medline: 17600449]
52. Dohan D, Garrett SB, Rendle KA, Halley M, Abramson C. The importance of integrating narrative into health care decision making. *Health Aff (Millwood)* 2016 Apr;35(4):720-725. [doi: 10.1377/hlthaff.2015.1373] [Medline: 27044974]
53. Koller KR, Flanagan CA, Day GE, Thomas TK, Smith CA, Wolfe AW, et al. Developing a biomarker feedback intervention to motivate smoking cessation during pregnancy: phase II MAW study. *Nicotine Tob Res* 2017 Aug 1;19(8):930-936 [FREE Full text] [doi: 10.1093/ntr/ntw330] [Medline: 28003506]
54. Patten C, Lando H, Resnicow K, Decker P, Smith C, Hanza M, et al. Developing health communication messaging for a social marketing campaign to reduce tobacco use in pregnancy among Alaska Native women. *J Commun Healthc* 2018;11(4):252-262 [FREE Full text] [doi: 10.1080/17538068.2018.1495929] [Medline: 31548863]
55. Ramo DE, Liu H, Prochaska JJ. A mixed-methods study of young adults' receptivity to using Facebook for smoking cessation: if you build it, will they come? *Am J Health Promot* 2015;29(4):e126-e135 [FREE Full text] [doi: 10.4278/ajhp.130326-QUAL-128] [Medline: 24575728]
56. Ploderer B, Smith W, Howard S, Pearce J, Borland R. Patterns of Support in an Online Community for Smoking Cessation. In: *Proceedings of the 6th International Conference on Communities and Technologies*. 2013 Presented at: C&T'13; June 29-July 2, 2013; Munich, Germany p. 26-35. [doi: 10.1145/2482991.2482992]
57. Ramo DE, Rodriguez TM, Chavez K, Sommer MJ, Prochaska JJ. Facebook recruitment of young adult smokers for a cessation trial: methods, metrics, and lessons learned. *Internet Interv* 2014 Apr;1(2):58-64 [FREE Full text] [doi: 10.1016/j.invent.2014.05.001] [Medline: 25045624]
58. Topolovec-Vranic J, Natarajan K. The use of social media in recruitment for medical research studies: a scoping review. *J Med Internet Res* 2016 Nov 7;18(11):e286 [FREE Full text] [doi: 10.2196/jmir.5698] [Medline: 27821383]
59. Fortune R. Historical notes on the introduction of tobacco into Alaska. *Alaska Med* 1996;38(1):3-7. [Medline: 8936092]
60. United States Census Bureau. 2015. American Community Survey. URL: <https://www.census.gov/programs-surveys/acs.html> [accessed 2017-03-31]
61. Pechmann C, Delucchi K, Lakon CM, Prochaska JJ. Randomised controlled trial evaluation of Tweet2Quit: a social network quit-smoking intervention. *Tob Control* 2017 Mar;26(2):188-194 [FREE Full text] [doi: 10.1136/tobaccocontrol-2015-052768] [Medline: 26928205]
62. Benowitz NL, Renner CC, Lanier AP, Tyndale RF, Hatsukami DK, Lindgren B, et al. Exposure to nicotine and carcinogens among Southwestern Alaskan Native cigarette smokers and smokeless tobacco users. *Cancer Epidemiol Biomarkers Prev* 2012 Jun;21(6):934-942 [FREE Full text] [doi: 10.1158/1055-9965.EPI-11-1178] [Medline: 22490317]
63. Pagoto S, Waring ME, May CN, Ding EY, Kunz WH, Hayes R, et al. Adapting behavioral interventions for social media delivery. *J Med Internet Res* 2016 Jan 29;18(1):e24 [FREE Full text] [doi: 10.2196/jmir.5086] [Medline: 26825969]
64. Biener L, Abrams DB. The Contemplation Ladder: validation of a measure of readiness to consider smoking cessation. *Health Psychol* 1991;10(5):360-365. [doi: 10.1037/0278-6133.10.5.360] [Medline: 1935872]
65. Baker TB, Gustafson DH, Shah D. How can research keep up with eHealth? Ten strategies for increasing the timeliness and usefulness of eHealth research. *J Med Internet Res* 2014 Feb 19;16(2):e36 [FREE Full text] [doi: 10.2196/jmir.2925] [Medline: 24554442]
66. Fagerström K. Determinants of tobacco use and renaming the FTND to the Fagerstrom Test for Cigarette Dependence. *Nicotine Tob Res* 2012 Jan;14(1):75-78. [doi: 10.1093/ntr/ntn137] [Medline: 22025545]
67. Heatherton TF, Kozlowski LT, Frecker RC, Fagerström KO. The Fagerström Test for Nicotine Dependence: a revision of the Fagerström Tolerance Questionnaire. *Br J Addict* 1991 Sep;86(9):1119-1127. [doi: 10.1111/j.1360-0443.1991.tb01879.x] [Medline: 1932883]
68. Patton MQ. *Qualitative Research & Evaluation Methods: Integrating Theory And Practice*. Fourth Edition. Thousand Oaks, CA: Sage Publications Inc; 2015.

69. Krueger RA, Casey MA. Focus Groups: A Practical Guide for Applied Research. Fifth Edition. Thousand Oaks, CA: Sage Publications Inc; 2014.
70. Krippendorff K. Content Analysis: An Introduction To Its Methodology. Third Edition. Thousand Oaks, CA: Sage Publications Inc; 2013.
71. QSR International. 2015. NVivo Qualitative Data Analysis Software Version 10. URL: <https://www.qsrinternational.com/nvivo/home> [accessed 2019-10-09]
72. Davis KC, Duke J, Shafer P, Patel D, Rodes R, Beistle D. Perceived effectiveness of antismoking ads and association with quit attempts among smokers: evidence from the tips from former smokers campaign. *Health Commun* 2017 Aug;32(8):931-938. [doi: [10.1080/10410236.2016.1196413](https://doi.org/10.1080/10410236.2016.1196413)] [Medline: [27435919](https://pubmed.ncbi.nlm.nih.gov/27435919/)]
73. Biener L. Adult and youth response to the Massachusetts anti-tobacco television campaign. *J Public Health Manag Pract* 2000 May;6(3):40-44. [doi: [10.1097/00124784-200006030-00007](https://doi.org/10.1097/00124784-200006030-00007)] [Medline: [10848481](https://pubmed.ncbi.nlm.nih.gov/10848481/)]
74. Ramo DE, Thrul J, Delucchi KL, Ling PM, Hall SM, Prochaska JJ. The Tobacco Status Project (TSP): Study protocol for a randomized controlled trial of a Facebook smoking cessation intervention for young adults. *BMC Public Health* 2015 Sep 15;15:897 [FREE Full text] [doi: [10.1186/s12889-015-2217-0](https://doi.org/10.1186/s12889-015-2217-0)] [Medline: [26374203](https://pubmed.ncbi.nlm.nih.gov/26374203/)]
75. Ramo DE, Thrul J, Chavez K, Delucchi KL, Prochaska JJ. Feasibility and quit rates of the tobacco status project: a Facebook smoking cessation intervention for young adults. *J Med Internet Res* 2015 Dec 31;17(12):e291 [FREE Full text] [doi: [10.2196/jmir.5209](https://doi.org/10.2196/jmir.5209)] [Medline: [26721211](https://pubmed.ncbi.nlm.nih.gov/26721211/)]
76. Lund AM. Measuring usability with the USE questionnaire. *Usability Interface* 2001;8(2):3-6 [FREE Full text]
77. Kraemer HC, Kupfer DJ. Size of treatment effects and their importance to clinical research and practice. *Biol Psychiatry* 2006 Jun 1;59(11):990-996. [doi: [10.1016/j.biopsych.2005.09.014](https://doi.org/10.1016/j.biopsych.2005.09.014)] [Medline: [16368078](https://pubmed.ncbi.nlm.nih.gov/16368078/)]
78. Redwood D, Lanier AP, Renner C, Smith J, Tom-Orme L, Slattery ML. Differences in cigarette and smokeless tobacco use among American Indian and Alaska Native people living in Alaska and the Southwest United States. *Nicotine Tob Res* 2010 Jul;12(7):791-796 [FREE Full text] [doi: [10.1093/ntr/ntq087](https://doi.org/10.1093/ntr/ntq087)] [Medline: [20525781](https://pubmed.ncbi.nlm.nih.gov/20525781/)]
79. Smith JJ, Ferucci ED, Dillard DA, Lanier AP. Tobacco use among Alaska Native people in the EARTH study. *Nicotine Tob Res* 2010 Aug;12(8):839-844 [FREE Full text] [doi: [10.1093/ntr/ntq091](https://doi.org/10.1093/ntr/ntq091)] [Medline: [20547558](https://pubmed.ncbi.nlm.nih.gov/20547558/)]
80. Clark MS, Ouellette R, Powell MC, Milberg S. Recipient's mood, relationship type, and helping. *J Pers Soc Psychol* 1987 Jul;53(1):94-103. [doi: [10.1037//0022-3514.53.1.94](https://doi.org/10.1037//0022-3514.53.1.94)] [Medline: [3612495](https://pubmed.ncbi.nlm.nih.gov/3612495/)]
81. Cohen S, Lemay EP. Why would social networks be linked to affect and health practices? *Health Psychol* 2007 Jul;26(4):410-417. [doi: [10.1037/0278-6133.26.4.410](https://doi.org/10.1037/0278-6133.26.4.410)] [Medline: [17605560](https://pubmed.ncbi.nlm.nih.gov/17605560/)]
82. Rubin DB. Multiple Imputation for Nonresponse in Surveys. Hoboken, NJ: John Wiley & Sons; 2004.
83. Schafer J. Analysis of Incomplete Multivariate Data. Boca Raton, FL: CRC Press; 1997.
84. Schafer JL. Multiple imputation: a primer. *Stat Methods Med Res* 1999 Mar;8(1):3-15. [doi: [10.1177/096228029900800102](https://doi.org/10.1177/096228029900800102)] [Medline: [10347857](https://pubmed.ncbi.nlm.nih.gov/10347857/)]
85. MacKinnon DP. Introduction to Statistical Mediation Analysis. First Edition. New York, NY: Routledge: Taylor & Francis Group; 2008.
86. MacKinnon DP, Fairchild AJ, Fritz MS. Mediation analysis. *Annu Rev Psychol* 2007;58:593-614 [FREE Full text] [doi: [10.1146/annurev.psych.58.110405.085542](https://doi.org/10.1146/annurev.psych.58.110405.085542)] [Medline: [16968208](https://pubmed.ncbi.nlm.nih.gov/16968208/)]
87. Smith PH, Bessette AJ, Weinberger AH, Sheffer CE, McKee SA. Sex/gender differences in smoking cessation: A review. *Prev Med* 2016 Nov;92:135-140 [FREE Full text] [doi: [10.1016/j.ypmed.2016.07.013](https://doi.org/10.1016/j.ypmed.2016.07.013)] [Medline: [27471021](https://pubmed.ncbi.nlm.nih.gov/27471021/)]

Abbreviations

- AI:** American Indian
- AK:** Alaska
- AN:** Alaska Native
- ANMC:** Alaska Native Medical Center
- ANTHC:** The Alaska Native Tribal Health Consortium
- CDC:** Centers for Disease Control
- COS:** Communal Orientation Scale
- FB:** Facebook
- NIDA:** National Institute on Drug Abuse
- NRT:** nicotine replacement therapy
- PE:** perceived effectiveness

Edited by G Eysenbach; submitted 02.07.19; peer-reviewed by N Baskerville, L Akers; comments to author 28.08.19; accepted 05.09.19; published 22.11.19.

Please cite as:

Sinicrope PS, Koller KR, Prochaska JJ, Hughes CA, Bock MJ, Decker PA, Flanagan CA, Merritt ZT, Meade CD, Willetto AL, Resnicow K, Thomas TK, Patten CA

Social Media Intervention to Promote Smoking Treatment Utilization and Cessation Among Alaska Native People Who Smoke: Protocol for the Connecting Alaska Native People to Quit Smoking (CAN Quit) Pilot Study

JMIR Res Protoc 2019;8(11):e15155

URL: <http://www.researchprotocols.org/2019/11/e15155/>

doi: [10.2196/15155](https://doi.org/10.2196/15155)

PMID: [31755867](https://pubmed.ncbi.nlm.nih.gov/31755867/)

©Pamela S Sinicrope Sinicrope, Kathryn R Koller, Judith J Prochaska, Christine A Hughes, Martha J Bock, Paul A Decker, Christie A Flanagan, Zoe T Merritt, Crystal D Meade, Abbie L Willetto, Ken Resnicow, Timothy K Thomas, Christi A Patten. Originally published in JMIR Research Protocols (<http://www.researchprotocols.org>), 22.11.2019. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in JMIR Research Protocols, is properly cited. The complete bibliographic information, a link to the original publication on <http://www.researchprotocols.org>, as well as this copyright and license information must be included.

Protocol

Delivering a Post-Partum Weight Loss Intervention via Facebook or In-Person Groups: Protocol for a Randomized Feasibility Pilot Trial

Molly E Waring¹, PhD; Brooke A Libby¹, MPH; Tiffany A Moore Simas^{2,3,4,5}, MPH, MEd, MD; Madison L Bracken^{1,6}, MA; Jessica L Bibeau¹, MA; Valeria Herrera¹, BS, RD; Justin Wang⁷, PhD; Sherry L Pagoto¹, PhD

¹Department of Allied Health Sciences, UConn Center for mHealth and Social Media, University of Connecticut, Storrs, CT, United States

²Department of Obstetrics and Gynecology, University of Massachusetts Medical School/UMass Memorial Health Care, Worcester, MA, United States

³Department of Pediatrics, University of Massachusetts Medical School/UMass Memorial Health Care, Worcester, MA, United States

⁴Department of Psychiatry, University of Massachusetts Medical School/UMass Memorial Health Care, Worcester, MA, United States

⁵Department of Population and Quantitative Health Sciences, University of Massachusetts Medical School, Worcester, MA, United States

⁶Department of Psychological and Brain Sciences, University of Massachusetts, Amherst, MA, United States

⁷Social Sciences Department, Community College of Rhode Island, Warwick, RI, United States

Corresponding Author:

Molly E Waring, PhD

Department of Allied Health Sciences

UConn Center for mHealth and Social Media

University of Connecticut

358 Mansfield Road, Unit 1101

Storrs, CT, 06269

United States

Phone: 1 8604861446

Email: molly.waring@uconn.edu

Abstract

Background: Postpartum weight retention contributes to long-term weight gain and obesity for many women. Lifestyle interventions with numerous visits are logistically challenging for many postpartum women. Delivering a lifestyle intervention via social media may overcome logistic challenges to participation in in-person weight loss programs.

Objective: The objective of this study is to conduct a randomized feasibility pilot trial of a 6-month postpartum weight loss intervention delivered via Facebook or in-person groups with 72 postpartum women with overweight or obesity.

Methods: Women with overweight or obesity who are 8 weeks to 12 months postpartum (N=72) will be recruited from the Hartford, Connecticut community. Eligible participants must also own an iPhone or Android smartphone and be an active Facebook user. Participants will receive a 6-month postpartum weight loss intervention based on the Diabetes Prevention Program lifestyle intervention and adapted for postpartum women. Participants will be randomized to receive the intervention via a private Facebook group or in-person group meetings. Assessments will occur at baseline, weekly during the intervention, at 6 months (at the end of the intervention), and at 12 months. Primary feasibility outcomes are recruitment, sustained participation, contamination, retention, and feasibility of assessment procedures including measurement of costs to deliver and receive the intervention. We will describe 6- and 12-month weight loss as an exploratory outcome.

Results: Recruitment began in September 2018. The first wave of the intervention began in February 2019, and the second wave of the intervention is expected to begin in fall 2019. We anticipate completing follow-up assessments in fall 2020, and results will be analyzed at that time.

Conclusions: Results will inform the design of a large randomized controlled trial to assess whether delivering a postpartum weight loss intervention via Facebook is noninferior for weight loss and more cost-effective than delivering the intervention via traditional in-person groups.

International Registered Report Identifier (IRRID): DERR1-10.2196/15530

(*JMIR Res Protoc* 2019;8(11):e15530) doi:[10.2196/15530](https://doi.org/10.2196/15530)

KEYWORDS

postpartum period; weight loss; social media; pilot study

Introduction

Postpartum weight retention contributes to long-term weight gain and obesity for many women [1-3]. Although average postpartum weight retention ranges from 0.5 kg to 3 kg [2,4,5], it is variable [6,7], with as many as 50% of women retaining 5 kg or more [2,4,5]. In addition to failing to lose weight gained during pregnancy, some women gain weight in the year following childbirth [8]. Having parents who are obese, especially a mother, greatly increases a child's risk of becoming obese [9,10]. The postpartum period provides a critical period for obesity intervention [11]. Although lifestyle interventions have shown to be modestly efficacious for postpartum weight loss in randomized controlled trials [12,13], interventions with numerous in-person sessions are logistically challenging for many postpartum women [14], adding yet another strain on women at an already stressful and demanding period of life [14-20]. Treatment models for weight loss that fit into the busy lives of new moms are needed [21].

Facebook may be an effective platform for delivering evidence-based weight loss programming to postpartum women. Facebook is currently the most popular online social network [22], used by 81% of online moms [23]. Overall, 70% of Facebook users engage daily, including 43% multiple times per day [24], for at least 50 min a day on average [25]. Many women seek support about health and parenting from their Facebook network [23,26]. Facebook can connect postpartum women seeking to lose weight with each other, even across wide geographic regions. Moms, especially first-time moms, often look to other women for advice and support [26-29].

Postpartum weight loss interventions that deliver at least some content via Facebook appear promising [30-32], and additional research is ongoing [33]. We developed a postpartum weight loss intervention based on the Diabetes Prevention Program (DPP) lifestyle intervention, tailored to needs of postpartum women and for delivery by a trained weight loss counselor via a private Facebook group [30]. Our pilot work demonstrated that (1) this approach is feasible and acceptable; (2) we were able to engage participants; and (3) on average, participants achieved meaningful weight loss (average 12-week weight loss was 4.8% [SD 4.2%]; 58% lost $\geq 5\%$) [30]. Although delivering intervention content via Facebook offers many advantages, we have no reason to believe that it will be more efficacious than a traditionally delivered intervention (ie, via in-person group sessions). Instead, we hypothesize that in a large randomized trial, delivery via Facebook will be not inferior for weight loss and more cost-effective than in-person delivery. Our previous single-arm pilot study [30] did not allow us to explore the feasibility of (1) recruitment rates under conditions of randomization into online versus in-person conditions; (2) sustained participation in the Facebook-delivered intervention after 12 weeks; (3) contamination in both conditions; and (4) the feasibility of assessment procedures, particularly the measurement of costs associated with delivering and receiving the intervention. Answers to these feasibility questions are

needed before conducting a large-scale noninferiority trial ([Multimedia Appendix 1](#)).

The aim of this study is to conduct a randomized feasibility pilot trial of a 6-month postpartum weight loss intervention delivered via a private Facebook group or in-person groups with 72 postpartum women with overweight or obesity to answer these feasibility questions and finalize the design of the subsequent noninferiority trial. We will examine the feasibility of recruitment, sustained participation, contamination, retention, and assessment procedures in both conditions. We will describe weight loss as an exploratory outcome. Results will provide critical preliminary data to finalize the design of a subsequent noninferiority trial.

Methods**Study Design**

The study is a randomized feasibility pilot trial comparing delivery of a postpartum weight loss intervention via Facebook or in-person groups among women with overweight or obesity. The trial will be conducted in 2 waves. In each wave, participants will be randomized in a 1:1 ratio to either the Facebook-delivered or in-person intervention condition. The University of Connecticut institutional review board (IRB) approved this study.

Study Population

We will recruit 72 adult women with overweight or obesity who are 8 weeks to 12 months postpartum at the time of enrollment. To be eligible to participate in this study, women will have to meet the following inclusion criteria: aged 18 years or older; body mass index ≥ 25 kg/m² per measured height and weight at baseline; either own a scale or be willing to be provided one if needed; comfortable reading and writing in English; own an Android or iPhone smartphone; active Facebook user (defined as daily Facebook use and posts or comments at least weekly over the past 4 weeks); clearance from their primary care provider or obstetrician/gynecologist; willing to participate in either treatment condition (Facebook or in-person); available to attend in-person meetings over the 6-month study period in Hartford, Connecticut; less than 45 min travel time to intervention meetings; and willing and able to provide informed consent.

Participants who meet the following criteria will be excluded: currently pregnant; plans to become pregnant during the study period; current participation in a clinical weight loss program (online or in-person); diagnosed with type 1 or type 2 diabetes as self-reported or reported by their health care provider; medical conditions or medications affecting weight; incapable of walking a quarter of a mile unaided without stopping; pain that prevents engagement in exercise; previous bariatric surgery; planned surgery during the study period; plans to move out of the area during the study period; high depressive symptoms or suicidal ideation (a total score of 12 or higher or positive response on question number 10 on the Edinburgh Postnatal Depression

Scale [EPDS] [34]); positive screen for binge eating disorder (BED) [35]; or failure to complete baseline survey, orientation webinar, or prerandomization survey. Additionally, key study personnel; spouses, dependents, or relatives of key study personnel; University of Connecticut employees who report to key study personnel; and University of Connecticut students taught by key study personnel will be excluded from participation.

Recruitment

We will recruit postpartum women from the Hartford, Connecticut community. We will distribute flyers in local obstetric or pediatric clinics or practices; Special Supplemental Nutrition Program for Women, Infants, and Children offices; community organizations; and community venues and events. We will also recruit by posting study advertisements on ResearchMatch, Craigslist, and online social networks, including Facebook, Instagram, and Twitter. We will identify local Facebook groups relevant to postpartum women (eg, parenting groups and general community groups such as buy/sell groups) and contact the group administrators for permission to post our recruitment messages in their groups. We will also use paid advertisements on Facebook and Instagram. We will submit announcements to be included in email distribution lists at the University of Connecticut and UConn Health. Recruitment messages will include the study team's email address and phone number and ask interested individuals to contact the team for more information about the study. If a woman contacts the study team by email, we will reply and ask her to provide her phone number or call the team. We will attempt to contact interested individuals' phone 3 times, with a final contact via email. Research staff will screen potential participants for eligibility via phone.

In addition to recruiting postpartum women, we will post recruitment messages online targeting pregnant women whose expected due dates put them in the eligible postpartum window (eg, "are you pregnant and due before June 2019?"). Interested individuals will be asked to complete a brief online form that includes their name, contact information, and expected due date. Approximately 2 months after their expected due date, we will contact them via email or phone about their interest in the study and, if interested, screen them for eligibility.

Baseline Assessment

A 30- to 45-min in-person baseline assessment will include provision of informed consent, measurement of height and weight, completion of a contact information sheet, and screenings for elevated depressive symptoms and BED. Study personnel will also help participants download the MyFitnessPal app and provide instruction on how to use this app to track their diet and activity. Study personnel will provide instructions on how to locate Facebook app usage data within the Facebook app and how to locate Facebook app usage data using the battery settings (iPhone users) or help participants download and use a free app to track time on Facebook (Android users).

After the baseline visit, staff will email participants a link to complete a survey via Research Electronic Data Capture (REDCap) [36]. The survey is designed to take 30 min to

complete and includes measures of demographics; reproductive history [37], including gestational weight gain during the index pregnancy [38]; previous postpartum weight loss attempts [39]; quality of life [40,41]; infant feeding [42,43]; social support for diet and physical activity changes [44]; and social media use [45]. Participants will also report their Facebook use habits, including what device(s) they used to access Facebook, what proportion of use was from their smartphone (vs other devices), and the extent to which other people used Facebook on their phone [46].

We will email participants a US \$20 gift card after they have completed the baseline visit and online survey. Following the baseline assessment, research staff will fax the medical clearance form to participants' primary care provider or obstetrician/gynecologist.

Orientation Webinar and Prerandomization Survey

Next, participants will complete a 60-min orientation webinar. The purpose of the webinar is to educate participants about what research is, review study procedures, review the importance of participation by enrolled participants, and engage them in a discussion about the advantages and challenges of participating in each treatment condition, which previous research has suggested may help participants have more realistic expectations of study participation [47], which may lead to higher retention. Following the orientation webinar, we will email participants a short online survey that includes completion of a randomization agreement, report of app-tracked time on Facebook over the past 7 days, and report of their Facebook use habits, including what device(s) they used to access Facebook, what proportion of use was from their smartphone (vs other devices), and the extent to which other people used Facebook on their phone [46].

Randomization

Only participants who have completed the telephone screening, baseline assessments (visit and survey), orientation webinar, and prerandomization survey and for whom medical clearance has been obtained will be randomized. Randomization will occur after completing recruitment for the wave, approximately a week before the start of the intervention. We will randomize participants in a 1:1 ratio to the Facebook and in-person conditions in randomly permuted blocks of size 4 and 6. Randomization will be stratified by weeks postpartum at enrollment (8 weeks to <6 months vs 6-12 months postpartum) and smartphone type (iPhone vs Android). We will stratify randomization by months postpartum because in the absence of intervention, weight change varies across the postpartum period [48,49]. We will stratify randomization by smartphone type to ensure balance in methods for assessing time on Facebook because available tools differed by phone type during the design phase, and app or phone operating system updates may impact measurement unequally.

Intervention

Over 6 months (25 weeks), a trained weight loss counselor will deliver a lifestyle intervention based on the DPP lifestyle intervention [50] and adapted for the needs of postpartum women. The DPP lifestyle intervention is a gold standard

lifestyle intervention with ample efficacy data for weight loss [51,52]. In addition, the DPP lifestyle intervention has been successfully translated to numerous settings and populations [53], including primary care via the internet [54] and the postpartum period [55-57]. The DPP curriculum includes behavioral strategies such as self-monitoring, stimulus control, problem solving, social support, environmental restructuring, and relapse prevention [50]. The interventions will be delivered by weight loss counselors with backgrounds in nutrition/dietetics who have completed National DPP training and training by a licensed clinical psychologist with extensive experience using the DPP in our specific intervention protocols. Weight loss counselors will be supervised by a licensed clinical psychologist with extensive experience in developing and delivering in-person and online lifestyle interventions.

The intervention goals are 5% to 10% weight loss and increasing physical activity to 150 min per week of moderate-intensity physical activity. Participants will receive calorie and physical activity goals to help them achieve a healthy weight loss of 1 to 2 pounds per week. Calorie goals will account for breastfeeding, as appropriate [58]. Intervention content, individualized calorie goals, tools for self-monitoring, and access to a Pinterest board of existing online resources will be consistent across conditions; the 2 treatment conditions differ only in delivery modality.

We include intervention content specific to the needs and challenges of postpartum women, including information about energy intake needs while breastfeeding [59]; adjusted calorie goals for women who are breastfeeding [60]; quick, easy recipe ideas with emphasis on foods that appeal to children [55]; gradually increasing physical activity goals for women who were inactive during pregnancy [61]; physical activity ideas that engage infant/children; discussion around feelings of guilt for taking time away from family to exercise; discussion of barriers common to postpartum women [14-20]; managing stress related to parenting [62]; tips for getting baby on a regular sleep schedule; and partner communication skills to help to mobilize social support and assistance [63].

We will ask all participants to use MyFitnessPal to track their energy intake, physical activity, and weight. We will provide participants instructions for downloading the MyFitnessPal app and setting up their account, including setting a passcode to allow the weight loss counselor to review their diet/activity records, and tips for general use. Staff will be available to answer questions about using the website or mobile app. The weight loss counselor will email participants in both treatment conditions feedback on data entered into MyFitnessPal weekly or every 2 weeks (corresponding to the frequency of intervention sessions in the in-person condition). Participants will be

withdrawn from the intervention if they report becoming pregnant to the weight loss counselor or study staff.

In-Person Condition

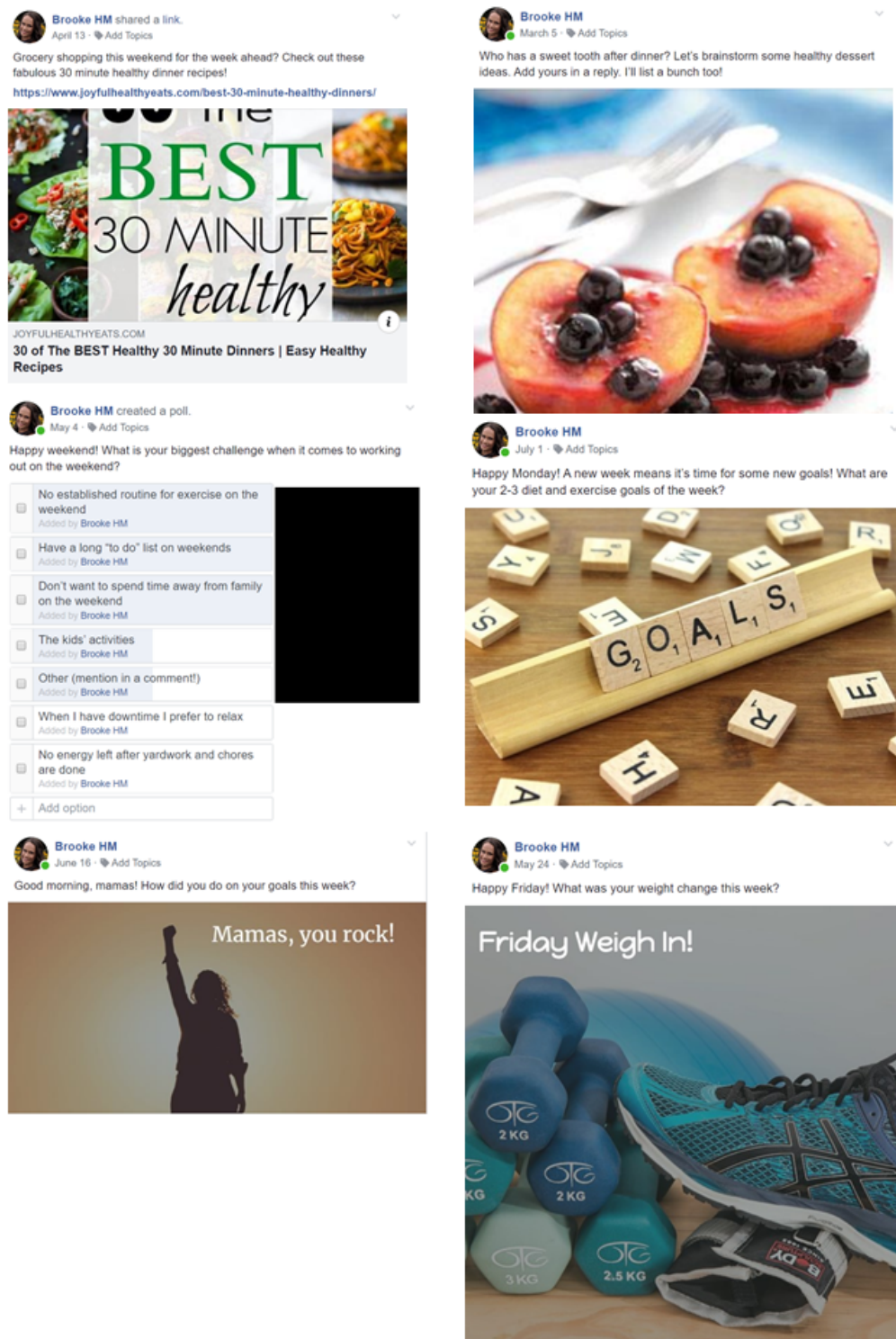
In the in-person condition, the intervention will be delivered via weekly 90-min group meetings for the first 15 weeks and then every other week in weeks 16 to 25. Intervention materials will be provided via handouts. The weight loss counselor will facilitate discussions about weekly topics. During recruitment and baseline procedures, participants will be told that they may bring their babies to in-person intervention meetings but that older children are not allowed to attend. Participants will receive up to US \$5 to reimburse them for parking or bus fare.

Facebook Condition

The intervention will be delivered via a private (*secret*) Facebook group. *Secret* Facebook groups are restricted such that group membership is by invitation only, membership in the group does not appear in member profiles or search results, and only members can see content posted within the group [64]. During consent and the orientation webinar, study staff will outline how participants are encouraged to engage with each other (eg, read intervention posts and respond to the weight loss counselor and other participants daily), different ways to access intervention posts (eg, view in news feed and visit the group directly), and encourage participants to adjust their settings to get notifications of new posts in the group. On the first day of the intervention, the weight loss counselor posts a reminder of the format of the intervention, including encouraging participants to post at least one update a week.

We will schedule daily intervention posts to be posted from the weight loss counselor's account using the Facebook post scheduling tool. There will be 2 posts daily for the first 15 weeks, and 1 post daily for weeks 16 to 25, corresponding to the decrease in contact in the in-person condition. Intervention posts have been developed based on our previous research [30,65-67] to cover the intervention content in that intervention module of the DPP lifestyle intervention through posts that provide information or resources, solicit sharing of thoughts or experiences or challenges related to the topic of the week, ask participants to set goals (posted on Mondays), ask participants to report their progress toward these goals (posted on Sundays), and ask participants to report their weekly weight change (posted on Fridays). Sample intervention posts are shown in Figure 1. The weight loss counselor will facilitate discussions about weekly topics by engaging participants in problem solving, assisting them in setting SMART goals (ie, goals that are Specific, Measurable, Attainable, Relevant, Time-Based), providing constructive feedback, sharing resources, providing positive reinforcement, and answering questions.

Figure 1. Sample intervention posts from the Facebook-delivered postpartum weight loss intervention by post type. For the middle post on the left, participants' responses have been obscured with a black rectangle to protect participants' confidentiality.



Assessments

Weekly Surveys

Weekly during the intervention, participants in both treatment conditions will complete a brief (5-min) online survey to report current weight; app-tracked time on Facebook over the past 7 days; and their Facebook use habits, including what device(s) they used to access Facebook, what proportion of use was from

their smartphone (vs other devices), and the extent to which other people used Facebook on their phone [46].

Six-Month Follow-Up Assessment

At 6 months, immediately following the intervention, participants will attend a focus group with other members of their weight loss group. Research staff will measure participants' weight at the focus group visit. We will ask participants in both

treatment conditions to elaborate on barriers and facilitators to participation. Participants in the Facebook condition will be asked for their reactions to and ratings of intervention posts that received low engagement. We will use their feedback to refine the format of low-engagement intervention posts to make them more engaging. Participants who do not attend the focus group will complete an individual follow-up visit that includes measurement of weight and an individual interview.

At 6 months, participants will also complete an online survey that includes assessment of current pregnancy, depressive symptoms [34], quality of life [40,41], infant feeding [42,43], social support for diet and physical activity changes [44], social media use [45], group cohesion [68,69], contamination, and intervention acceptability [30]. Participants will also report app-tracked time on Facebook over the past 7 days and their Facebook use habits, including what device(s) they used to access Facebook, what proportion of use was from their smartphone (vs other devices), the extent to which other people used Facebook on their phone [46], and whether they consciously changed their Facebook use as a result of becoming aware of the time spent on Facebook and, if so, in what way [70].

We expect that this follow-up visit will take 1 to 1.5 hours, and the survey will take 30 to 45 min. We will email participants a US \$40 gift card after they complete the focus group and survey.

Twelve-Month Follow-Up Assessment

At 12 months (6 months after the end of the intervention), participants will attend a follow-up visit to measure weight and complete an online survey. Research staff will provide participants with instructions on how to remove the MyFitnessPal and time tracking apps from their phones. We will email participants a link to complete an online survey that includes measures of current pregnancy, depressive symptoms [34], quality of life [40,41], infant feeding [42,43], social support for diet and physical activity changes [44], and social media use [30,45]. Participants will also report app-tracked time on Facebook over the past 7 days and their Facebook use habits, including what device(s) they used to access Facebook, what proportion of use was from their smartphone (vs other devices), and the extent to which other people used Facebook on their phone [46]. We expect that the survey will take about 30 min, and the visit will take about 15 to 45 min. We will email participants a US \$40 gift card after they complete the study visit and survey.

Measures

Primary Outcomes: Feasibility

We will examine the feasibility of recruitment, sustained participation, contamination, retention, and feasibility of assessment procedures, particularly measurement of costs related to delivering and receiving the intervention.

Recruitment

We will calculate recruitment rates from the number of individuals contacted, screened, consented, and randomized, overall and by recruitment source. We will record the reasons

for ineligibility and nonparticipation, including unwillingness to be randomized to either an online or in-person condition.

Sustained Participation

We will assess sustained participation in the intervention, that is, treatment retention. For the in-person condition, we will calculate sustained participation as time to last intervention session attended. Attendance at in-person intervention sessions will be recorded by the weight loss counselor at each meeting. For the Facebook condition, we will calculate sustained participation as time to last post, comment, or reaction (based on the date of post or comment reacted to) in the Facebook group. We will download objective engagement data from Facebook and calculate the date of last engagement.

Contamination

At 6 months, participants will complete a survey that includes questions about whether they participated in other weight loss programs (online or in-person) and whether they sought weight loss support on Facebook or other online social networks [71]; and, if so, to what extent and reasons why they sought this support.

Retention

We will calculate retention as the proportion of participants who complete the 6- and 12-month follow-up assessments in each condition.

Feasibility of Assessment Procedures

We will examine the extent and mechanisms of missing data on each measure to be included in the subsequent noninferiority trial, especially procedures used to capture costs. We will systematically track costs associated with delivery of both intervention conditions, capturing information on the costs that would be required to implement each intervention in practice (ie, outside the research context) using methods developed by others [72-74]. We have created an accounting system that captures administrative (eg, setting up the Facebook group and copying participants' handouts), intervention delivery (eg, leading in-person intervention meetings and counseling via the Facebook group), and participant costs (eg, travel time to intervention meetings, time spent attending intervention meetings, and time spent on Facebook to participate in the intervention) for both conditions [75]. We will document any challenges with procedures for collecting data, including study records, participant-reported measures, measurement of weight, engagement data from Facebook, and time data recorded from tracking tools.

Exploratory Outcome: Weight Change

At baseline, 6 months, and 12 months, weight will be measured twice and averaged. We will calculate percent weight change from baseline to 6 months and from baseline to 12 months. We will define clinically significant weight loss as 5% or greater [76,77] and will calculate the proportion of participants achieving this degree of weight loss at both follow-up points. For women who become pregnant during the study, we will use self-reported prepregnancy weight as their follow-up weight.

Treatment Fidelity and Participant Safety

Treatment Fidelity

We will randomly select 20% of intervention modules, stratified by phase of the intervention: in-person group meetings weekly (weeks 1-15) or every other week (weeks 16-25). Study staff will review audiotapes from the in-person group sessions and content library of intervention posts from the Facebook condition and rate whether content objectives were met in each module. The weight loss counselor will receive feedback for intervention modules with less than 90% adherence to the protocol.

Participant Safety

The possible risks of participating in this study include an injury while being physically active, possible discomfort from completing questionnaires, and breach of confidentiality. Participants will be screened for ability to engage in physical activity, and we will obtain medical clearance from each participant's primary care provider or obstetrician/gynecologist. Participants will be encouraged to participate in physical activity they are comfortable with, while gradually scaling to meet intensity recommendations, and avoid any exercises that could lead to injury, pain, or discomfort. Participants who experience injury or discomfort from exercise will be asked to meet with a health care provider before returning to physical activity. We will keep study data stored on REDCap [36], on password-protected research drives, or in locked filing cabinets. We will encourage participants to review privacy policies of Facebook, MyFitnessPal, and any time tracking apps, and during the informed consent process, we will review with participants the privacy considerations of participating in an intervention delivered via a secret Facebook group (eg, who can see what they post and what access Facebook has to content they share in the group). We will record and follow up on any adverse events that occur during the intervention, regardless of likely relation to the intervention. We will report any events that are related or possibly related to study procedures to the University of Connecticut IRB within 24 to 48 hours regardless of level of severity, and all other adverse events those that are not related or unlikely related to study procedures, during annual continuing IRB review.

Although not expected to be related to study participation, over the course of the study, research staff may become aware of elevated depressive symptoms among our participants, as depression is common among postpartum women [78]. Study assessments at baseline, 6 months, and 12 months include the EPDS [34]. Elevated depressive symptoms and/or suicidal ideation at baseline are exclusionary. The weight loss counselor will monitor participants' posts on the Facebook group and discussions at in-person intervention sessions for disclosures of feelings of depressed mood during the intervention phase and will call participants disclosing such feelings to assess for clinical depression and make appropriate referrals if necessary. At any point during the study, we will refer participants for mental health care and/or arrange immediate psychiatric evaluation, as appropriate, and will alert referring providers of elevated depressive symptomology as identified by the EPDS [34].

Statistical Analysis

We will use REDCap [36] to administer participant surveys and for participant tracking and data management. We will use SAS 9.4 (SAS Institute, Inc) to analyze quantitative data. Reporting of the feasibility outcomes and exploratory outcome of weight change will be descriptive (eg, percent retention at 6 and 12 months).

Primary Outcomes: Feasibility

Examination of feasibility outcomes will inform the design of the subsequent full-scale noninferiority trial.

Recruitment

We will report recruitment using a Consolidated Standards of Reporting Trials (CONSORT) diagram [79,80]. We will compare yield from different recruitment approaches and will examine whether any eligibility criteria are excluding an inordinate proportion of otherwise eligible women. In particular, we will examine the number of otherwise eligible women excluded from participation because one or the other delivery mode is not feasible or unwillingness to be randomized to either treatment condition. If recruitment rates are lower than expected, we will adjust recruitment timelines as we plan the subsequent noninferiority trial.

Sustained Participation

We will compare sustained participation in both conditions. We will modify the delivery of both intervention conditions to address logistical and other barriers to sustained participation.

Contamination

We will describe the extent of contamination and reasons women sought these extra sources of support. If a significant proportion of women report seeking weight loss support from other sources, we will adapt our intervention to better meet their needs to reduce the occurrence of contamination in the subsequent trial.

Retention

We will report retention rates in each condition using a CONSORT diagram [79,80]. If retention is lower than expected, we will explore reasons for dropout and make changes to the protocol to address these challenges. We will also examine the proportion of participants who become pregnant during the study period.

Feasibility of Assessment Procedures

We will examine the extent and mechanisms of missing data, particularly measures of costs associated with delivering and receiving the intervention. For measures with an unacceptable amount of missingness, we will consider alternative measures in the subsequent noninferiority trial. We will resolve any issues arising in the collection of cost-related data and develop procedures for assessing time spent on Facebook to participate in the intervention.

Weight Loss (Exploratory)

We will report average percent weight loss in each treatment condition and the proportion that achieved clinically significant weight loss ($\geq 5\%$).

Power

The purpose of this pilot trial is to examine the feasibility, thus identifying modifications required before examining noninferiority in a large randomized controlled trial. Leon et al [81] state that “power analyses should not be presented in an application for a pilot study that does not propose inferential results.” As they and others recommend [81,82], we based the sample size on necessities for examining the feasibility, thus identifying modifications required to the design of the trial or study procedures before conducting a full-scale noninferiority trial. Conducting 2 waves allows us to iteratively refine how we deliver intervention content via Facebook while assessing the feasibility of recruitment and engagement under the conditions of the subsequent trial. Although we will aim to maximize retention in both conditions, with retention of 80% or greater to be acceptable, a priori, we decided that a retention rate in either condition lower than 60% would indicate that the noninferiority trial is not feasible as designed. With 36 participants per treatment condition, the 95% CI for the estimated retention rate will be within $\pm 13\%$ if observed retention is 80%. Given 36 participants per condition, the lower limit of the 95% CI for the observed retention rate in either treatment condition should not be lower than 60%.

Owing to the variability in estimated standard errors from pilot studies, estimated effect sizes from small pilot studies should not be used to determine sample size to adequately power randomized controlled trials to assess intervention efficacy [81,83]. Thus, as recommended [81,83], we will calculate sample size requirements for the subsequent full-scale noninferiority trial based on a clinically meaningful noninferiority margin for percent weight loss and variance in weight loss observed in previous adequately powered trials of postpartum weight loss interventions [84].

Results

Recruitment began in September 2018. The first wave of the intervention began in February 2019, and the second wave of the intervention began in October 2019. We anticipate completing follow-up assessments in fall 2020, and results will be analyzed at that time.

Discussion

This randomized feasibility pilot trial will provide the necessary data to support a fully powered noninferiority trial comparing the Facebook-delivered postpartum weight loss intervention with traditional in-person delivery. A feasibility trial is important for several reasons. First, we need to demonstrate the feasibility of recruiting a sample of postpartum women who are willing and able to participate in either treatment condition. Barriers to attending numerous in-person sessions include work schedules, lack of childcare, and unreliable transportation [14-20], which may limit the available participant pool. In addition, women who have a strong preference for 1 condition may be more likely to drop out of treatment if they do not get randomized to their preferred condition. For this reason, we need to test recruitment and enrollment procedures to ensure adequate pacing of recruitment of eligible postpartum women who are able and

willing to participate in either the in-person or Facebook condition to achieve the higher sample size required for efficacy testing.

Second, we need to establish that we can sustain participation in the Facebook-delivered condition adequately for 6 months. Previous studies using social media platforms for weight loss intervention delivery were either shorter than 6 months or had highly variable engagement [85]. In our 1-arm pilot of a 12-week version of the Facebook-delivered intervention, 63% of women sustained participation until the last week of the intervention, including 42% who engaged on the last day of the intervention [30]. Although this rate of treatment retention is promising, this study will provide information about sustained participation in the intervention throughout the full 6-month intervention. We have refined our intervention content after pretesting it in this and other pilot studies by identifying posts that received low engagement and rewording them to be more succinct; adding high-quality graphics; and including features known to elicit engagement such as polls, gifs, and challenges [65,86]. As attrition from treatment is a common challenge in postpartum weight loss intervention studies regardless of treatment modality [12,13], this study will also provide an opportunity to examine sustained participation in the in-person condition.

Third, we need to establish the feasibility of assessment procedures, particularly the measurement of costs related to delivering and receiving the intervention. We will systematically track costs that would be required to implement each intervention in practice (ie, outside the research context) [72-74] using a tracking system and procedures we previously developed [67]. The time participants spend using Facebook to participate in the intervention is a critical component of estimating the cost of receiving the intervention. Many Facebook users log in multiple times a day for short periods to scan their feed [87]. Within those periods, only a fraction of time might be dedicated to reading intervention posts and engaging with the counselor and other participants. Currently, no best practice exists for accurately measuring time spent on a particular Facebook feed [88]. We propose to use a difference-in-differences approach to compare changes in total Facebook use from preintervention across treatment conditions to estimate time spent to participate in the Facebook-delivered intervention. This approach requires accurate measures of total time on Facebook throughout the intervention for participants in both treatment conditions. As part of this project, we will develop procedures for measuring time spent on Facebook to participate in the intervention that maximize accuracy while not placing undue burden on participants nor changing their behavior as a result of surveilling their social media activities [70]. We will ask participants in both conditions to report the average time spent using Facebook recorded by the Facebook app's time tracking tool or another app for tracking app usage and compare changes in Facebook use between the conditions over the course of the study. We will also query use patterns (eg, from other devices) and use this information to explore the likely accuracy of app-tracked time on Facebook. This formative work is needed before moving to a large-scale trial to assess cost-effectiveness.

Both social media and in-person treatment modalities have advantages and disadvantages that may impact efficacy for

weight loss. The Facebook-delivered condition, by not requiring group visits, has the advantage of allowing participants to receive intervention content and participate in discussions where and when it works for them and providing more ready access to support from the counselor and other moms. They also do not need to carve out time in their schedule to attend intervention sessions, which may result in more time available for lifestyle activities such as exercise and meal preparation. A disadvantage is that intervention content competes with other highly engaging content in participants' Facebook feeds and can easily be scrolled past. To compete for attention, intervention posts should be designed using similar features as other content on social media (eg, high-quality images). To this end, our team applies popular social media marketing trends when designing posts, and solicited feedback from postpartum women on intervention posts that received low engagement in our previous pilot study to refine intervention posts to elicit greater engagement from participants. Although an advantage of using a commercial social media platform for intervention delivery is the ability to capitalize on Facebook's attractive technology (website and mobile app) and software for scheduling content, intervention research using Facebook as a delivery platform can be complicated by Facebook's proprietary algorithm that determines how content is prioritized. Recently, Facebook announced an effort to put greater priority on content from Facebook groups; however, researchers have no way of knowing how much content ends up in each participants' newsfeeds and have no ability to control that. New post notifications can be set up to circumvent this challenge. To the extent that data support the efficacy of Facebook-delivered intervention approaches, privacy protection will need to be secured before delivery in clinical settings.

An advantage of in-person delivery is that participants who attend receive face time with the counselor and each other, which provides more opportunity to develop tighter interpersonal bonds. Emotional support can be expressed through nonverbal behaviors such as smiling, nodding, and eye contact, all of which cannot be communicated online. Social media platforms attempt to fill this gap by allowing users to use clickable reactions (eg, like button) and gifs that create emotion through 1- to 2-second animations. A disadvantage is that missed visits are fairly

common and, when repeated, often lead to attrition from treatment. This negatively affects treatment receipt and ultimately outcomes. Barriers to attending in-person sessions include work schedules, lack of childcare, and unreliable transportation [14-20]. Given the unique advantages and disadvantages of each treatment modality, we hypothesize that delivery via Facebook will not be appreciably worse on weight loss outcomes compared with delivery via in-person groups.

We hypothesize that social media delivery will be more cost-effective (ie, cost per participant, per kg lost, and per participant who lost $\geq 5\%$) than in-person delivery. Online interventions do not require physical space or travel time for interventionists or participants. In an era of limited health care dollars, data on cost-effectiveness can influence decision making about the provision of treatments or preventive interventions and the willingness to pay for these programs [73,74]. Previous cost-effectiveness analyses of weight loss interventions have suggested that technology-based approaches may be cost-effective compared with traditional in-person counseling [89,90], but available data on technology-delivered weight loss interventions are sparse [91]. This feasibility pilot trial will provide information on the feasibility of collection of cost-related data needed to evaluate cost-effectiveness of the Facebook-delivered intervention compared with in-person delivery in a subsequent large-scale noninferiority trial. Demonstration of cost-effectiveness in addition to efficacy can support the coverage of online lifestyle interventions by employers and health insurers.

Conclusions

In summary, results from this randomized feasibility pilot trial will inform the design of a large-scale randomized controlled trial to assess whether delivering a postpartum weight loss intervention via Facebook is noninferior for weight loss and more cost-effective than delivering the intervention via traditional in-person groups. Following the noninferiority trial, we will assess the effectiveness of the Facebook-delivered intervention when implemented in real-world settings. Efficacious, cost-effective, and scalable strategies for postpartum weight loss have potential for high impact on the obesity epidemic and long-term maternal health.

Acknowledgments

This project was supported by National Institutes of Health (NIH) grant R34HL136979 (principal investigator [PI]: MEW). Additional support was provided by NIH grant K24HL124366 (PI: SLP).

Conflicts of Interest

None declared.

Multimedia Appendix 1

Peer-review report from NIH for Grant R34HL136979.

[[PDF File \(Adobe PDF File\), 167 KB - resprot_v8i11e15530_app1.pdf](#)]

References

1. Gunderson E, Quesenberry CP, Lewis CE, Tsai AL, Sternfeld B, Smith West D, et al. Development of overweight associated with childbearing depends on smoking habit: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. *Obes Res* 2004 Dec;12(12):2041-2053 [FREE Full text] [doi: [10.1038/oby.2004.255](https://doi.org/10.1038/oby.2004.255)] [Medline: [15687406](https://pubmed.ncbi.nlm.nih.gov/15687406/)]
2. Endres LK, Straub H, McKinney C, Plunkett B, Minkovitz CS, Schetter CD, Community Child Health Network of the Eunice Kennedy Shriver National Institute of Child Health and Human Development. Postpartum weight retention risk factors and relationship to obesity at 1 year. *Obstet Gynecol* 2015 Jan;125(1):144-152 [FREE Full text] [doi: [10.1097/AOG.0000000000000565](https://doi.org/10.1097/AOG.0000000000000565)] [Medline: [25560116](https://pubmed.ncbi.nlm.nih.gov/25560116/)]
3. Rooney BL, Schauburger CW, Mathiason MA. Impact of perinatal weight change on long-term obesity and obesity-related illnesses. *Obstet Gynecol* 2005 Dec;106(6):1349-1356. [doi: [10.1097/01.AOG.0000185480.09068.4a](https://doi.org/10.1097/01.AOG.0000185480.09068.4a)] [Medline: [16319262](https://pubmed.ncbi.nlm.nih.gov/16319262/)]
4. Gore SA, Brown DM, West DS. The role of postpartum weight retention in obesity among women: a review of the evidence. *Ann Behav Med* 2003 Oct;26(2):149-159. [doi: [10.1207/S15324796ABM2602_07](https://doi.org/10.1207/S15324796ABM2602_07)] [Medline: [14534032](https://pubmed.ncbi.nlm.nih.gov/14534032/)]
5. Gould Rothberg BE, Magriples U, Kershaw TS, Rising SS, Ickovics JR. Gestational weight gain and subsequent postpartum weight loss among young, low-income, ethnic minority women. *Am J Obstet Gynecol* 2011 Jan;204(1):52.e1-52.11 [FREE Full text] [doi: [10.1016/j.ajog.2010.08.028](https://doi.org/10.1016/j.ajog.2010.08.028)] [Medline: [20974459](https://pubmed.ncbi.nlm.nih.gov/20974459/)]
6. Østbye T, Krause KM, Swamy GK, Lovelady CA. Effect of breastfeeding on weight retention from one pregnancy to the next: results from the North Carolina WIC program. *Prev Med* 2010 Nov;51(5):368-372. [doi: [10.1016/j.ypmed.2010.07.017](https://doi.org/10.1016/j.ypmed.2010.07.017)] [Medline: [20655944](https://pubmed.ncbi.nlm.nih.gov/20655944/)]
7. Sonnevile KR, Rifas-Shiman SL, Oken E, Peterson KE, Gortmaker SL, Gillman MW, et al. Longitudinal association of maternal attempt to lose weight during the postpartum period and child obesity at age 3 years. *Obesity (Silver Spring)* 2011 Oct;19(10):2046-2052 [FREE Full text] [doi: [10.1038/oby.2011.25](https://doi.org/10.1038/oby.2011.25)] [Medline: [21350436](https://pubmed.ncbi.nlm.nih.gov/21350436/)]
8. Walker LO. Low-income women's reproductive weight patterns empirically based clusters of prepregnant, gestational, and postpartum weights. *Womens Health Issues* 2009;19(6):398-405. [doi: [10.1016/j.whi.2009.08.003](https://doi.org/10.1016/j.whi.2009.08.003)] [Medline: [19766016](https://pubmed.ncbi.nlm.nih.gov/19766016/)]
9. Whitaker K, Jarvis MJ, Beeken RJ, Boniface D, Wardle J. Comparing maternal and paternal intergenerational transmission of obesity risk in a large population-based sample. *Am J Clin Nutr* 2010 Jun;91(6):1560-1567. [doi: [10.3945/ajcn.2009.28838](https://doi.org/10.3945/ajcn.2009.28838)] [Medline: [20375189](https://pubmed.ncbi.nlm.nih.gov/20375189/)]
10. Pachucki MC, Lovenheim MF, Harding M. Within-family obesity associations: evaluation of parent, child, and sibling relationships. *Am J Prev Med* 2014 Oct;47(4):382-391. [doi: [10.1016/j.amepre.2014.05.018](https://doi.org/10.1016/j.amepre.2014.05.018)] [Medline: [25015563](https://pubmed.ncbi.nlm.nih.gov/25015563/)]
11. Herring SJ, Oken E. Obesity and diabetes in mothers and their children: can we stop the intergenerational cycle? *Curr Diab Rep* 2011 Feb;11(1):20-27 [FREE Full text] [doi: [10.1007/s11892-010-0156-9](https://doi.org/10.1007/s11892-010-0156-9)] [Medline: [20963519](https://pubmed.ncbi.nlm.nih.gov/20963519/)]
12. Amorim Adegboye AR, Linne YM. Diet or exercise, or both, for weight reduction in women after childbirth. *Cochrane Database Syst Rev* 2013 Jul 23(7):CD005627. [doi: [10.1002/14651858.CD005627.pub3](https://doi.org/10.1002/14651858.CD005627.pub3)] [Medline: [23881656](https://pubmed.ncbi.nlm.nih.gov/23881656/)]
13. Dodd J, Deussen AR, O'Brien CM, Schoenaker DA, Poprzeczny A, Gordon A, et al. Targeting the postpartum period to promote weight loss: a systematic review and meta-analysis. *Nutr Rev* 2018 Aug 1;76(8):639-654 [FREE Full text] [doi: [10.1093/nutrit/nuy024](https://doi.org/10.1093/nutrit/nuy024)] [Medline: [29889259](https://pubmed.ncbi.nlm.nih.gov/29889259/)]
14. Carter-Edwards L, Østbye T, Bastian LA, Yarnall KS, Krause KM, Simmons T. Barriers to adopting a healthy lifestyle: insight from postpartum women. *BMC Res Notes* 2009 Aug 17;2:161 [FREE Full text] [doi: [10.1186/1756-0500-2-161](https://doi.org/10.1186/1756-0500-2-161)] [Medline: [19686601](https://pubmed.ncbi.nlm.nih.gov/19686601/)]
15. Montgomery KS, Bushee TD, Phillips JD, Kirkpatrick T, Catledge C, Braveboy K, et al. Women's challenges with postpartum weight loss. *Matern Child Health J* 2011 Nov;15(8):1176-1184. [doi: [10.1007/s10995-010-0681-9](https://doi.org/10.1007/s10995-010-0681-9)] [Medline: [20844941](https://pubmed.ncbi.nlm.nih.gov/20844941/)]
16. Groth SW, David T. New mothers' views of weight and exercise. *MCN Am J Matern Child Nurs* 2008;33(6):364-370 [FREE Full text] [doi: [10.1097/01.NMC.0000341257.26169.30](https://doi.org/10.1097/01.NMC.0000341257.26169.30)] [Medline: [18997572](https://pubmed.ncbi.nlm.nih.gov/18997572/)]
17. Mailey EL, Huberty J, Dinkel D, McAuley E. Physical activity barriers and facilitators among working mothers and fathers. *BMC Public Health* 2014 Jun 27;14:657 [FREE Full text] [doi: [10.1186/1471-2458-14-657](https://doi.org/10.1186/1471-2458-14-657)] [Medline: [24974148](https://pubmed.ncbi.nlm.nih.gov/24974148/)]
18. Graham M, Uesugi K, Olson C. Barriers to weight-related health behaviours: a qualitative comparison of the socioecological conditions between pregnant and post-partum low-income women. *Matern Child Nutr* 2016 Apr;12(2):349-361 [FREE Full text] [doi: [10.1111/mcn.12135](https://doi.org/10.1111/mcn.12135)] [Medline: [25040706](https://pubmed.ncbi.nlm.nih.gov/25040706/)]
19. Evenson KR, Aytur SA, Borodulin K. Physical activity beliefs, barriers, and enablers among postpartum women. *J Womens Health (Larchmt)* 2009 Dec;18(12):1925-1934 [FREE Full text] [doi: [10.1089/jwh.2008.1309](https://doi.org/10.1089/jwh.2008.1309)] [Medline: [20044854](https://pubmed.ncbi.nlm.nih.gov/20044854/)]
20. Chang M, Nitzke S, Guilford E, Adair CH, Hazard DL. Motivators and barriers to healthful eating and physical activity among low-income overweight and obese mothers. *J Am Diet Assoc* 2008 Jun;108(6):1023-1028. [doi: [10.1016/j.jada.2008.03.004](https://doi.org/10.1016/j.jada.2008.03.004)] [Medline: [18502238](https://pubmed.ncbi.nlm.nih.gov/18502238/)]
21. Hutchesson MJ, Hulst J, Collins CE. Weight management interventions targeting young women: a systematic review. *J Acad Nutr Diet* 2013 Jun;113(6):795-802. [doi: [10.1016/j.jand.2013.01.015](https://doi.org/10.1016/j.jand.2013.01.015)] [Medline: [23473986](https://pubmed.ncbi.nlm.nih.gov/23473986/)]
22. Chasan-Taber L, Silveira M, Waring ME, Pekow P, Braun B, Manson JE, et al. Gestational weight gain, body mass index, and risk of hypertensive disorders of pregnancy in a predominantly Puerto Rican population. *Matern Child Health J* 2016 Sep;20(9):1804-1813 [FREE Full text] [doi: [10.1007/s10995-016-1983-3](https://doi.org/10.1007/s10995-016-1983-3)] [Medline: [27003150](https://pubmed.ncbi.nlm.nih.gov/27003150/)]
23. Duggan M, Lenhart A, Lampe C, Ellison NB. Pew Research Center. 2015 Jul 16. Parents and Social Media. URL: <http://www.pewinternet.org/2015/07/16/parents-and-social-media/> [accessed 2019-10-17]

24. Duggan M. Pew Research Center. 2015 Aug 19. Mobile Messaging and Social Media 2015. URL: <https://www.pewinternet.org/2015/08/19/mobile-messaging-and-social-media-2015/> [accessed 2019-10-17]
25. Owens JC. MarketWatch. 2016 Apr 28. People Spend More Time With Facebook Than Actual Friends. URL: <http://www.marketwatch.com/story/people-spend-more-time-with-facebook-friends-than-with-actual-friends-2016-04-27> [accessed 2019-10-17]
26. Holtz B, Smock A, Reyes-Gastelum D. Connected motherhood: social support for moms and moms-to-be on Facebook. *Telemed J E Health* 2015 May;21(5):415-421. [doi: [10.1089/tmj.2014.0118](https://doi.org/10.1089/tmj.2014.0118)] [Medline: [25665177](https://pubmed.ncbi.nlm.nih.gov/25665177/)]
27. Cupples ME, Stewart MC, Percy A, Hepper P, Murphy C, Halliday HL. A RCT of peer-mentoring for first-time mothers in socially disadvantaged areas (the MOMENTS Study). *Arch Dis Child* 2011 Mar;96(3):252-258. [doi: [10.1136/adc.2009.167387](https://doi.org/10.1136/adc.2009.167387)] [Medline: [20522466](https://pubmed.ncbi.nlm.nih.gov/20522466/)]
28. Jago R, Steeds JK, Bentley GF, Sebire SJ, Lucas PJ, Fox KR, et al. Designing a physical activity parenting course: parental views on recruitment, content and delivery. *BMC Public Health* 2012 Jul 5;12:356 [FREE Full text] [doi: [10.1186/1471-2458-12-356](https://doi.org/10.1186/1471-2458-12-356)] [Medline: [22591593](https://pubmed.ncbi.nlm.nih.gov/22591593/)]
29. Walsh A, Kearney L, Dennis N. Factors influencing first-time mothers' introduction of complementary foods: a qualitative exploration. *BMC Public Health* 2015 Sep 22;15:939 [FREE Full text] [doi: [10.1186/s12889-015-2250-z](https://doi.org/10.1186/s12889-015-2250-z)] [Medline: [26395331](https://pubmed.ncbi.nlm.nih.gov/26395331/)]
30. Waring ME, Simas TA, Oleski J, Xiao RS, Mulcahy JA, May CN, et al. Feasibility and acceptability of delivering a postpartum weight loss intervention via Facebook: a pilot study. *J Nutr Educ Behav* 2018 Jan;50(1):70-4.e1 [FREE Full text] [doi: [10.1016/j.jneb.2017.09.025](https://doi.org/10.1016/j.jneb.2017.09.025)] [Medline: [29325665](https://pubmed.ncbi.nlm.nih.gov/29325665/)]
31. Herring SJ, Cruice JF, Bennett GG, Davey A, Foster GD. Using technology to promote postpartum weight loss in urban, low-income mothers: a pilot randomized controlled trial. *J Nutr Educ Behav* 2014;46(6):610-615 [FREE Full text] [doi: [10.1016/j.jneb.2014.06.002](https://doi.org/10.1016/j.jneb.2014.06.002)] [Medline: [25069621](https://pubmed.ncbi.nlm.nih.gov/25069621/)]
32. Silfee VJ, Lopez-Cepero A, Lemon SC, Estabrook B, Nguyen O, Wang ML, et al. Adapting a behavioral weight loss intervention for delivery via Facebook: a pilot series among low-income postpartum women. *JMIR Form Res* 2018 Sep 10;2(2):e18 [FREE Full text] [doi: [10.2196/formative.9597](https://doi.org/10.2196/formative.9597)] [Medline: [30684423](https://pubmed.ncbi.nlm.nih.gov/30684423/)]
33. Wilcox S, Liu J, Addy CL, Turner-McGrievy G, Burgis JT, Wingard E, et al. A randomized controlled trial to prevent excessive gestational weight gain and promote postpartum weight loss in overweight and obese women: Health In Pregnancy and Postpartum (HIPPP). *Contemp Clin Trials* 2018 Mar;66:51-63 [FREE Full text] [doi: [10.1016/j.cct.2018.01.008](https://doi.org/10.1016/j.cct.2018.01.008)] [Medline: [29371061](https://pubmed.ncbi.nlm.nih.gov/29371061/)]
34. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. *Br J Psychiatry* 1987 Jun;150:782-786. [doi: [10.1192/bjp.150.6.782](https://doi.org/10.1192/bjp.150.6.782)] [Medline: [3651732](https://pubmed.ncbi.nlm.nih.gov/3651732/)]
35. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. Fifth Edition. United States: American Psychiatric Publishing; 2013.
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](https://doi.org/10.1016/j.jbi.2008.08.010)] [Medline: [18929686](https://pubmed.ncbi.nlm.nih.gov/18929686/)]
37. Carter EB, Stuart JJ, Farland LV, Rich-Edwards JW, Zera CA, McElrath TF, et al. Pregnancy complications as markers for subsequent maternal cardiovascular disease: validation of a maternal recall questionnaire. *J Womens Health (Larchmt)* 2015 Sep;24(9):702-712 [FREE Full text] [doi: [10.1089/jwh.2014.4953](https://doi.org/10.1089/jwh.2014.4953)] [Medline: [26061196](https://pubmed.ncbi.nlm.nih.gov/26061196/)]
38. Institute of Medicine, National Research Council. In: Rasmussen KM, Yaktine AL, editors. *Weight Gain During Pregnancy: Reexamining the Guidelines*. Washington, DC: National Academies Press; 2009. [Medline: [20669500](https://pubmed.ncbi.nlm.nih.gov/20669500/)]
39. Moore Simas TA, Corvera S, Lee MM, Zhang N, Leung K, Olendzki B, et al. Understanding multifactorial influences on the continuum of maternal weight trajectories in pregnancy and early postpartum: study protocol, and participant baseline characteristics. *BMC Pregnancy Childbirth* 2015 Mar 28;15:71 [FREE Full text] [doi: [10.1186/s12884-015-0490-7](https://doi.org/10.1186/s12884-015-0490-7)] [Medline: [25885002](https://pubmed.ncbi.nlm.nih.gov/25885002/)]
40. Dewitt B, Feeny D, Fischhoff B, Cella D, Hays RD, Hess R, et al. Estimation of a preference-based summary score for the patient-reported outcomes measurement information system: the PROMIS-preference (PROPr) scoring system. *Med Decis Making* 2018 Aug;38(6):683-698 [FREE Full text] [doi: [10.1177/0272989X18776637](https://doi.org/10.1177/0272989X18776637)] [Medline: [29944456](https://pubmed.ncbi.nlm.nih.gov/29944456/)]
41. Hanmer J, Dewitt B, Yu L, Tsevat J, Roberts M, Revicki D, et al. Cross-sectional validation of the PROMIS-Preference scoring system. *PLoS One* 2018;13(7):e0201093 [FREE Full text] [doi: [10.1371/journal.pone.0201093](https://doi.org/10.1371/journal.pone.0201093)] [Medline: [30063733](https://pubmed.ncbi.nlm.nih.gov/30063733/)]
42. Grummer-Strawn LM, Scanlon KS, Fein SB. Infant feeding and feeding transitions during the first year of life. *Pediatrics* 2008 Oct;122(Suppl 2):S36-S42. [doi: [10.1542/peds.2008-1315d](https://doi.org/10.1542/peds.2008-1315d)] [Medline: [18829829](https://pubmed.ncbi.nlm.nih.gov/18829829/)]
43. Lakshman RR, Landsbaugh JR, Schiff A, Hardeman W, Ong KK, Griffin SJ. Development of a questionnaire to assess maternal attitudes towards infant growth and milk feeding practices. *Int J Behav Nutr Phys Act* 2011 Apr 21;8:35 [FREE Full text] [doi: [10.1186/1479-5868-8-35](https://doi.org/10.1186/1479-5868-8-35)] [Medline: [21510900](https://pubmed.ncbi.nlm.nih.gov/21510900/)]
44. Rieder S, Ruderman A. The development and validation of the weight management support inventory. *Eat Behav* 2007 Jan;8(1):39-47. [doi: [10.1016/j.eatbeh.2005.05.010](https://doi.org/10.1016/j.eatbeh.2005.05.010)] [Medline: [17174850](https://pubmed.ncbi.nlm.nih.gov/17174850/)]
45. Smith A, Anderson M. Pew Research Center. 2018 Mar 1. Social Media Use in 2018. URL: <http://www.pewinternet.org/2018/03/01/social-media-use-in-2018/> [accessed 2019-10-17]

46. Revilla M, Ochoa C, Loewe G. Using passive data from a meter to complement survey data in order to study online behavior. *Soc Sci Comput Rev* 2016;35(4):521-536. [doi: [10.1177/0894439316638457](https://doi.org/10.1177/0894439316638457)]
47. Xiao L, Lv N, Rosas LG, Karve S, Luna V, Jameiro E, et al. Use of a motivational interviewing-informed strategy in group orientations to improve retention and intervention attendance in a randomized controlled trial. *Health Educ Res* 2016 Dec;31(6):729-737 [FREE Full text] [doi: [10.1093/her/cyw048](https://doi.org/10.1093/her/cyw048)] [Medline: [27923862](https://pubmed.ncbi.nlm.nih.gov/27923862/)]
48. Lee C, Hwang F, Liou Y, Chien L. A preliminary study on the pattern of weight change from pregnancy to 6 months postpartum: a latent growth model approach. *Int J Obes (Lond)* 2011 Aug;35(8):1079-1086. [doi: [10.1038/ijo.2010.225](https://doi.org/10.1038/ijo.2010.225)] [Medline: [21042322](https://pubmed.ncbi.nlm.nih.gov/21042322/)]
49. Onyango AW, Nommsen-Rivers L, Siyam A, Borghi E, de Onis M, Garza C, WHO Multicentre Growth Reference Study Group. Post-partum weight change patterns in the WHO Multicentre Growth Reference Study. *Matern Child Nutr* 2011 Jul;7(3):228-240. [doi: [10.1111/j.1740-8709.2010.00295.x](https://doi.org/10.1111/j.1740-8709.2010.00295.x)] [Medline: [21338469](https://pubmed.ncbi.nlm.nih.gov/21338469/)]
50. Diabetes Prevention Program (DPP) Research Group. The Diabetes Prevention Program (DPP): description of lifestyle intervention. *Diabetes Care* 2002 Dec;25(12):2165-2171 [FREE Full text] [doi: [10.2337/diacare.25.12.2165](https://doi.org/10.2337/diacare.25.12.2165)] [Medline: [12453955](https://pubmed.ncbi.nlm.nih.gov/12453955/)]
51. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 2002 Feb 7;346(6):393-403 [FREE Full text] [doi: [10.1056/NEJMoa012512](https://doi.org/10.1056/NEJMoa012512)] [Medline: [11832527](https://pubmed.ncbi.nlm.nih.gov/11832527/)]
52. Ratner R, Goldberg R, Haffner S, Marcovina S, Orchard R, Fowler S, Diabetes Prevention Program Research Group. Impact of intensive lifestyle and metformin therapy on cardiovascular disease risk factors in the diabetes prevention program. *Diabetes Care* 2005 Apr;28(4):888-894 [FREE Full text] [doi: [10.2337/diacare.28.4.888](https://doi.org/10.2337/diacare.28.4.888)] [Medline: [15793191](https://pubmed.ncbi.nlm.nih.gov/15793191/)]
53. Whittemore R. A systematic review of the translational research on the Diabetes Prevention Program. *Transl Behav Med* 2011 Sep;1(3):480-491 [FREE Full text] [doi: [10.1007/s13142-011-0062-y](https://doi.org/10.1007/s13142-011-0062-y)] [Medline: [24073067](https://pubmed.ncbi.nlm.nih.gov/24073067/)]
54. McTigue KM, Conroy MB, Hess R, Bryce CL, Fiorillo AB, Fischer GS, et al. Using the internet to translate an evidence-based lifestyle intervention into practice. *Telemed J E Health* 2009 Nov;15(9):851-858. [doi: [10.1089/tmj.2009.0036](https://doi.org/10.1089/tmj.2009.0036)] [Medline: [19919191](https://pubmed.ncbi.nlm.nih.gov/19919191/)]
55. Rosal MC, Lemon SC, Nguyen OH, Driscoll NE, Ditaranto L. Translation of the diabetes prevention program lifestyle intervention for promoting postpartum weight loss among low-income women. *Transl Behav Med* 2011 Dec;1(4):530-538 [FREE Full text] [doi: [10.1007/s13142-011-0069-4](https://doi.org/10.1007/s13142-011-0069-4)] [Medline: [24073075](https://pubmed.ncbi.nlm.nih.gov/24073075/)]
56. Ferrara A, Hedderson MM, Albright CL, Ehrlich SF, Quesenberry CP, Peng T, et al. A pregnancy and postpartum lifestyle intervention in women with gestational diabetes mellitus reduces diabetes risk factors: a feasibility randomized control trial. *Diabetes Care* 2011 Jul;34(7):1519-1525 [FREE Full text] [doi: [10.2337/dc10-2221](https://doi.org/10.2337/dc10-2221)] [Medline: [21540430](https://pubmed.ncbi.nlm.nih.gov/21540430/)]
57. Nicklas JM, Zera CA, England LJ, Rosner BA, Horton E, Levkoff SE, et al. A web-based lifestyle intervention for women with recent gestational diabetes mellitus: a randomized controlled trial. *Obstet Gynecol* 2014 Sep;124(3):563-570 [FREE Full text] [doi: [10.1097/AOG.0000000000000420](https://doi.org/10.1097/AOG.0000000000000420)] [Medline: [25162257](https://pubmed.ncbi.nlm.nih.gov/25162257/)]
58. Food and Nutrition Information Center. Dietary Reference Intake (DRI) Calculator for Healthcare Professionals. URL: <https://fnic.nal.usda.gov/fnic/dri-calculator/> [accessed 2019-10-17]
59. Lovelady C. Balancing exercise and food intake with lactation to promote post-partum weight loss. *Proc Nutr Soc* 2011 May;70(2):181-184. [doi: [10.1017/S002966511100005X](https://doi.org/10.1017/S002966511100005X)] [Medline: [21349230](https://pubmed.ncbi.nlm.nih.gov/21349230/)]
60. Otten JJ, Hellwig JP, Meyers LD. Dietary Reference Intakes: the Essential Guide to Nutrient Requirements. Washington, DC: The National Academics Press; 2006. URL: https://www.nal.usda.gov/sites/default/files/fnic_uploads/DRIEssentialGuideNutReq.pdf
61. American College of Obstetricians and Gynecologists. Exercise during pregnancy and the postpartum period. *Clin Obstet Gynecol* 2003 Jun;46(2):496-499. [doi: [10.1097/00003081-200306000-00028](https://doi.org/10.1097/00003081-200306000-00028)] [Medline: [12808399](https://pubmed.ncbi.nlm.nih.gov/12808399/)]
62. Epifanio MS, Genna V, De Luca C, Roccella M, La Grutta S. Paternal and maternal transition to parenthood: the risk of postpartum depression and parenting stress. *Pediatr Rep* 2015 May 25;7(2):5872 [FREE Full text] [doi: [10.4081/pr.2015.5872](https://doi.org/10.4081/pr.2015.5872)] [Medline: [26266033](https://pubmed.ncbi.nlm.nih.gov/26266033/)]
63. Negron R, Martin A, Almog M, Balbierz A, Howell EA. Social support during the postpartum period: mothers' views on needs, expectations, and mobilization of support. *Matern Child Health J* 2013 May;17(4):616-623 [FREE Full text] [doi: [10.1007/s10995-012-1037-4](https://doi.org/10.1007/s10995-012-1037-4)] [Medline: [22581378](https://pubmed.ncbi.nlm.nih.gov/22581378/)]
64. American College of Obstetricians and Gynecologists. ACOG Committee Opinion number 313, September 2005. The importance of preconception care in the continuum of women's health care. *Obstet Gynecol* 2005 Sep;106(3):665-666. [doi: [10.1097/00006250-200509000-00052](https://doi.org/10.1097/00006250-200509000-00052)] [Medline: [16135611](https://pubmed.ncbi.nlm.nih.gov/16135611/)]
65. Pagoto S, Waring ME, Jake-Schoffman DE, Goetz J, Michaels Z, Oleski J, et al. What Type of Engagement Predictors Success in a Facebook Weight Loss Group? In: Proceedings of the 51th Hawaii International Conference on System Sciences. 2018 Presented at: Hawaii International Conference on System Sciences; January 3-6, 2018; Honolulu, Hawaii p. 3304-3312 URL: <https://scholarspace.manoa.hawaii.edu/handle/10125/50307>
66. Pagoto S, Waring ME, Schneider KL, Oleski KL, Olendzki E, Hayes RB, et al. Twitter-delivered behavioral weight-loss interventions: a pilot series. *JMIR Res Protoc* 2015 Oct 23;4(4):e123 [FREE Full text] [doi: [10.2196/resprot.4864](https://doi.org/10.2196/resprot.4864)] [Medline: [26500186](https://pubmed.ncbi.nlm.nih.gov/26500186/)]

67. Wang ML, Waring ME, Jake-Schoffman DE, Oleski JL, Michaels Z, Goetz JM, et al. Clinic versus online social network-delivered lifestyle interventions: protocol for the Get Social Noninferiority randomized controlled trial. *JMIR Res Protoc* 2017 Dec 11;6(12):e243 [FREE Full text] [doi: [10.2196/resprot.8068](https://doi.org/10.2196/resprot.8068)] [Medline: [29229591](https://pubmed.ncbi.nlm.nih.gov/29229591/)]
68. Bollen KA, Hoyle RH. Perceived cohesion: a conceptual and empirical examination. *Soc Forces* 1990;69(2):479-504. [doi: [10.1093/sf/69.2.479](https://doi.org/10.1093/sf/69.2.479)]
69. Gesell SB, Barkin SL, Sommer EC, Thompson JR, Valente TW. Increases in network ties are associated with increased cohesion among intervention participants. *Health Educ Behav* 2016 Apr;43(2):208-216 [FREE Full text] [doi: [10.1177/1090198115599397](https://doi.org/10.1177/1090198115599397)] [Medline: [26286298](https://pubmed.ncbi.nlm.nih.gov/26286298/)]
70. McCambridge J, Kypri K, Elbourne D. In randomization we trust? There are overlooked problems in experimenting with people in behavioral intervention trials. *J Clin Epidemiol* 2014 Mar;67(3):247-253 [FREE Full text] [doi: [10.1016/j.jclinepi.2013.09.004](https://doi.org/10.1016/j.jclinepi.2013.09.004)] [Medline: [24314401](https://pubmed.ncbi.nlm.nih.gov/24314401/)]
71. Smith A. Pew Research Center. 2010 Jul 7. Mobile Access 2010. URL: <https://www.pewinternet.org/2010/07/07/mobile-access-2010/> [accessed 2019-10-17]
72. Hernan WH, Brandle M, Zhang P, Williamson DF, Matulik MJ, Ratner RE, Diabetes Prevention Program Research Group. Costs associated with the primary prevention of type 2 diabetes mellitus in the diabetes prevention program. *Diabetes Care* 2003 Jan;26(1):36-47 [FREE Full text] [doi: [10.2337/diacare.26.1.36](https://doi.org/10.2337/diacare.26.1.36)] [Medline: [12502656](https://pubmed.ncbi.nlm.nih.gov/12502656/)]
73. Ritzwoller DP, Sukhanova A, Gaglio B, Glasgow RE. Costing behavioral interventions: a practical guide to enhance translation. *Ann Behav Med* 2009 Apr;37(2):218-227. [doi: [10.1007/s12160-009-9088-5](https://doi.org/10.1007/s12160-009-9088-5)] [Medline: [19291342](https://pubmed.ncbi.nlm.nih.gov/19291342/)]
74. Ramsey SD, Willke RJ, Glick H, Reed SD, Augustovski F, Jonsson B, et al. Cost-effectiveness analysis alongside clinical trials II-An ISPOR Good Research Practices Task Force report. *Value Health* 2015 Mar;18(2):161-172 [FREE Full text] [doi: [10.1016/j.jval.2015.02.001](https://doi.org/10.1016/j.jval.2015.02.001)] [Medline: [25773551](https://pubmed.ncbi.nlm.nih.gov/25773551/)]
75. Frick KD. Microcosting quantity data collection methods. *Med Care* 2009 Jul;47(7 Suppl 1):S76-S81 [FREE Full text] [doi: [10.1097/MLR.0b013e31819bc064](https://doi.org/10.1097/MLR.0b013e31819bc064)] [Medline: [19536026](https://pubmed.ncbi.nlm.nih.gov/19536026/)]
76. Mertens I, Van Gaal LF. Overweight, obesity, and blood pressure: the effects of modest weight reduction. *Obes Res* 2000 May;8(3):270-278 [FREE Full text] [doi: [10.1038/oby.2000.32](https://doi.org/10.1038/oby.2000.32)] [Medline: [10832771](https://pubmed.ncbi.nlm.nih.gov/10832771/)]
77. Wing RR, Lang W, Wadden TA, Safford M, Knowler WC, Bertoni AG, Look AHEAD Research Group. Benefits of modest weight loss in improving cardiovascular risk factors in overweight and obese individuals with type 2 diabetes. *Diabetes Care* 2011 Jul;34(7):1481-1486 [FREE Full text] [doi: [10.2337/dc10-2415](https://doi.org/10.2337/dc10-2415)] [Medline: [21593294](https://pubmed.ncbi.nlm.nih.gov/21593294/)]
78. Woody CA, Ferrari AJ, Siskind DJ, Whiteford HA, Harris MG. A systematic review and meta-regression of the prevalence and incidence of perinatal depression. *J Affect Disord* 2017 Sep;219:86-92. [doi: [10.1016/j.jad.2017.05.003](https://doi.org/10.1016/j.jad.2017.05.003)] [Medline: [28531848](https://pubmed.ncbi.nlm.nih.gov/28531848/)]
79. Altman DG, Schulz KF, Moher D, Egger M, Davidoff F, Elbourne D, CONSORT GROUP (Consolidated Standards of Reporting Trials). The revised CONSORT statement for reporting randomized trials: explanation and elaboration. *Ann Intern Med* 2001 Apr 17;134(8):663-694. [doi: [10.7326/0003-4819-134-8-200104170-00012](https://doi.org/10.7326/0003-4819-134-8-200104170-00012)] [Medline: [11304107](https://pubmed.ncbi.nlm.nih.gov/11304107/)]
80. Moher D, Hopewell S, Schulz KF, Montori V, Gøtzsche PC, Devereaux PJ, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *Br Med J* 2010 Mar 23;340:c869 [FREE Full text] [doi: [10.1136/bmj.c869](https://doi.org/10.1136/bmj.c869)] [Medline: [20332511](https://pubmed.ncbi.nlm.nih.gov/20332511/)]
81. Leon AC, Davis LL, Kraemer HC. The role and interpretation of pilot studies in clinical research. *J Psychiatr Res* 2011 May;45(5):626-629 [FREE Full text] [doi: [10.1016/j.jpsychires.2010.10.008](https://doi.org/10.1016/j.jpsychires.2010.10.008)] [Medline: [21035130](https://pubmed.ncbi.nlm.nih.gov/21035130/)]
82. Thabane L, Ma J, Chu R, Cheng J, Ismaila A, Rios LP, et al. A tutorial on pilot studies: the what, why and how. *BMC Med Res Methodol* 2010 Jan 6;10:1 [FREE Full text] [doi: [10.1186/1471-2288-10-1](https://doi.org/10.1186/1471-2288-10-1)] [Medline: [20053272](https://pubmed.ncbi.nlm.nih.gov/20053272/)]
83. Kraemer HC, Mintz J, Noda A, Tinklenberg J, Yesavage JA. Caution regarding the use of pilot studies to guide power calculations for study proposals. *Arch Gen Psychiatry* 2006 May;63(5):484-489. [doi: [10.1001/archpsyc.63.5.484](https://doi.org/10.1001/archpsyc.63.5.484)] [Medline: [16651505](https://pubmed.ncbi.nlm.nih.gov/16651505/)]
84. Østbye T, Krause KM, Lovelady CA, Morey MC, Bastian LA, Peterson BL, et al. Active Mothers Postpartum: a randomized controlled weight-loss intervention trial. *Am J Prev Med* 2009 Sep;37(3):173-180 [FREE Full text] [doi: [10.1016/j.amepre.2009.05.016](https://doi.org/10.1016/j.amepre.2009.05.016)] [Medline: [19595557](https://pubmed.ncbi.nlm.nih.gov/19595557/)]
85. An R, Ji M, Zhang S. Effectiveness of social media-based interventions on weight-related behaviors and body weight status: review and meta-analysis. *Am J Health Behav* 2017 Nov 1;41(6):670-682. [doi: [10.5993/AJHB.41.6.1](https://doi.org/10.5993/AJHB.41.6.1)] [Medline: [29025495](https://pubmed.ncbi.nlm.nih.gov/29025495/)]
86. Waring ME, Jake-Schoffman DE, Holovatska MM, Mejia C, Williams JC, Pagoto SL. Social media and obesity in adults: a review of recent research and future directions. *Curr Diab Rep* 2018 Apr 18;18(6):34. [doi: [10.1007/s11892-018-1001-9](https://doi.org/10.1007/s11892-018-1001-9)] [Medline: [29671135](https://pubmed.ncbi.nlm.nih.gov/29671135/)]
87. Junco R. Too much face and not enough books: the relationship between multiple indices of Facebook use and academic performance. *Comput Human Behav* 2012;28(1):187-198. [doi: [10.1016/j.chb.2011.08.026](https://doi.org/10.1016/j.chb.2011.08.026)]
88. Sonnenberg B, Riediger M, Wrzus C, Wagner GG. Measuring time use in surveys - Concordance of survey and experience sampling measures. *Soc Sci Res* 2012 Sep;41(5):1037-1052. [doi: [10.1016/j.ssresearch.2012.03.013](https://doi.org/10.1016/j.ssresearch.2012.03.013)] [Medline: [23017916](https://pubmed.ncbi.nlm.nih.gov/23017916/)]
89. Archer E, Groessl EJ, Sui X, McClain AC, Wilcox S, Hand GA, et al. An economic analysis of traditional and technology-based approaches to weight loss. *Am J Prev Med* 2012 Aug;43(2):176-182. [doi: [10.1016/j.amepre.2012.04.018](https://doi.org/10.1016/j.amepre.2012.04.018)] [Medline: [22813682](https://pubmed.ncbi.nlm.nih.gov/22813682/)]

90. Meenan RT, Stevens VJ, Funk K, Bauck A, Jerome GJ, Lien LF, et al. Development and implementation cost analysis of telephone- and Internet-based interventions for the maintenance of weight loss. *Int J Technol Assess Health Care* 2009 Jul;25(3):400-410 [FREE Full text] [doi: [10.1017/S0266462309990018](https://doi.org/10.1017/S0266462309990018)] [Medline: [19619360](https://pubmed.ncbi.nlm.nih.gov/19619360/)]
91. Tate DF, Finkelstein EA, Khavjou O, Gustafson A. Cost effectiveness of internet interventions: review and recommendations. *Ann Behav Med* 2009 Aug;38(1):40-45 [FREE Full text] [doi: [10.1007/s12160-009-9131-6](https://doi.org/10.1007/s12160-009-9131-6)] [Medline: [19834778](https://pubmed.ncbi.nlm.nih.gov/19834778/)]

Abbreviations

BED: binge eating disorder
CONSORT: Consolidated Standards of Reporting Trials
DPP: Diabetes Prevention Program
EPDS: Edinburgh Postnatal Depression Scale
NIH: National Institutes of Health
IRB: institutional review board
PI: principal investigator
REDCap: Research Electronic Data Capture

Edited by G Eysenbach; submitted 17.07.19; peer-reviewed by D Arigo, T Stump, A Dahl, L Saslow; comments to author 11.09.19; revised version received 25.09.19; accepted 26.09.19; published 28.11.19.

Please cite as:

Waring ME, Libby BA, Moore Simas TA, Bracken ML, Bibeau JL, Herrera V, Wang J, Pagoto SL

Delivering a Post-Partum Weight Loss Intervention via Facebook or In-Person Groups: Protocol for a Randomized Feasibility Pilot Trial

JMIR Res Protoc 2019;8(11):e15530

URL: <http://www.researchprotocols.org/2019/11/e15530/>

doi: [10.2196/15530](https://doi.org/10.2196/15530)

PMID: [31778116](https://pubmed.ncbi.nlm.nih.gov/31778116/)

©Molly E E. Waring, Brooke A Libby, Tiffany A Moore Simas, Madison L Bracken, Jessica L Bibeau, Valeria Herrera, Justin Wang, Sherry L Pagoto. Originally published in JMIR Research Protocols (<http://www.researchprotocols.org>), 28.11.2019. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in JMIR Research Protocols, is properly cited. The complete bibliographic information, a link to the original publication on <http://www.researchprotocols.org>, as well as this copyright and license information must be included.

Protocol

Comparing the Impact of an Implicit Learning Approach With Standard Care on Recovery of Mobility Following Stroke: Protocol for a Pilot Cluster Randomized Controlled Trial

Louise Johnson^{1*}, PhD; Jane Burridge^{2*}, PhD; Sara Demain^{3*}, PhD; Sean Ewings^{2*}, PhD

¹Stroke Unit, Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust, Bournemouth, United Kingdom

²University of Southampton, Southampton, United Kingdom

³University of Plymouth, Plymouth, United Kingdom

* all authors contributed equally

Corresponding Author:

Louise Johnson, PhD

Stroke Unit

Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust

Castle Lane East

Bournemouth, BH7 7DW

United Kingdom

Phone: 44 7986596631

Email: Louise.johnson@rbch.nhs.uk

Abstract

Background: Although implicit and explicit learning approaches have been well investigated in healthy populations, there is less evidence regarding the relative benefits of each approach in clinical practice. Studies in stroke typically investigate single elements of an implicit learning approach (ILA; eg, reduced quantity feedback or an external focus of attention) within controlled environments. These studies predominantly evaluate performance, with few measuring this over time (ie, learning). The relevance and transferability of current research evidence into stroke rehabilitation is therefore limited.

Objective: The objective of this study was to compare the ILA with standard care in the acute phase following stroke, to generate data and insights to inform the design of a definitive trial, and to understand patient and therapist perceptions of the ILA.

Methods: This is a multicenter, assessor-blind, cluster randomized controlled pilot trial with nested qualitative evaluation. Stroke units (clusters) will be randomized to either ILA (intervention) or standard care (control) arms. Therapy teams at the intervention sites will be trained in the ILA and provided with an intervention manual. Those at the control sites will have minimal input from the research team, other than for data collection. Consent will be provided at the individual participant level. Once enrolled, participants will receive rehabilitation that focuses on lower limb recovery, using the designated approach. Measures will be taken at baseline, every 2 weeks until the point of discharge from hospital, and at 3 months post stroke onset. Measures include the Fugl Meyer Assessment (motor leg subsection), modified Rivermead Mobility Index, Swedish Postural Adjustment in Stroke Scale, and achievement of mobility milestones. Fidelity of the treatment approach will be monitored using observational video analysis. Focus groups and interviews will be used to gain insight into the perceptions of trial participants and clinical teams.

Results: The first site opened to recruitment in February 2019. The opening of a further 5 sites will be staggered throughout 2019. Results are expected in early 2021.

Conclusions: The findings from this mixed methods pilot study will be used to inform the design of a definitive study, comparing the ILA with standard care in acute stroke rehabilitation.

Trial Registration: ClinicalTrials.gov NCT03792126; <https://clinicaltrials.gov/ct2/show/NCT03792126>

International Registered Report Identifier (IRRID): DERR1-10.2196/14222

(*JMIR Res Protoc* 2019;8(11):e14222) doi:[10.2196/14222](https://doi.org/10.2196/14222)

KEYWORDS

stroke; rehabilitation; learning; attention

Introduction

Background

Regaining the ability to stand, step, and walk is an important goal for people who have experienced a stroke and is a common focus during early rehabilitation.

The process of functional recovery post stroke is underpinned by theories of motor learning, of which there are 2 broad categories—explicit and implicit. Explicit learning occurs when someone is thinking about what to do and about how to move; it is a conscious form of learning. Implicit learning occurs through trial and error and without thinking specifically about how to move; it is a subconscious form of learning. There is, already, agreement that 2 practice conditions are particularly important when differentiating explicit from implicit learning. These are as follows: (1) the *quantity* of instructions and feedback that therapists give and (2) the *focus of attention* (FOA) derived from these instructions and feedback statements [1].

Many factors can influence the process of motor learning. However, experts consider that high quantity of information and/or promotion of an internal FOA (ie, focusing on body movements) are synonymous with an explicit learning model, and that reduced quantity of information and/or an external FOA (ie, focusing on the environment) are synonymous with an implicit learning model [2]. Bias toward one or the other form of learning can be created in a number of ways, including the way that practice is structured, how the person is instructed, and how they receive feedback.

Implicit and explicit approaches have been well investigated with healthy participants. Research has shown that tasks learnt explicitly are less robust and are less likely to be retained over time than those learnt implicitly [3]. Research in sport broadly supports the view that giving excessive verbal information during task practice reduces movement automaticity [4,5] and that reducing the frequency of feedback can enhance learning [6-8]. However, a recent systematic review highlights that such benefits may be small, and the overall quality of evidence is poor [9]. In relation to FOA, there is strong evidence that people master skills more effectively if they are prompted to focus their attention toward the environment, rather than on their body [3].

Research in stroke rehabilitation is more limited. Although studies in stroke show the relative benefits of reduced quantity feedback [10] and an external FOA [11-14], limitations of study design restrict transferability and generalizability of these findings. Most studies measure performance and have not evaluated the benefits of the given approach over time (ie, learning). In 2 studies that have compared the benefits of internal and external focus conditions on longer-term practice, no group differences were found for upper limb function (trained using a robotic device) [15] or balance (trained using a balance board device) [16].

Therefore, although implicit learning is a promising concept in stroke rehabilitation, we do not know how this approach can be effectively delivered, tailored, and evaluated in a clinical setting. Likewise, given the heterogeneity of impairments caused by stroke, there may not be a single optimal approach; it is feasible

that an individualized motor learning approach is necessary to maximize recovery for an individual [17,16]. We currently lack evidence regarding who benefits most from each approach and at what time point in their recovery. Despite this, observational studies have shown rehabilitation practice to be largely explicit in nature [18-22].

Objectives

This paper outlines the protocol for a clinical trial, which will compare an implicit learning approach (ILA) with usual care during the rehabilitation of mobility in the acute phase following stroke. The focus is on lower limb recovery, that is, sitting, sit-to-stand, transfers, stepping, and gait. The broad aims are as follows:

- To establish the feasibility of delivering an ILA during stroke rehabilitation
- To test the integrity of the study protocol (pilot)
- To generate data to inform the design of a phase III trial.

Methods

Study Design

This is a multicenter, assessor-blind, cluster randomized controlled pilot trial, with embedded feasibility study. It also includes a nested qualitative evaluation designed to explore the views of participants and therapists. We aim to recruit 6 Stroke units (clusters) to take part in the trial. Each unit will be randomized to deliver either the ILA or standard care. Individuals within each cluster, who meet the inclusion criteria and agree to take part, will receive all of their lower limb rehabilitation using the designated approach for the duration of their inpatient stay. The study has been approved by the Berkshire Research Ethics Committee B (18/SC/0582).

Stage 1: Understanding and Describing Baseline

The success of this study is dependent on (1) the ability of therapy teams in the intervention sites to consistently and robustly deliver the ILA to trial participants (fidelity) and (2) there being a sufficient difference in the rehabilitation delivered to the ILA group, compared with control.

To understand current practice within each unit, we will conduct an observational study at the beginning of the trial. This will take place *before cluster randomization* and thus before clinicians have received any information or training related to the ILA. We will use nonprobability sampling to video record between 6 and 10 patient-therapist dyads (exact number to be agreed locally, depending on the size of the unit/team). Each recorded session will involve a different patient-therapist pair, but the individual patients and therapists may be recorded more than once. Therapists will be asked to continue with a routine therapy session aimed at improving sit-to-stand, stepping, transfers, or gait.

We will analyze the content of these recorded sessions using a previously validated method [21]. This will give us an indication of the likely content of standard care in each participating organization and will help us to tailor the required training (for the intervention sites). By later comparing the collective content of these recordings with those taken during the main trial, we

will also get insight into the scale of the differences between the trial interventions and standard care.

Stage 2: Cluster Randomized Controlled Trial

Recruitment and Randomization of Clusters

Criteria for stroke unit eligibility are a dedicated unit that (1) routinely admits patients with acute stroke and (2) has a dedicated therapy (occupational therapy and physiotherapy) service for at least 5 days per week.

Stroke units do not need to provide hyperacute care to be involved, but they must admit patients within 5 days of stroke onset. Written informed consent will be obtained by the cluster guardian (senior clinician) at each site. The cluster guardian is consenting for the *stroke unit* to take part in the trial.

The unit of randomization (cluster) is the stroke unit. The trial statistician (SE) will use a Web-based randomization system to allocate sites to control or intervention.

Recruitment and Consent of Individual Participants

Within each cluster, all new admissions will be screened for eligibility within 72 hours. Screening will be performed by the local stroke research nurse or therapist. They will consult other members of the multidisciplinary team, if necessary, to confirm eligibility. Those that meet the inclusion criteria will be provided with verbal and written information, which they will be given a minimum of 24 hours to consider. Those willing to participate will be asked to sign a consent form.

There may be individuals who do not meet the inclusion criteria at the beginning of their stroke unit stay but regain sufficient function to meet the criteria at a later date. We will continue to monitor potential participants and will recruit up to 14 days post stroke, if eligibility changes.

Inclusion Criteria

The inclusion criteria are as follows:

- Clinical diagnosis of stroke, presenting with lower limb paresis
- Has rehabilitation goals relating to lower limb mobility or function
- Within 14 days of stroke onset
- Medically stable
- Able to tolerate daily therapy for a minimum of 30 min per session, sit for more than 5 seconds without support, and understand and follow single stage commands.

Exclusion Criteria

The exclusion criteria are as follows:

- Previous stroke with residual impairments
- Other neurological diagnosis (eg, Parkinson disease, Multiple Sclerosis)
- Clinically relevant premorbid disability levels (required physical assistance of 1-2 people to transfer from bed to chair and/or unable to mobilize without physical assistance of 1-2 people).

Intervention

For those enrolled at the intervention sites, all mobility-focused rehabilitation sessions will utilize the ILA for all rehabilitation (whether delivered by a physiotherapist, occupational therapist, or therapy assistant) that focuses on sitting, sit-to-stand, standing, stepping, transfers, and walking. The content of therapy will be based on the treatment guidelines and intervention manual, which have been developed with input from an international expert group (using Delphi methodology). As this is a clinically grounded, pragmatic trial, therapists will have freedom to tailor the specific content of each treatment session to patient need, while remaining true to the ILA. Specifically, the intervention is not prescriptive with regard to the exercises and tasks that are practiced; these are selected by the treating therapist. However, the therapist will be asked to minimize the use of instructions and feedback *during* practice and to set the task up to promote an external focus. If a task is being performed incorrectly, the therapist can either provide a further instruction or amend the task to facilitate correct performance. This approach gives the therapist autonomy to tailor the content of therapy to the individual patient, while working within the framework for implicit learning that is outlined in the intervention guidelines.

Other therapy interventions, such as upper limb rehabilitation, will be provided as per usual practice. Although the content of this additional therapy will not be monitored, the quantity of other therapy, outside of the trial interventions, will be recorded and compared between groups. Frequency of treatment will be based on the usual practice of the treating hospital. The actual number of sessions received by each participant will be recorded. Specific details relating to the ILA intervention will be shared with intervention sites once randomization has taken place.

Control

Standard care is as per the usual working practice for the stroke unit. Standard care clusters will not have access to the trial materials (eg, treatment manual) or details about the specific elements of the intervention. They will be aware of the broad aims of the study but not the specific detail of the intervention. Although standard care has been shown to be typically explicit, we will verify this through the baseline observations for each site and the ongoing fidelity monitoring (see *Monitoring Fidelity* section). Contact with the research team will be kept to a minimum. An overview is given in [Multimedia Appendix 1](#). The guidance for standard care is based on published observational studies describing usual practice in stroke rehabilitation [1,10,11].

Training for Intervention Sites

For sites randomized to the intervention arm, all physiotherapists, occupational therapists, and therapy assistants will be trained in the ILA. Training is anticipated to last no more than 3 hours and will be delivered by the chief investigator (LJ) as group sessions. Training will include the following:

- Theoretical background to implicit and explicit motor learning
- Research design, methodology, and process (overview)

- Content of the ILA, including video examples and case studies to highlight application
- Opportunity for discussion and questions.

Additional training sessions will be offered if new members join the team during the recruitment phase. A manual including written, photographic, and video resources will demonstrate how to adapt standard care interventions to the ILA. Therapists will be able to refer to the manual throughout their involvement in the study. Therapists' skill in delivering the intervention will be measured as part of the fidelity monitoring (see below).

Although the wider multidisciplinary team (eg, nurses, doctors, other Allied Health Professionals) will not be asked to change their approach with patients, those at intervention sites will be invited to attend a short educational session to raise their awareness of the trial and will be provided with written information about the study and the concepts under investigation. As these professions would not typically be analyzing movement or giving specific instructions and feedback, this level of engagement is deemed appropriate and realistic.

Duration of Treatment

Patients will be recruited as soon as eligible, up to a maximum of 14 days post stroke onset. Trial interventions will be delivered for the duration of each participant's inpatient stay, as deemed appropriate by the treating team. This approach is pragmatic and will ensure that the intervention can be fitted into the current care pathway, but accepting that discharge will be at different times for different patients. We will record length of stay for each participant to gain a better understanding of any variability across sites.

Bias Protection

Outcome assessors will be blind as to the intervention group. Video recording of outcome measures will be used to achieve this, with the blind assessments being conducted by a research assistant, who is not otherwise involved in the trial (EW).

Participants will be informed that the study is investigating different approaches to providing instructions and feedback to patients during rehabilitation. They will be aware that this involves differences in the amount and the type of instructions and feedback given by therapists. However, they will be blind as to whether their stroke unit is providing control or intervention. Whether or not participants have guessed their treatment arm will be explored in the qualitative interviews.

Therapists will be involved in delivering the intervention and cannot therefore be blind. As part of their training, therapists at the intervention sites will receive information about both implicit and explicit learning. We deem this to be important to engage teams in delivering the intervention to the best of their ability. We accept that this may introduce unintended bias, but consider this risk to be small. The priority is for the intervention to be delivered consistently, and an understanding of the theoretical basis and the research hypothesis will aid this.

Monitoring Fidelity (Adherence)

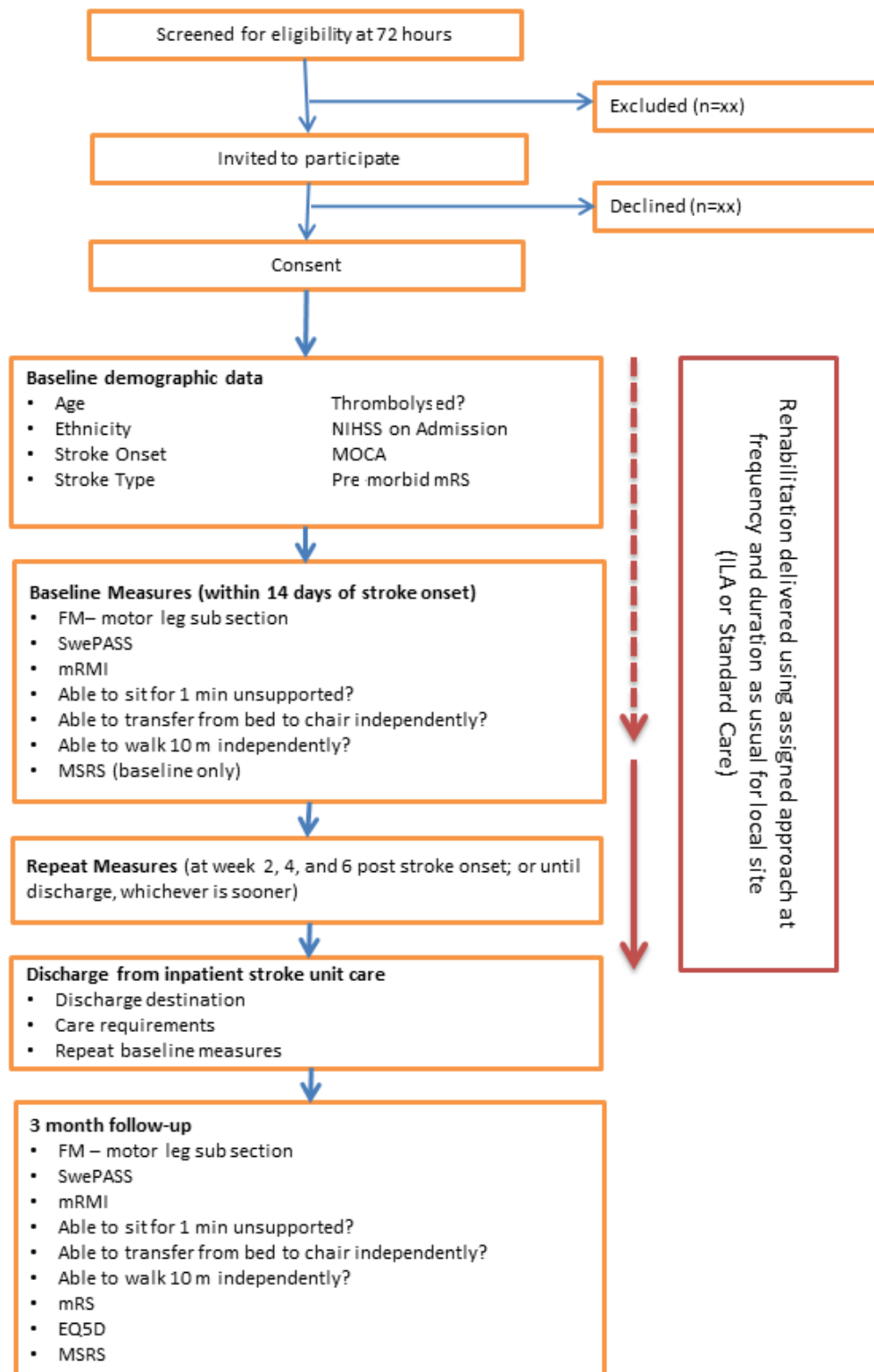
We will endeavor to record all trial treatment sessions. A small and unobtrusive video camera will be used to do this. For practicality, and to avoid observer bias, the treating therapists will be asked to set up the video camera for each session.

For each individual treating therapist (at intervention sites), the first 3 video recordings will be analyzed. We will provide each therapist with objective feedback regarding their adherence to the ILA guidelines (eg, proportion of internal to external focus instruction). In cases where adherence is low, this feedback will include practical solutions on how to improve fidelity and may involve further monitoring until adherence is achieved. For all other sessions, a random sample of videos (minimum of 1 in 6) will be selected for analysis; the sample will be stratified to ensure an equal proportion of videos from each site. Videos will be analyzed using a previously validated method [21] and will be compared for coherence with the written records of the treatment session. We will use a recognized framework to guide this process [23] through the systematic and transparent identification and appraisal of potential problems and solutions relating to fidelity.

Measures

Measures will be performed and recorded by the stroke research practitioner(s) or designated clinician at each site. As the research practitioner is unlikely to remain blind to the intervention arm, all measures will be video recorded and later scored by a blinded second assessor. Frequent measures are required to understand the *rate* of change. Outcome measures have been selected with consideration of international recommendations for measurement of sensorimotor recovery in stroke [24]. Measures include the Movement Specific Reinvestment Scale [25], Fulg Meyer – motor leg subsection [26], modified Postural Adjustment in Stroke Scale (SwePASS) [27,28], modified Rivermead Mobility Index (mRMI) [29], Modified Rankin Scale [30], and the EuroQol 5 Dimension questionnaire (EQ5D) [31]. An overview is given in [Figure 1](#).

Figure 1. Trial flow chart. EQ5D: EuroQol 5 Dimension questionnaire; FM: Fugl Meyer; ILA: implicit learning approach; MOCA: Montreal cognitive assessment; mRS: modified Rankin Scale; mRMI: modified Rivermead Mobility Index; MSRS: Movement Specific Reinvestment Scale; SwePASS: modified Postural Adjustment in Stroke Scale; NIHSS: National Institutes of Health Stroke Scale; SU: stroke unit.



Proposed Sample Size

The sample size is based on estimating the recruitment rate to a desired level, while also remaining mindful of the study’s other objectives. We anticipate being able to recruit 50.0% (60/120) of all eligible people. To ensure that our estimate of this rate has a 95% confidence interval no wider than 20% (ie, ±10%), we must approach 104 people (based on exact

confidence intervals [32]). As the study is cluster randomized, we must also account for this in our sample size. We aim to recruit 6 stroke units (chosen based on practicalities and ensuring we get a range of sites in which to implement the intervention, ie, hospitals of different sizes, and in different geographical locations). Assuming an intracluster correlation of 0.01, we require 120 people in total (15 per cluster). On the basis of 50%

recruitment rate, we anticipate 60 people will consent to the study, allowing us to estimate retention to within $\pm 14\%$. Each of the 6 sites will, therefore, be required to recruit 10 participants; keeping recruitment focused over a short time frame may also help to maintain treatment fidelity.

Analysis

Data will be stored and managed using the Statistical Package for Social Sciences software. Analysis will be performed by the trial statistician (SE) who will be blind to group allocation.

The unit of analysis is the individual patient. As this is a pilot study, analysis will primarily be descriptive. Descriptive methods will be used to estimate practicality of factors relating to the protocol, such as recruitment (proportion of eligible people who consent to the study) and retention (completion of outcome measures at 3 months).

Fidelity of the interventions will be established by comparing the number and type of coaching statements delivered to each group. We will describe the mean number of coaching statements per person (and the breakdown of these statements as externally or internally focused) in each group. Although we expect large differences, we will not formally test the difference as the study is not designed to do so; we will instead provide an estimate of the difference with corresponding 95% confidence interval. Differences in outcome and potential effect size for the Fugl Meyer SwePASS and mRMI be calculated using confidence interval estimation.

The CONSORT (Consolidated Standards of Reporting Trials) diagram can be found in [Multimedia Appendix 2](#).

Stage 3: Qualitative Evaluation

To enable us to understand patient and therapist perceptions and experiences of the ILA, we will invite a subset of participants to take part in the qualitative evaluation.

Patient Interviews

We will invite 20 participants (10 from the intervention arm and 10 from the control arm) to take part in a semistructured interview. These will be conducted within 1 week of the final treatment session to ensure that the intervention is recent enough for the patient to recall. The purpose is to provide an understanding of patient perceptions of the ILA (compared with standard care); identify if there are any differences in the experience of those receiving the ILA, versus standard care (eg, motivation); and determine the extent to which participants were aware of what was being learnt during their treatment sessions. Interviews will be conducted by the chief investigator (LJ). They will focus on patients' experiences of therapy and their perceptions of the benefits and disadvantages of the therapeutic style received. We will use maximum variation sampling to identify the sample and to include those with differing stroke severities (including differing levels of language and cognitive impairments), age, gender, and family/care situations.

Interviews will take place in hospital or in the patient's home, will last for approximately 45 min, and will be audio recorded. They will later be transcribed verbatim and thematically

analyzed by the chief investigator (LJ) and a second researcher. The topic guide can be found in [Multimedia Appendix 3](#).

Therapist Discussion Groups

Three discussion groups (1 at each *intervention* site), involving therapists who took part in the study, will take place at the end of the trial, after all treatment sessions have been delivered. All therapists and therapy assistants who are involved in delivering the ILA will be invited to take part. The structure and analysis of these groups will be based on Normalization Process Theory (NPT) [33,34]. NPT is a sociological theory that focuses on the process by which complex interventions are made workable and integrated into everyday practice. It is concerned with identifying and understanding the ways that people make sense of the work of implementing and integrating a complex intervention (coherence); how they engage with it (cognitive participation); enact it (collective action); and appraise its effects (reflexive monitoring) [33]. The topic guide for the discussion groups will be broadly structured around the NPT framework, using a similar approach to that described previously [35]. For example, we will explore therapists' views and beliefs relating to motor learning models, including their perceived impact and applicability within clinical practice. The insights gained from the discussion groups will give us a more valid understanding of the potential application of the ILA in clinical practice, thereby considering future implementation from the outset.

Results

Recruitment commenced in February 2019 and will take place over an 18-month period. We anticipate results to be available in 2021. The anticipated outputs from this trial will be as follows:

- A description of current therapy practice across the 6 sites, in relation to the application of implicit and explicit learning models
- An understanding of how well therapy teams can adapt their practice and maintain fidelity of the ILA within clinical practice (by comparing the quantity and focus of instructions/feedback given between intervention and control sites, alongside quantitative data from therapist focus groups and patient interviews)
- An estimate of the difference in treatment received between the intervention and control groups, based on the frequency of instructions and feedback and their FOA
- Evidence to inform the design of a phase III trial, including the following:
 - An estimate of recruitment and retention rates to inform the future recruitment strategy
 - Agreed randomization procedures
 - Identification of appropriate primary and secondary outcome measures
 - A measure of effect size and an estimation of the required sample size
- An understanding of both patient and therapist perceptions of the ILA.

Discussion

Overview

Retraining of movement following stroke requires knowledge of how to apply behavioral principles of learning within the clinical setting. To date, a number of researchers have highlighted implicit learning as an important concept in stroke rehabilitation [36-40], and the factors that promote implicit learning have been defined through expert consensus [2]. Namely, implicit learning can be biased through restricting the use of instructions and feedback, adopting an external FOA, and practicing the whole task where possible [2]. Given that many people with stroke will have impairments of cognition and/or language, it is feasible that ILAs, which reduce attentional demand and promote automaticity, are particularly valuable in this group. However, these concepts have not been robustly tested in clinical settings, and we lack evidence to guide rehabilitation professionals in how these approaches can be applied following stroke. We need to better understand how we can adopt fundamental principles of motor learning within the clinical setting, what works best, and for whom.

To date, much of the research in this field has investigated discrete aspects of an ILA. For example, simplifying the way in which multidisciplinary teams use instructions within an acute stroke setting [41] or promoting an external FOA [11,13,14,16]. Others have used different learning paradigms as a means of applying implicit learning in practice, including analogy learning [42,43] and errorless learning [12].

Strengths and Limitations

Despite a clear conceptual framework for how implicit learning can be biased [40], operationalizing an implicit approach is challenging within the complexities of stroke rehabilitation. To our knowledge, this is one of the first studies to examine the implicit learning paradigm in the acute phase following stroke. It is also one of the first studies to investigate implicit learning as a complex intervention, involving multiple contributory

elements. Thus, we are trialing the principle of the ILA, rather than a fixed version of it, accepting that practice may vary from therapist to therapist and from session to session. We are asking rehabilitation teams at the intervention sites to alter their whole approach to lower limb rehabilitation to maximize the bias toward implicit learning pathways and to do this throughout their intervention. The cluster randomized design is an important enabler of this and will give us the best chance of gaining fidelity among the intervention sites.

However, this approach has several methodological challenges, which will be explored through this pilot trial. In particular, how well therapy teams can maintain fidelity to an implicit approach, particularly when asked to apply it with a range of patients and over a period of time. Another key challenge relates to the “dose” of the implicit learning intervention, that is, how we ensure that there is sufficient bias toward implicit learning, such that there is a strong difference between the rehabilitation received by the intervention and the control groups in this study. This challenge is confounded by the fact that there is likely to be variability in the specific components of rehabilitation delivery received by the control groups. These differences may arise between individual therapists as well as between different sites. Our baseline period of observational data collection will allow us to understand and describe these differences, which will be further explored through the qualitative arm of the trial.

Conclusions

Findings from this pilot study will be used to design a phase III trial. The use of qualitative and quantitative methodologies, within a study design that is embedded within clinical services, will help to ensure that the trial remains clinically grounded. This enables us to best understand if and how implicit learning models can be applied within clinical settings. It will help us to design a future pragmatic (effectiveness) trial and will maximize potential for our future findings to be readily translated into clinical practice. This phased approach aligns to the model for developing, testing, and evaluating complex interventions, as outlined in the Medical Research Council guidelines [44].

Acknowledgments

LJ is funded by a National Institute of Health Research (NIHR) Clinical Lectureship for this research project. This project is funded by the NIHR (ICA-CL-2017-03-011). The views expressed are those of the author(s) and not necessarily those of the National Health Service, NIHR, or Department of Health and Social Care.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Overview of trial intervention.

[[PNG File, 44 KB - resprot_v8i11e14222_app1.png](#)]

Multimedia Appendix 2

CONSORT (Consolidated Standards of Reporting Trials) diagram.

[[PDF File \(Adobe PDF File\), 239 KB - resprot_v8i11e14222_app2.pdf](#)]

Multimedia Appendix 3

Participant interviews - topic guide.

[[PDF File \(Adobe PDF File\), 240 KB](#) - [resprot_v8i11e14222_app3.pdf](#)]

Multimedia Appendix 4

Peer-review report from the Department of Health, National Institute for Health Research.

[[PDF File \(Adobe PDF File\), 464 KB](#) - [resprot_v8i11e14222_app4.pdf](#)]

References

1. Kleynen M, Braun SM, Bleijlevens MH, Lexis MA, Rasquin SM, Halfens J, et al. Using a Delphi technique to seek consensus regarding definitions, descriptions and classification of terms related to implicit and explicit forms of motor learning. *PLoS One* 2014;9(6):e100227 [[FREE Full text](#)] [doi: [10.1371/journal.pone.0100227](https://doi.org/10.1371/journal.pone.0100227)] [Medline: [24968228](#)]
2. Kleynen M, Braun SM, Rasquin SM, Bleijlevens MH, Lexis M, Halfens J, et al. Multidisciplinary views on applying explicit and implicit motor learning in practice: an international survey. *PLoS One* 2015;10(8):e0135522 [[FREE Full text](#)] [doi: [10.1371/journal.pone.0135522](https://doi.org/10.1371/journal.pone.0135522)] [Medline: [26296203](#)]
3. Wulf G. Attentional focus and motor learning: a review of 15 years. *Int Rev Sport Exerc Psychol* 2013 Sep;6(1):77-104 [[FREE Full text](#)] [doi: [10.1080/1750984X.2012.723728](https://doi.org/10.1080/1750984X.2012.723728)]
4. Wulf G, Prinz W. Directing attention to movement effects enhances learning: a review. *Psychon Bull Rev* 2001 Dec;8(4):648-660. [doi: [10.3758/BF03196201](https://doi.org/10.3758/BF03196201)] [Medline: [11848583](#)]
5. Poolton JM, Maxwell JP, Masters RS, Raab M. Benefits of an external focus of attention: common coding or conscious processing? *J Sports Sci* 2006 Jan;24(1):89-99. [doi: [10.1080/02640410500130854](https://doi.org/10.1080/02640410500130854)] [Medline: [16368617](#)]
6. Winstein C, Schmidt RA. Reduced frequency of knowledge of results enhances motor skill learning. *J Exp Psychol* 1990;16(4):677-691. [doi: [10.1037/0278-7393.16.4.677](https://doi.org/10.1037/0278-7393.16.4.677)]
7. Lai Q, Shea CH. Generalized motor program (GMP) learning: effects of reduced frequency of knowledge of results and practice variability. *J Mot Behav* 1998 Mar;30(1):51-59. [doi: [10.1080/00222899809601322](https://doi.org/10.1080/00222899809601322)] [Medline: [20037020](#)]
8. Weeks DL, Kordus RN. Relative frequency of knowledge of performance and motor skill learning. *Res Q Exerc Sport* 1998 Sep;69(3):224-230. [doi: [10.1080/02701367.1998.10607689](https://doi.org/10.1080/02701367.1998.10607689)] [Medline: [9777659](#)]
9. Kal E, Prosée R, Winters M, van der Kamp J. Does implicit motor learning lead to greater automatization of motor skills compared to explicit motor learning? A systematic review. *PLoS One* 2018;13(9):e0203591 [[FREE Full text](#)] [doi: [10.1371/journal.pone.0203591](https://doi.org/10.1371/journal.pone.0203591)] [Medline: [30183763](#)]
10. Croce R, Horvat M, Roswal G. Augmented feedback for enhanced skill acquisition in individuals with traumatic brain injury. *Percept Mot Skills* 1996 Apr;82(2):507-514. [doi: [10.2466/pms.1996.82.2.507](https://doi.org/10.2466/pms.1996.82.2.507)] [Medline: [8724923](#)]
11. Fasoli SE, Trombly CA, Tickle-Degnen L, Verfaellie MH. Effect of instructions on functional reach in persons with and without cerebrovascular accident. *Am J Occup Ther* 2002;56(4):380-390. [doi: [10.5014/ajot.56.4.380](https://doi.org/10.5014/ajot.56.4.380)] [Medline: [12125827](#)]
12. Orrell AJ, Eves FF, Masters RS. Motor learning of a dynamic balancing task after stroke: implicit implications for stroke rehabilitation. *Phys Ther* 2006 Mar;86(3):369-380. [doi: [10.1093/ptj/86.3.369](https://doi.org/10.1093/ptj/86.3.369)] [Medline: [16506873](#)]
13. Durham KF, Sackley CM, Wright CC, Wing AM, Edwards MG, van Vliet P. Attentional focus of feedback for improving performance of reach-to-grasp after stroke: a randomised crossover study. *Physiotherapy* 2014 Jun;100(2):108-115. [doi: [10.1016/j.physio.2013.03.004](https://doi.org/10.1016/j.physio.2013.03.004)] [Medline: [23796803](#)]
14. Mückel S, Mehrholz J. Immediate effects of two attention strategies on trunk control on patients after stroke. A randomized controlled pilot trial. *Clin Rehabil* 2014 Jul;28(7):632-636. [doi: [10.1177/0269215513513963](https://doi.org/10.1177/0269215513513963)] [Medline: [24452700](#)]
15. Kim G, Hinojosa J, Rao A, Batavia M, O'Dell M. Randomized trial on the effects of attentional focus on motor training of the upper extremity using robotics with individuals after chronic stroke. *Arch Phys Med Rehabil* 2017 Oct;98(10):1924-1931. [doi: [10.1016/j.apmr.2017.06.005](https://doi.org/10.1016/j.apmr.2017.06.005)] [Medline: [28652064](#)]
16. Kal E, Houdijk H, van der Kamp J, Verhoef M, Prosée R, Groet E, et al. Are the effects of internal focus instructions different from external focus instructions given during balance training in stroke patients? A double-blind randomized controlled trial. *Clin Rehabil* 2019 Feb;33(2):207-221. [doi: [10.1177/0269215518795243](https://doi.org/10.1177/0269215518795243)] [Medline: [30168348](#)]
17. Piccoli A, Rossetini G, Cecchetto S, Viceconti A, Ristori D, Turolla A, et al. Effect of attentional focus instructions on motor learning and performance of patients with central nervous system and musculoskeletal disorders: a systematic review. *J Funct Morphol Kinesiol* 2018 Jul 25;3(3):40. [doi: [10.3390/jfmk3030040](https://doi.org/10.3390/jfmk3030040)]
18. Talvitie U. Socio-affective characteristics and properties of extrinsic feedback in physiotherapy. *Physiother Res Int* 2000;5(3):173-189. [doi: [10.1002/pri.197](https://doi.org/10.1002/pri.197)] [Medline: [10998774](#)]
19. Talvitie U, Reunanen M. Interaction between physiotherapists and patients in stroke treatment. *Physiotherapy* 2002 Feb;88(2):77-88. [doi: [10.1016/S0031-9406\(05\)60931-5](https://doi.org/10.1016/S0031-9406(05)60931-5)]
20. Durham K, van Vliet PM, Badger F, Sackley C. Use of information feedback and attentional focus of feedback in treating the person with a hemiplegic arm. *Physiother Res Int* 2009 Jun;14(2):77-90. [doi: [10.1002/pri.431](https://doi.org/10.1002/pri.431)] [Medline: [19107706](#)]
21. Johnson L, Burrige JH, Demain SH. Internal and external focus of attention during gait re-education: an observational study of physical therapist practice in stroke rehabilitation. *Phys Ther* 2013 Jul;93(7):957-966. [doi: [10.2522/ptj.20120300](https://doi.org/10.2522/ptj.20120300)] [Medline: [23559523](#)]

22. Stanton R, Ada L, Dean CM, Preston E. Feedback received while practicing everyday activities during rehabilitation after stroke: an observational study. *Physiother Res Int* 2015 Sep;20(3):166-173. [doi: [10.1002/pri.1612](https://doi.org/10.1002/pri.1612)] [Medline: [25451759](https://pubmed.ncbi.nlm.nih.gov/25451759/)]
23. Bugge C, Williams B, Hagen B, Logan J, Glazener C, Pringle S, et al. A process for Decision-making after pilot and feasibility trials (ADePT): development following a feasibility study of a complex intervention for pelvic organ prolapse. *Trials* 2013 Oct 25;14:353 [FREE Full text] [doi: [10.1186/1745-6215-14-353](https://doi.org/10.1186/1745-6215-14-353)] [Medline: [24160371](https://pubmed.ncbi.nlm.nih.gov/24160371/)]
24. Kwakkel G, Lannin NA, Borschmann K, English C, Ali M, Churilov L, et al. Standardized measurement of sensorimotor recovery in stroke trials: consensus-based core recommendations from the stroke recovery and rehabilitation roundtable. *Neurorehabil Neural Repair* 2017 Sep;31(9):784-792. [doi: [10.1177/1545968317732662](https://doi.org/10.1177/1545968317732662)] [Medline: [28934918](https://pubmed.ncbi.nlm.nih.gov/28934918/)]
25. Masters R, Maxwell J. The theory of reinvestment. *Int Rev Sport Exerc Psychol* 2008 Sep;1(2):160-183 [FREE Full text] [doi: [10.1080/17509840802287218](https://doi.org/10.1080/17509840802287218)]
26. Fugl-Meyer AR, Jääskö L, Leyman I, Olsson S, Stegling S. The post-stroke hemiplegic patient. 1. a method for evaluation of physical performance. *Scand J Rehabil Med* 1975;7(1):13-31. [doi: [10.4236/health.2012.412183_3,900](https://doi.org/10.4236/health.2012.412183_3,900)] [Medline: [1135616](https://pubmed.ncbi.nlm.nih.gov/1135616/)]
27. Persson CU, Sunnerhagen KS, Lundgren-Nilsson AJ. Rasch analysis of the modified version of the postural assessment scale for stroke patients: postural stroke study in Gothenburg (POSTGOT). *BMC Neurol* 2014 Jun 19;14:134 [FREE Full text] [doi: [10.1186/1471-2377-14-134](https://doi.org/10.1186/1471-2377-14-134)] [Medline: [24946807](https://pubmed.ncbi.nlm.nih.gov/24946807/)]
28. Persson CU, Linder A, Hagell P. Measurement properties of the Swedish modified version of the postural assessment scale for stroke patients (SwePASS) using Rasch analysis. *Eur J Phys Rehabil Med* 2017 Dec;53(6):848-855. [doi: [10.23736/S1973-9087.17.04607-X](https://doi.org/10.23736/S1973-9087.17.04607-X)] [Medline: [28497929](https://pubmed.ncbi.nlm.nih.gov/28497929/)]
29. Lennon S, Johnson L. The modified rivermead mobility index: validity and reliability. *Disabil Rehabil* 2000 Dec 15;22(18):833-839. [doi: [10.1080/09638280050207884](https://doi.org/10.1080/09638280050207884)] [Medline: [11197520](https://pubmed.ncbi.nlm.nih.gov/11197520/)]
30. van Swieten JC, Koudstaal PJ, Visser MC, Schouten HJ, van Gijn J. Interobserver agreement for the assessment of handicap in stroke patients. *Stroke* 1988 May;19(5):604-607. [doi: [10.1161/01.str.19.5.604](https://doi.org/10.1161/01.str.19.5.604)] [Medline: [3363593](https://pubmed.ncbi.nlm.nih.gov/3363593/)]
31. 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](https://doi.org/10.1007/s11136-011-9903-x)] [Medline: [21479777](https://pubmed.ncbi.nlm.nih.gov/21479777/)]
32. Morisette JT, Khorram S. Exact binomial confidence interval for proportions. *Photogramm Eng Rem S* 1998;64(4):281-282 [FREE Full text]
33. May CR, Mair F, Finch T, MacFarlane A, Dowrick C, Treweek S, et al. Development of a theory of implementation and integration: normalization process theory. *Implement Sci* 2009 May 21;4:29 [FREE Full text] [doi: [10.1186/1748-5908-4-29](https://doi.org/10.1186/1748-5908-4-29)] [Medline: [19460163](https://pubmed.ncbi.nlm.nih.gov/19460163/)]
34. Murray E, Treweek S, Pope C, MacFarlane A, Ballini L, Dowrick C, et al. Normalisation process theory: a framework for developing, evaluating and implementing complex interventions. *BMC Med* 2010 Oct 20;8:63 [FREE Full text] [doi: [10.1186/1741-7015-8-63](https://doi.org/10.1186/1741-7015-8-63)] [Medline: [20961442](https://pubmed.ncbi.nlm.nih.gov/20961442/)]
35. Blakeman T, Protheroe J, Chew-Graham C, Rogers A, Kennedy A. Understanding the management of early-stage chronic kidney disease in primary care: a qualitative study. *Br J Gen Pract* 2012 Apr;62(597):e233-e242 [FREE Full text] [doi: [10.3399/bjgp12X636056](https://doi.org/10.3399/bjgp12X636056)] [Medline: [22520910](https://pubmed.ncbi.nlm.nih.gov/22520910/)]
36. Boyd L, Winstein C. Providing explicit information disrupts implicit motor learning after basal ganglia stroke. *Learn Mem* 2004;11(4):388-396 [FREE Full text] [doi: [10.1101/lm.80104](https://doi.org/10.1101/lm.80104)] [Medline: [15286181](https://pubmed.ncbi.nlm.nih.gov/15286181/)]
37. Boyd L, Winstein C. Explicit information interferes with implicit motor learning of both continuous and discrete movement tasks after stroke. *J Neurol Phys Ther* 2006 Jun;30(2):46-57; discussion 58. [doi: [10.1097/01](https://doi.org/10.1097/01)] [Medline: [16796767](https://pubmed.ncbi.nlm.nih.gov/16796767/)]
38. Orrell A, Masters R, Eves FJ. Reinvestment and movement disruption following stroke. *Neurorehabil Neural Repair* 2009 Feb;23(2):177-183. [doi: [10.1177/1545968308317752](https://doi.org/10.1177/1545968308317752)] [Medline: [18987385](https://pubmed.ncbi.nlm.nih.gov/18987385/)]
39. Kal E, Winters M, van der Kamp J, Houdijk H, Groet E, van Bennekom C, et al. Is implicit motor learning preserved after stroke? A systematic review with meta-analysis. *PLoS One* 2016;11(12):e0166376 [FREE Full text] [doi: [10.1371/journal.pone.0166376](https://doi.org/10.1371/journal.pone.0166376)] [Medline: [27992442](https://pubmed.ncbi.nlm.nih.gov/27992442/)]
40. Kleynen M, Beurskens A, Olijve H, Kamphuis J, Braun S. Application of motor learning in neurorehabilitation: a framework for health-care professionals. *Physiother Theory Pract* 2018 Jun 19:1-20 (epub ahead of print)(forthcoming). [doi: [10.1080/09593985.2018.1483987](https://doi.org/10.1080/09593985.2018.1483987)] [Medline: [29920128](https://pubmed.ncbi.nlm.nih.gov/29920128/)]
41. Pavol MA, Bassile CC, Lehman JR, Harmon E, Ferreira N, Shinn B, et al. Modified approach to stroke rehabilitation (MAStR): feasibility study of a method to apply procedural memory concepts to transfer training. *Top Stroke Rehabil* 2018 Jul;25(5):351-358. [doi: [10.1080/10749357.2018.1458462](https://doi.org/10.1080/10749357.2018.1458462)] [Medline: [29609504](https://pubmed.ncbi.nlm.nih.gov/29609504/)]
42. Liao CM, Masters R. Analogy learning: a means to implicit motor learning. *J Sports Sci* 2001 May;19(5):307-319. [doi: [10.1080/02640410152006081](https://doi.org/10.1080/02640410152006081)] [Medline: [11354610](https://pubmed.ncbi.nlm.nih.gov/11354610/)]
43. Jie LJ, Kleynen M, Meijer K, Beurskens A, Braun S. The effects of implicit and explicit motor learning in gait rehabilitation of people after stroke: protocol for a randomized controlled trial. *JMIR Res Protoc* 2018 May 24;7(5):e142 [FREE Full text] [doi: [10.2196/resprot.9595](https://doi.org/10.2196/resprot.9595)] [Medline: [29793902](https://pubmed.ncbi.nlm.nih.gov/29793902/)]

44. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M, Medical Research Council Guidance. Developing and evaluating complex interventions: the new Medical Research Council guidance. *Br Med J* 2008 Sep 29;337:a1655 [FREE Full text] [doi: [10.1136/bmj.a1655](https://doi.org/10.1136/bmj.a1655)] [Medline: [18824488](https://pubmed.ncbi.nlm.nih.gov/18824488/)]

Abbreviations

CONSORT: Consolidated Standards of Reporting Trials

FOA: focus of attention

ILA: implicit learning approach

mRMI: modified Rivermead Mobility Index

NIHR: National Institute of Health Research

NPT: Normalization Process Theory

SwePASS: modified Postural Adjustment in Stroke Scale

Edited by G Eysenbach; submitted 01.04.19; peer-reviewed by M Pavol, E Kal; comments to author 11.05.19; revised version received 17.06.19; accepted 16.07.19; published 05.11.19.

Please cite as:

Johnson L, BurrIDGE J, Demain S, Ewings S

Comparing the Impact of an Implicit Learning Approach With Standard Care on Recovery of Mobility Following Stroke: Protocol for a Pilot Cluster Randomized Controlled Trial

JMIR Res Protoc 2019;8(11):e14222

URL: <https://www.researchprotocols.org/2019/11/e14222>

doi: [10.2196/14222](https://doi.org/10.2196/14222)

PMID: [31687935](https://pubmed.ncbi.nlm.nih.gov/31687935/)

©Louise Johnson, Jane BurrIDGE, Sara Demain, Sean Ewings. Originally published in JMIR Research Protocols (<http://www.researchprotocols.org>), 05.11.2019. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in JMIR Research Protocols, is properly cited. The complete bibliographic information, a link to the original publication on <http://www.researchprotocols.org>, as well as this copyright and license information must be included.

Protocol

A Mobile Health App to Improve HIV Medication Adherence: Protocol for a Pilot Randomized Controlled Trial

Susan Ramsey^{1,2}, PhD; Evan Ames², MA; Julia Uber², MA; Samia Habib², BS; Seth Clark^{1,2}, MD, MPH

¹The Warren Alpert Medical School of Brown University, Providence, RI, United States

²Rhode Island Hospital, Providence, RI, United States

Corresponding Author:

Susan Ramsey, PhD

The Warren Alpert Medical School of Brown University

111 Plain Street

Providence, RI, 02903

United States

Phone: 1 4014447831

Email: Susan_Ramsey@brown.edu

Abstract

Background: Adherence to antiretroviral therapy (ART) is essential for allowing persons living with HIV to live longer, healthier lives. However, a large portion of this population has suboptimal adherence and are not virally suppressed. Conventional interventions aimed at improving ART adherence lack portability and scalability, and improvements in adherence are not often sustained. Mobile health (mHealth) ART interventions offer a low-cost and accessible method of improving adherence, but many have limited functionality and do not offer comprehensive support. The combination of an mHealth intervention with a face-to-face adherence intervention and interactive health coaching feature may offer sufficient support in a manner that is sensitive to resource limitations that are often found in HIV treatment settings. This paper details the protocol of a study designed to evaluate the potential of an enhanced mHealth intervention for improving ART adherence.

Objective: The primary objective of this study is to assess the feasibility and acceptability of the Fitbit Plus app enhanced with a face-to-face LifeSteps session (Fitbit Plus condition) for improving ART adherence. In addition, we will determine the preliminary efficacy of the intervention by calculating treatment effect sizes.

Methods: This study will be conducted in 2 phases. The intervention will be developed and piloted with a small group of participants during phase 1. Pilot participants will provide feedback that will be used to refine the intervention for phase 2. In phase 2, a preliminary randomized controlled trial (RCT) comparing Fitbit Plus with a condition that approximates the standard of care (SOC) will be conducted with 60 persons living with HIV. Interviews will be conducted with RCT participants at baseline, and follow-up interviews will be conducted at 1, 3, 6, and 12 months. ART adherence is the primary outcome and will be monitored throughout the study via electronic pill boxes. Effect sizes will be generated using a fractional logit model estimated by generalized estimating equations.

Results: Phase 1 of this trial is complete; data collection for phase 2 is ongoing. Follow-ups with enrolled participants will conclude in January 2020.

Conclusions: This study will contribute to the literature on ART adherence and may produce an efficacious intervention. Owing to a small sample size, there may be insufficient power to detect statistically significant differences between Fitbit Plus and SOC. However, if Fitbit Plus is found to be acceptable and feasible and yields promising effect size estimates, this pilot study could serve as the foundation for a larger, fully powered trial of Fitbit Plus.

Trial Registration: ClinicalTrials.gov NCT02676128; <https://clinicaltrials.gov/ct2/show/NCT02676128>

International Registered Report Identifier (IRRID): DERR1-10.2196/15356

(*JMIR Res Protoc* 2019;8(11):e15356) doi:[10.2196/15356](https://doi.org/10.2196/15356)

KEYWORDS

HIV; medication adherence; mobile health

Introduction

Background

The Centers for Disease Control and Prevention estimates that 1.1 million people living in the United States are infected with HIV [1], with an estimated 38,739 new HIV diagnoses in 2017 alone [2]. Antiretroviral therapy (ART) is highly effective and allows persons living with HIV (PLWH) to live longer, healthier lives [3,4]. Despite the effectiveness of ART, only 60% of PLWH living in the United States achieve viral suppression [5]. Medication nonadherence is a significant contributor to unsuccessful viral suppression; a meta-analysis found that only an estimated 59% of participants in North American studies were adherent at the commonly accepted minimal threshold for successful viral suppression of 90% [6]. Although newer medications can produce viral suppression at lower levels of adherence, relatively high adherence is still necessary to avoid disease progression and shortened lifespan [7-9].

Given the significant public health problem presented by poor adherence to ART, a great deal of research has been devoted to improving adherence. Interventions have been developed to address poor ART adherence, with most studies demonstrating some degree of success [10]. LifeSteps, one of the early interventions in this area, is a single session intervention that incorporates motivational interviewing, cognitive-behavioral skills, and problem-solving components and is grounded in the Information-Motivation-Behavioral Skills Model of ART adherence [11-13]. It was found to improve adherence more rapidly when compared with a self-monitoring condition [12] and has been used in conjunction with cognitive behavioral therapy (CBT) interventions to improve ART adherence and reduce depressive symptoms in PLWH [11,14,15]. A noted shortcoming of ART adherence interventions is the tendency of their treatment effects to diminish over time [10]; most real-world clinical settings lack the resources necessary to sustain any adherence improvements that are achieved [10].

To address concerns of portability and sustainability of improvements from traditional ART adherence interventions, effort has also been directed at the development of mobile health (mHealth) ART adherence interventions. mHealth ART interventions allow greater accessibility than clinical settings and provide a low-cost option for continued intervention. To date, the bulk of the research in this area has focused on text message-based ART adherence interventions. A meta-analysis of text messaging interventions [16] found fairly modest but significant support for these interventions. However, most of the interventions examined were of short duration, which is noteworthy given the well-known challenges of habituation and response fatigue with these types of interventions.

Currently, there are hundreds of HIV-related mHealth apps marketed for PLWH on either Android or Apple platforms. Fortunately, a number of mHealth apps for PLWH have been found to be effective, as well as feasible and acceptable [17]. However, most current mHealth interventions have limited functionality, such as only offering medication reminders [17]. Another review highlighted key content areas that are not currently addressed by existing apps: resources regarding

psychological and emotional support and components that enhance linkage to treatment providers [18]. Therefore, more comprehensive mHealth interventions, which address multiple self-management needs of PLWH, are needed.

Evidence suggests that treatment supporters result in better adherence to ART [19]. Examples of treatment supporters include peer support sessions, home visits by nurses or counselors, case management, and provision of training in treatment support to a friend or family member of the patient. The importance of this type of adherence support has been found in other reviews as well [20,21].

Health coaches represent one type of treatment supporter. Health coaching has a patient-centered focus, involving patients in the process of goal setting [22]. Health coaches assist the patient in achieving a greater understanding of the patient's medical condition and encourage patient accountability [22]. Reviews of the general literature regarding health coaching conclude that the approach shows great promise for improving health outcomes [23,24].

Objective

One particular smartphone app that has shown promise in improving ART adherence incorporated personalized health-related information with medication reminders [25]. This paper outlines the protocol behind a study designed to extend and enhance this previous work. These enhancements include a face-to-face adherence intervention and an interactive health coaching feature, which were selected to address barriers and limitations of typical mobile adherence aids. At the conclusion of the study, we will be able to determine the feasibility, acceptability, and preliminary efficacy of this intervention.

Methods

Overview

To assess the feasibility, acceptability, and preliminary efficacy of the study intervention, we will develop and test the intervention through 2 phases. In phase 1, we will pilot and refine our face-to-face intervention and the use of our smartphone app (Fitbit Plus). In phase 2, we will conduct a randomized controlled trial (RCT) of 60 PLWH to examine the effect of the face-to-face intervention followed by Fitbit Plus (Fitbit Plus condition) compared with the face-to-face intervention alone, which approximates standard of care (SOC condition) in most HIV treatment settings. Participants in the RCT will complete a baseline interview and follow-up interviews at 1, 3, 6, and 12 months. The primary outcome will be ART adherence based on electronic pill box (EPB) data.

Participants and Recruitment

A total of 80 PLWH (n=20 in phase 1 and n=60 in phase 2) will be recruited from the Northeast region of the United States via community advertisement and in-person recruitment at an outpatient HIV treatment center. Persons will be eligible for the study if they are at least 18 years of age, have been prescribed ART, are living with HIV, have had a detectable viral load (>20 copies/mL) within the past 6 months, report less than 100% self-reported medication adherence, and have a smartphone that

is compatible with Fitbit Plus. Persons living with physical or cognitive impairment that could impede completion of the intervention or jeopardize informed consent, active psychosis, or who are not fluent in English will be excluded from participation. This study has been reviewed and approved by the first author's institutional review board.

After receiving a description of the study from research staff, anyone interested in participating will be asked to complete a screening interview. The screening interview, which will include a review of medical information, will assess eligibility and will be used to ensure no exclusion criteria are met. Demographic information, including age, gender, time since HIV diagnosis, mode of HIV transmission, and type of cell phone used will be collected as a part of the screening interview. For screening purposes, a single-item visual analog scale [26] will be used to measure ART adherence for the past month. In this measure, respondents are asked to rate percentage of prescribed doses taken in the past month on a visual analog scale ranging from 0% to 100%. We will confirm the absence of cognitive impairment using the University of California, San Diego Brief Assessment of Capacity to Consent measure [27] and the absence of active psychosis using the Mini-International Neuropsychiatric Interview (MINI) [28], with positive responses to the MINI further queried by doctoral-level study staff. Written informed consent will be obtained from those who are eligible; this will be obtained at the time of the screening interview for those who are screened in person or during the first in-person visit for those who are screened over the phone.

Phase 1: Development and Piloting Phase

Procedures

During phase 1, we will test the face-to-face adherence intervention followed by the use of Fitbit Plus with 5 to 10 PLWH. In-depth interviews will be conducted with these pilot participants after they have used Fitbit Plus for 3 months, in addition to brief phone interviews after 1 month of Fitbit Plus use, to gain an understanding of the strengths and limitations of the app as well as to garner feedback regarding the face-to-face session content. This feedback will guide refinement, and this process will then be repeated with another 5 to 10 PLWH. To enhance follow-up rates, participants in phase 1 will be paid US \$50 for completing the postintervention interview. The data collected from these participants regarding feasibility, acceptability, and barriers or challenges that would limit effectiveness will guide modifications to the intervention.

Face-to-Face Antiretroviral Therapy Adherence Intervention

Our single session face-to-face ART adherence intervention will be based on the LifeSteps intervention [11,12,14,15]. Consistent with the literature regarding efficacious adherence interventions [21,29], LifeSteps combines brief motivational interviewing, CBT, and problem-solving skills and is grounded in the IMB Skills Model of ART adherence [13]. During the development phase of the study, Fitbit Plus orientation material will be added to the face-to-face intervention that will be delivered to pilot participants and to RCT participants assigned to the Fitbit Plus condition. The introduction to Fitbit Plus will

include downloading the app to the participant's phone, entering the participant's ART medication schedule, and assisting the participant in formulating an ART adherence goal, which will be entered into the app so that both the patient and health coach can track progress toward the goal. Participants who do not have password protection enabled on their phones will be encouraged to activate this feature to protect the privacy of their information. During the orientation to Fitbit Plus, we will highlight that the interactive coaching feature is not intended for use in medical or other emergencies and that side effect and other medical questions should be directed to clinic treatment providers. Pilot participant feedback will guide refinement of the face-to-face intervention, including the Fitbit Plus orientation content, during phase 1 of the study.

The Mobile Health Antiretroviral Therapy Adherence App (Fitbit Plus)

An earlier version of Fitbit Plus (previously known as Twine) was found to show promise in improving ART adherence [25]. Fitbit Plus is fully Health Insurance Portability and Accountability Act compliant. The participant version of Fitbit Plus runs on an iPhone with iOS version 9.0+ or an Android phone with version 4.4+. The vast majority (94%) of smartphones in the United States use a platform (iOS or Android) that is compatible with Fitbit Plus [30]. Therefore, the proposed intervention could be disseminated readily. In addition to running on smartphones, the health coach version also runs on a Chrome, Firefox, or Safari Web browser or an iPad with iOS version 9.0+. The Fitbit Plus app that is compatible with any medication, includes medication reminders and tracking, and secure 2-way messaging. Fitbit Plus will generate a push notification at the time ART dosing should occur each day. After each push reminder, participants are prompted to click *yes* or *no* that they have taken their medication. Responding to the prompt requires only the single click of a text box, minimizing respondent burden.

On their "dashboards," health coaches will be able to monitor participants' adherence to ART in real time and identify participants whose adherence falls below optimal levels and may be in need of support, in addition to responding to participant requests for support or information. There is general support in the extant ART adherence literature for adherence monitoring and feedback [31,32]. Health coaches will support ART adherence through interactive secure messaging. Health coaches will provide support, encouragement, and resources, including links and attachments, via the messaging feature. At a minimum, health coaches will message participants at least weekly. In the development phase of the project, we will develop content that health coaches can send via the app to address commonly encountered situations that impede ART adherence (eg, stress/anxiety, depressive symptoms, substance use, and treatment fatigue). Coaching materials and strategies will also be refined based on pilot participant feedback. Fitbit Plus will allow us to examine utilization data for both the adherence tracking and interactive features.

Training and Supervision of Health Coaches

Health coaches will receive training and supervision in the face-to-face intervention and the interactive coaching component

of the mHealth ART adherence app from the first author who has extensive experience in the training, supervision, and delivery of interventions grounded in motivational interviewing and CBT. Training will include didactics, role-playing, and review of audiotaped sessions. Weekly supervision will be held to ensure competent and standardized delivery. All face-to-face sessions will be audiotaped, and the content of the interactive coaching messages delivered via Fitbit Plus will be logged. A randomly selected 30% (18/60) of face-to-face session recordings and Fitbit Plus coaching messages will be rated for health coach competence and adherence to intervention protocol.

Phase 2: Randomized Controlled Trial Phase

Procedures

After informed consent has been obtained, participants will complete a baseline interview (see [Table 1](#) for timeline of procedures). EPBs will be distributed at the conclusion of the baseline interview, with instructions to begin storing their ART medication in the EPB and to continue to adhere to their regimen as they normally would. Adherence will then be monitored for a 2-week period to establish a baseline adherence level. Participants will be randomized to Fitbit Plus or SOC using urn randomization [33] to ensure that the 2 groups are comparable

on important prognostic variables (number of years on ART, percent self-reported adherence on the visual analog scale [26], level of substance use reported on the Timeline Followback (TLFB) interview [34], and level of depressive symptoms reported on the Centers for Epidemiologic Studies-Depression Scale [35]). Participants assigned to the Fitbit Plus condition will receive the face-to-face intervention followed by 12 months of access to Fitbit Plus, whereas the SOC condition will receive the face-to-face session alone. Participants will be informed whether or not they are receiving the app during the face-to-face session, and only Fitbit Plus participants will receive an introduction to the app. Follow-up interviews will be conducted 1, 3, 6, and 12 months after the baseline interview. Participants in phase 2 will be compensated US \$25 for completion of the baseline interview and US \$30, US \$35, US \$40, and US \$50, respectively, for completion of the 1-, 3-, 6-, and 12-month follow-ups.

Measures

All data collection will be captured with a secure electronic data capture system developed by Vanderbilt University, REDCap. Paper versions of the assessments can be provided upon request but then will be entered by research staff into REDCap (see [Table 2](#) for schedule of assessments).

Table 1. Timing of participant enrollment, receipt of interventions, and assessment activities during phase 2.

| Timepoint | Enrollment (-t1) | Baseline (0) | Intervention start (+2 weeks) | Post allocation | | | |
|----------------------|------------------|----------------|-------------------------------|-----------------|-----------|-----------|------------|
| | | | | +1 month | +3 months | +6 months | +12 months |
| Enrollment | | | | | | | |
| Eligibility screen | ✓ ^a | — ^b | — | — | — | — | — |
| Informed consent | ✓ | — | — | — | — | — | — |
| Allocation | — | ✓ | — | — | — | — | — |
| Interventions | | | | | | | |
| Fitbit Plus | — | — | ✓ | ✓ | ✓ | ✓ | ✓ |
| Standard of care | — | — | ✓ | — | — | — | — |
| Assessments | | | | | | | |
| Primary outcomes | — | ✓ | — | ✓ | ✓ | ✓ | ✓ |
| Secondary outcomes | — | ✓ | — | ✓ | ✓ | ✓ | ✓ |
| Other outcomes | — | ✓ | — | ✓ | ✓ | ✓ | ✓ |

^aIndicates study activity will occur at the corresponding time-point.

^bNot applicable.

Table 2. Schedule of assessments.

| Measures | Baseline | 1-month follow-up | 3-month follow-up | 6-month follow-up | 12-month follow-up |
|--|----------------|-------------------|-------------------|-------------------|--------------------|
| ART^a adherence | | | | | |
| Electronic pill box data | ✓ ^b | ✓ | ✓ | ✓ | ✓ |
| Adult AIDS Clinical Trials Group medication questionnaire | ✓ | ✓ | ✓ | ✓ | ✓ |
| 3-item ART adherence questions | ✓ | ✓ | ✓ | ✓ | ✓ |
| Viral load | ✓ | — ^c | — | ✓ | ✓ |
| Potential treatment mechanisms | | | | | |
| LifeWindows information-motivation-behavioral skills ART questionnaire | ✓ | ✓ | ✓ | ✓ | ✓ |
| HIV Treatment Adherence Self-Efficacy Scale | ✓ | ✓ | ✓ | ✓ | ✓ |
| Potential moderators of treatment effects | | | | | |
| Timeline Followback | ✓ | ✓ | ✓ | ✓ | ✓ |
| Center for Epidemiological Studies-Depression Scale | ✓ | ✓ | ✓ | ✓ | ✓ |
| Fägerstrom Test for Nicotine Dependence | ✓ | ✓ | ✓ | ✓ | ✓ |
| Treatment received | | | | | |
| Treatment services review | ✓ | ✓ | ✓ | ✓ | ✓ |
| Use of medications | ✓ | ✓ | ✓ | ✓ | ✓ |
| Feasibility and acceptability | | | | | |
| Fitbit Plus satisfaction questionnaire | — | — | — | ✓ | ✓ |
| Semistructured interview | — | — | — | — | ✓ |

^aART: antiretroviral therapy.

^b✓ indicates measure will be administered at the corresponding time-point.

^cNot applicable.

Antiretroviral Therapy Adherence

MEMS Cap

ART adherence will be measured via EPB throughout the course of the study. Participants will be asked to bring the EPB to each follow-up interview. At each follow-up interview, adherence data (dates and times of pill bottle openings) will be downloaded from the EPB and then returned to the participant for continued medication adherence monitoring. At the last study visit (12-month follow-up), EPBs will be collected from participants, and all data will be downloaded and then deleted from the device.

Although this is an objective measure of adherence, there are limitations that should be noted. As the data from most EPBs must be downloaded using a specific device, there is a potential for data loss if a participant never brings the EPB to a study visit or misplaces it entirely. We will attempt to mitigate this in the following ways: (1) by reminding participants to bring the cap to every visit and (2) having replacements available should a participant report misplacing their EPB. These strategies have successfully minimized data loss in previous longitudinal studies of medication adherence [36-39].

In addition, adherence rates may be artificially inflated as EPBs record the date and time every time it is opened. It does not differentiate purposes for opening (eg, taking medication vs refilling pill bottle). EPBs could also potentially underestimate adherence rates owing to situations in which participants open the device, take out multiple doses, and then do not open the device again for several days but still take their medication (eg, pocketing doses for weekend travel). At each study appointment, participants will be asked if they can recall any instances in which they (1) opened the EPB but did not take medication or (2) took their medication but did not open the EPB. This information will be added to the EPB data to create a self-report corrected version of the EPB data. As is typically done in ART adherence studies (eg, [40]), we will consider the self-report corrected EPB data to be the primary ART adherence data. However, we will also conduct our planned data analyses on the uncorrected EPB data to bolster our confidence in the findings.

Self-Reported Adherence

Self-reported adherence will be collected at baseline and follow-up interviews using the Adult AIDS Clinical Trials Group medication questionnaire that asks participants to report

on the number of doses missed of their prescribed ART within the last 4 days [41]. We will also assess self-reported adherence with a 3-item ART adherence measure developed by Wilson and colleagues [42]. This brief measure has been found to have good psychometric properties and good construct validity when compared with electronic drug monitoring [42].

Viral Load

Viral load data will be collected at baseline and at the 6- and 12-month follow-up appointments. These data will be collected through a laboratory belonging to a hospital system in the Northeastern region of the United States. The laboratories use assays with sensitivity to detect viral load >20 copies/mL.

Potential Treatment Mechanisms

A total of 2 factors that may be mechanisms of successful treatment for improving ART adherence are motivation and self-efficacy. The LifeWindows IMB ART Adherence Questionnaire (LW-IMB-AAQ) [43] is designed to measure barriers to ART adherence that fall within the information, motivation, and behavioral skills areas. These areas are consistent with the IMB model of adherence [13]. Self-efficacy for adherence to HIV medications will be assessed using the HIV Treatment Adherence Self-Efficacy Scale (HIV-ASES), which has been shown to have robust internal consistency and reliability [44]. The HIV-ASES is a 12-item scale of patient confidence in their ability to carry out behaviors related to adhering to medication regimens. Responses range from 1 (“cannot do it at all”) to 10 (“completely certain can do it”). Item scores are averaged, with higher scores indicating higher adherence self-efficacy. The LW-IMB-AAQ and HIV-ASES will be administered at the baseline and follow-up interviews.

Potential Moderators of Treatment Effects

There are well established links between substance use, depressive symptoms, and poor ART adherence among PLWH [45-47]. Therefore, we will evaluate whether substance use and/or depressive symptoms moderate treatment effects. The TLFB interview will be administered to assess daily alcohol and drug use at baseline, as well as during the follow-up interviews. The TLFB interview is a calendar-assisted structured interview that provides a way to cue memory so that accurate recall of prior substance use is enhanced [48,49]. The TLFB interview has excellent reliability [50] and validity [48] and will provide data on the number of standard drinks consumed per day and types of drug classes used each day. At baseline, it will be administered to assess substance use during the 3 months before the interview. The Center for Epidemiological Studies-Depression Scale [35] will be used to measure level of depressive symptoms at baseline and follow-up interviews. This 20-item measure is widely used and has good sensitivity and specificity and high internal consistency [51]. Finally, nicotine dependence has also been associated with poor ART adherence [52,53]; thus, we will collect information about nicotine dependence during the baseline and follow-up interviews with the widely used Fagerstrom Test for Nicotine Dependence [54].

Treatment Received

The Treatment Services Review (TSR) [55] will be used to assess receipt of case management, psychiatric, substance use,

and other treatment services. At baseline, participants will be asked about services received in the previous 3 months. At follow-up interviews, they will be asked about services received since the previous interview. We will modify the TSR to ask specifically about HIV-related services received, including medical treatment for any ART-related side effects or HIV-related sequelae. Participants will also be asked to provide information regarding the use of medications for medical, psychiatric, or substance use indications. At baseline, patients will be asked to provide information regarding medications used in the past 3 months. At each follow-up interview, they will be asked to provide information concerning use of medications since the previous interview.

Feasibility and Acceptability

At the conclusion of the study, we will compile a patient eligibility rate, enrollment refusal rate, rate of recruitment, and follow-up completion rate to evaluate the feasibility of conducting a subsequent larger scale study using this protocol. We will also compile a study dropout rate and intervention session completion rate as indices of acceptability. Intervention acceptability and feasibility will also be assessed by asking participants randomized to receive Fitbit Plus satisfaction questions at the 6- and 12-month follow-ups. These questions will allow us to collect participants' overall opinions of the smartphone app and will allow us to observe whether satisfaction changes between 6 and 12 months. In addition, a semistructured interview will be completed with these participants at the 12-month follow-up to solicit additional information about the acceptability and feasibility of the intervention. More specifically, the semistructured interview will allow us to ask questions about different features of the app, what their favorite and least favorite aspects were, and if they have any recommendations for improvement.

Planned Analyses

Tests of the effects of treatment on the primary outcome variable (percent ART adherence based on corrected EPB data at 1-, 3-, 6-, and 12-month follow-ups) will be conducted using a fractional logit model [56] estimated by generalized estimating equations (GEEs) [57-59]. GEE is a quasi-likelihood estimation method of repeated measures analysis that allows for the inclusion of both categorical and continuous independent variables and for appropriate modeling of covariance structures when outcomes are correlated across time. The primary, between groups, independent variable in the above regression analysis is treatment group assignment. Variables measured at baseline will be examined using screening runs before primary analyses to see which of these baseline variables are most strongly associated with the primary outcome (adherence based on EPB data) in our sample. Those that show significant relationships with outcome will be entered as additional covariates in the primary analyses. The linear effect of time will also be included as a covariate in these analyses, as we assume that adherence rates will show a tendency to decrease over time. We will also test for nonlinear (ie, higher order) effects of time. Testing the time by group interaction will indicate the extent to which treatment differences are more or less pronounced closer in time to the intervention.

The same process described above for EPB adherence data will be employed to examine the impact of Fitbit Plus, relative to SOC, on the secondary measures of self-reported adherence percentage and viral load (dichotomized). Changes in viral load test assays have created inconsistencies in the literature in regard to level of viral load that is detectable. To be able to compare our results with the extant literature, we will dichotomize viral load at the 3 most commonly used levels (20, 50, and 200 copies/mL) and examine intervention effects using each of these levels. We will then explore potential mediators (motivation and self-efficacy) of the intervention effect on HIV medication adherence. This will be done using 2 common approaches to evaluating mediation mechanisms; Baron and Kenny's approach [60] and structural equation modeling [61,62].

In addition to the analyses that address the specific aims of the study, our data set will allow us to perform exploratory analyses that could enhance our understanding of ART adherence and may suggest avenues for future research. We will examine the temporal association between alcohol and drug use (TLFB) and missed ART doses. Using hierarchical linear models, we will regress daily ART adherence (based on EPB data) onto daily substance use. This will allow for the calculation of odds ratios that reflect the extent to which alcohol and drug use on a given day are associated with ART adherence on that day, relative to days in which participants refrained from using substances. Given that ART adherence will be examined dichotomously for these analyses, a logistic regression model will be specified in all analyses. More fine grained analyses will allow us to examine whether certain classes of drugs or level of alcohol consumption are temporally associated with missed ART doses.

Results

Funding for this project began in July 2015. Recruitment for phase 1 of this trial began in February 2016 and was completed in October 2016. Recruitment for phase 2 of this trial began in November 2016, and data collection is ongoing. A total of 53 participants have been enrolled in phase 2 and were randomized to treatment condition. At this time, the follow-up rate at the 12-month follow-up is 90%. It is anticipated that the final follow-up appointment will occur in January 2020. Formal analysis of deidentified data will proceed after the conclusion of data collection.

Discussion

There is a pressing need for more effective and accessible interventions for improving ART adherence given the high number of PLWH who are nonadherent and have not achieved

viral suppression [5,6]. This paper provides an outline of a protocol for a research study that aims to evaluate the acceptability, feasibility, and preliminary efficacy of an enhanced smartphone app intervention for improving adherence to ART among PLWH. Over a 2-phase design, this study will refine the Fitbit Plus intervention and compare this with an SOC condition in a preliminary RCT. The Fitbit Plus intervention is designed to overcome barriers and limitations of traditional mHealth apps for ART adherence [17]. Given the extant literature, we anticipate that Fitbit Plus will be feasible and acceptable and will improve ART adherence [31,32].

Although this study promises to contribute to the literature on ART adherence, there are also important limitations that need to be considered. As this is a pilot study, the sample size that will be recruited is sufficient for establishing acceptability and feasibility of the intervention. However, we may not be adequately powered to detect statistically significant differences between groups. This is especially true regarding analyses containing higher order effects and multiple predictors. Rather, our goal is to yield a stable effect size estimate of treatment effects that can be used to justify a larger scale RCT. In addition, persons younger than 18 years will be excluded from participation, limiting the generalizability of study findings. ART adherence among adolescents living with HIV is also a major public health concern [63]. Should this intervention be found efficacious within the current population, it will need to be tested among teenagers and young adults to determine if modification is required.

Despite the limitations outlined above, this study will contribute to the literature in very important ways. First, we will gain a preliminary understanding of whether the inclusion of an in-person adherence intervention session and a smartphone app with interactive health coaching improves ART adherence. In addition, we will also be able to explore whether Fitbit Plus helps to sustain treatment effects over a 12-month period. A further contribution of the proposed study is the examination of measures of putative mechanisms, grounded in the IMB model [13,64], through which Fitbit Plus may impact adherence. These analyses hold the potential to increase our understanding of the adherence intervention treatment mechanisms. Finally, our battery of assessment measures will allow us to conduct very interesting exploratory analyses. For example, we will be able to examine the temporal association between substance use and missed ART doses using data collected for each day during the course of the study. In summary, this study has the potential to produce an efficacious intervention for improving adherence to ART.

Acknowledgments

Research reported in this publication was supported by the National Institute of Mental Health of the National Institutes of Health under Award Number R34MH108431 to SR. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Conflicts of Interest

SR has an investigator-sponsored research agreement with Gilead Sciences, Inc, for the provision of medication for another trial.

References

1. Centers for Disease Control and Prevention. 2019. Estimated HIV Incidence and Prevalence in the United States 2010–2016 URL: https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-supplemental-report-vol-24-1.pdf?source=npin_highlight [accessed 2019-10-07]
2. Centers for Disease Control and Prevention. 2018. Diagnoses of HIV Infection in the United States and Dependent Areas, 2017 URL: <https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-2017-vol-29.pdf> [accessed 2019-10-07]
3. Chen LF, Hoy J, Lewin SR. Ten years of highly active antiretroviral therapy for HIV infection. *Med J Aust* 2007 Feb 5;186(3):146-151. [doi: [10.5694/j.1326-5377.2007.tb00839.x](https://doi.org/10.5694/j.1326-5377.2007.tb00839.x)] [Medline: [17309405](https://pubmed.ncbi.nlm.nih.gov/17309405/)]
4. Antiretroviral Therapy Cohort Collaboration. Life expectancy of individuals on combination antiretroviral therapy in high-income countries: a collaborative analysis of 14 cohort studies. *Lancet* 2008 Jul 26;372(9635):293-299 [FREE Full text] [doi: [10.1016/S0140-6736\(08\)61113-7](https://doi.org/10.1016/S0140-6736(08)61113-7)] [Medline: [18657708](https://pubmed.ncbi.nlm.nih.gov/18657708/)]
5. Centers for Disease Control and Prevention. 2018. Monitoring Selected National HIV Prevention and Care Objectives by Using HIV Surveillance Data United States and 6 Dependent Areas, 2016 URL: <https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-supplemental-report-vol-23-4.pdf> [accessed 2019-10-07]
6. Ortego C, Huedo-Medina TB, Llorca J, Sevilla L, Santos P, Rodríguez E, et al. Adherence to highly active antiretroviral therapy (HAART): a meta-analysis. *AIDS Behav* 2011 Oct;15(7):1381-1396. [doi: [10.1007/s10461-011-9942-x](https://doi.org/10.1007/s10461-011-9942-x)] [Medline: [21468660](https://pubmed.ncbi.nlm.nih.gov/21468660/)]
7. Paterson DL, Swindells S, Mohr J, Brester M, Vergis EN, Squier C, et al. Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Ann Intern Med* 2000 Jul 4;133(1):21-30. [doi: [10.7326/0003-4819-133-1-200007040-00004](https://doi.org/10.7326/0003-4819-133-1-200007040-00004)] [Medline: [10877736](https://pubmed.ncbi.nlm.nih.gov/10877736/)]
8. Bangsberg DR, Perry S, Charlebois ED, Clark RA, Roberston M, Zolopa AR, et al. Non-adherence to highly active antiretroviral therapy predicts progression to AIDS. *AIDS* 2001 Jun 15;15(9):1181-1183. [doi: [10.1097/00002030-200106150-00015](https://doi.org/10.1097/00002030-200106150-00015)] [Medline: [11416722](https://pubmed.ncbi.nlm.nih.gov/11416722/)]
9. Lima VD, Harrigan R, Bangsberg DR, Hogg RS, Gross R, Yip B, et al. The combined effect of modern highly active antiretroviral therapy regimens and adherence on mortality over time. *J Acquir Immune Defic Syndr* 2009 Apr 15;50(5):529-536 [FREE Full text] [doi: [10.1097/QAI.0b013e31819675e9](https://doi.org/10.1097/QAI.0b013e31819675e9)] [Medline: [19223785](https://pubmed.ncbi.nlm.nih.gov/19223785/)]
10. Simoni JM, Amico KR, Smith L, Nelson K. Antiretroviral adherence interventions: translating research findings to the real world clinic. *Curr HIV/AIDS Rep* 2010 Feb;7(1):44-51 [FREE Full text] [doi: [10.1007/s11904-009-0037-5](https://doi.org/10.1007/s11904-009-0037-5)] [Medline: [20425057](https://pubmed.ncbi.nlm.nih.gov/20425057/)]
11. Safren SA, Otto MW, Worth J. Life-steps: applying cognitive behavioral therapy to HIV medication adherence. *Cogn Behav Pract* 1999 Sep;6(4):332-341. [doi: [10.1016/S1077-7229\(99\)80052-2](https://doi.org/10.1016/S1077-7229(99)80052-2)]
12. Safren SA, Otto MW, Worth JL, Salomon E, Johnson W, Mayer K, et al. Two strategies to increase adherence to HIV antiretroviral medication: life-steps and medication monitoring. *Behav Res Ther* 2001 Oct;39(10):1151-1162. [doi: [10.1016/s0005-7967\(00\)00091-7](https://doi.org/10.1016/s0005-7967(00)00091-7)] [Medline: [11579986](https://pubmed.ncbi.nlm.nih.gov/11579986/)]
13. Fisher JD, Fisher WA, Amico KR, Harman JJ. An information-motivation-behavioral skills model of adherence to antiretroviral therapy. *Health Psychol* 2006 Jul;25(4):462-473. [doi: [10.1037/0278-6133.25.4.462](https://doi.org/10.1037/0278-6133.25.4.462)] [Medline: [16846321](https://pubmed.ncbi.nlm.nih.gov/16846321/)]
14. Safren SA, O'Cleirigh C, Tan JY, Raminani SR, Reilly LC, Otto MW, et al. A randomized controlled trial of cognitive behavioral therapy for adherence and depression (CBT-AD) in HIV-infected individuals. *Health Psychol* 2009 Jan;28(1):1-10 [FREE Full text] [doi: [10.1037/a0012715](https://doi.org/10.1037/a0012715)] [Medline: [19210012](https://pubmed.ncbi.nlm.nih.gov/19210012/)]
15. Safren SA, O'Cleirigh CM, Bullis JR, Otto MW, Stein MD, Pollack MH. Cognitive behavioral therapy for adherence and depression (CBT-AD) in HIV-infected injection drug users: a randomized controlled trial. *J Consult Clin Psychol* 2012 Jun;80(3):404-415 [FREE Full text] [doi: [10.1037/a0028208](https://doi.org/10.1037/a0028208)] [Medline: [22545737](https://pubmed.ncbi.nlm.nih.gov/22545737/)]
16. Finitis DJ, Pellowski JA, Johnson BT. Text message intervention designs to promote adherence to antiretroviral therapy (ART): a meta-analysis of randomized controlled trials. *PLoS One* 2014;9(2):e88166 [FREE Full text] [doi: [10.1371/journal.pone.0088166](https://doi.org/10.1371/journal.pone.0088166)] [Medline: [24505411](https://pubmed.ncbi.nlm.nih.gov/24505411/)]
17. Cooper V, Clatworthy J, Whetham J, Consortium E. mHealth interventions to support self-management in HIV: a systematic review. *Open AIDS J* 2017;11:119-132 [FREE Full text] [doi: [10.2174/1874613601711010119](https://doi.org/10.2174/1874613601711010119)] [Medline: [29290888](https://pubmed.ncbi.nlm.nih.gov/29290888/)]
18. Muessig KE, Pike EC, Legrand S, Hightow-Weidman LB. Mobile phone applications for the care and prevention of HIV and other sexually transmitted diseases: a review. *J Med Internet Res* 2013 Jan 4;15(1):e1 [FREE Full text] [doi: [10.2196/jmir.2301](https://doi.org/10.2196/jmir.2301)] [Medline: [23291245](https://pubmed.ncbi.nlm.nih.gov/23291245/)]
19. Chaiyachati KH, Ogbuoi O, Price M, Suthar AB, Negussie EK, Bärnighausen T. Interventions to improve adherence to antiretroviral therapy: a rapid systematic review. *AIDS* 2014 Mar;28(Suppl 2):S187-S204. [doi: [10.1097/QAD.0000000000000252](https://doi.org/10.1097/QAD.0000000000000252)] [Medline: [24849479](https://pubmed.ncbi.nlm.nih.gov/24849479/)]
20. Amico KR, Orrell C. Antiretroviral therapy adherence support: recommendations and future directions. *J Int Assoc Provid AIDS Care* 2013;12(2):128-137. [doi: [10.1177/1545109712459041](https://doi.org/10.1177/1545109712459041)] [Medline: [23334155](https://pubmed.ncbi.nlm.nih.gov/23334155/)]
21. Sandelowski M, Voils CI, Chang Y, Lee E. A systematic review comparing antiretroviral adherence descriptive and intervention studies conducted in the USA. *AIDS Care* 2009 Aug;21(8):953-966 [FREE Full text] [doi: [10.1080/09540120802626212](https://doi.org/10.1080/09540120802626212)] [Medline: [20024751](https://pubmed.ncbi.nlm.nih.gov/20024751/)]

22. Wolever RQ, Simmons LA, Sforzo GA, Dill D, Kaye M, Bechard EM, et al. A systematic review of the literature on health and wellness coaching: defining a key behavioral intervention in healthcare. *Glob Adv Health Med* 2013 Jul;2(4):38-57 [FREE Full text] [doi: [10.7453/gahmj.2013.042](https://doi.org/10.7453/gahmj.2013.042)] [Medline: [24416684](https://pubmed.ncbi.nlm.nih.gov/24416684/)]
23. Hill B, Richardson B, Skouteris H. Do we know how to design effective health coaching interventions: a systematic review of the state of the literature. *Am J Health Promot* 2015;29(5):e158-e168. [doi: [10.4278/ajhp.130510-LIT-238](https://doi.org/10.4278/ajhp.130510-LIT-238)] [Medline: [24720388](https://pubmed.ncbi.nlm.nih.gov/24720388/)]
24. Kivelä K, Elo S, Kyngäs H, Kääriäinen M. The effects of health coaching on adult patients with chronic diseases: a systematic review. *Patient Educ Couns* 2014 Nov;97(2):147-157. [doi: [10.1016/j.pec.2014.07.026](https://doi.org/10.1016/j.pec.2014.07.026)] [Medline: [25127667](https://pubmed.ncbi.nlm.nih.gov/25127667/)]
25. Perera AI, Thomas MG, Moore JO, Faasse K, Petrie KJ. Effect of a smartphone application incorporating personalized health-related imagery on adherence to antiretroviral therapy: a randomized clinical trial. *AIDS Patient Care STDS* 2014 Nov;28(11):579-586 [FREE Full text] [doi: [10.1089/apc.2014.0156](https://doi.org/10.1089/apc.2014.0156)] [Medline: [25290556](https://pubmed.ncbi.nlm.nih.gov/25290556/)]
26. Walsh JC, Mandalia S, Gazzard BG. Responses to a 1 month self-report on adherence to antiretroviral therapy are consistent with electronic data and virological treatment outcome. *AIDS* 2002 Jan 25;16(2):269-277. [doi: [10.1097/00002030-200201250-00017](https://doi.org/10.1097/00002030-200201250-00017)] [Medline: [11807312](https://pubmed.ncbi.nlm.nih.gov/11807312/)]
27. Jeste DV, Palmer BW, Appelbaum PS, Golshan S, Glorioso D, Dunn LB, et al. A new brief instrument for assessing decisional capacity for clinical research. *Arch Gen Psychiatry* 2007 Aug;64(8):966-974. [doi: [10.1001/archpsyc.64.8.966](https://doi.org/10.1001/archpsyc.64.8.966)] [Medline: [17679641](https://pubmed.ncbi.nlm.nih.gov/17679641/)]
28. First M, Spitzer R, Gibbon M, Williams J. Structured Clinical Interview for DSM-IV Axis I Disorders-Patient Edition. New York: New York State Psychiatric Institute; 1997.
29. Simoni JM, Pearson CR, Pantalone DW, Marks G, Crepaz N. Efficacy of interventions in improving highly active antiretroviral therapy adherence and HIV-1 RNA viral load. A meta-analytic review of randomized controlled trials. *J Acquir Immune Defic Syndr* 2006 Dec 1;43(Suppl 1):S23-S35 [FREE Full text] [doi: [10.1097/01.qai.0000248342.05438.52](https://doi.org/10.1097/01.qai.0000248342.05438.52)] [Medline: [17133201](https://pubmed.ncbi.nlm.nih.gov/17133201/)]
30. Nielsen. 2016. Millennials Are Top Smartphone Users URL: <http://www.nielsen.com/us/en/insights/news/2016/millennials-are-top-smartphone-users.html> [accessed 2017-12-27]
31. Sabin LL, DeSilva MB, Hamer DH, Xu K, Zhang J, Li T, et al. Using electronic drug monitor feedback to improve adherence to antiretroviral therapy among HIV-positive patients in China. *AIDS Behav* 2010 Jun;14(3):580-589 [FREE Full text] [doi: [10.1007/s10461-009-9615-1](https://doi.org/10.1007/s10461-009-9615-1)] [Medline: [19771504](https://pubmed.ncbi.nlm.nih.gov/19771504/)]
32. Krummenacher I, Cavassini M, Bugnon O, Schneider MP. An interdisciplinary HIV-adherence program combining motivational interviewing and electronic antiretroviral drug monitoring. *AIDS Care* 2011 May;23(5):550-561. [doi: [10.1080/09540121.2010.525613](https://doi.org/10.1080/09540121.2010.525613)] [Medline: [21271406](https://pubmed.ncbi.nlm.nih.gov/21271406/)]
33. Stout R, Wirtz P, Carbonari J, Boca F. Ensuring balanced distribution of prognostic factors in treatment outcome research. *J Stud Alcohol Suppl* 1994 Dec;12:70-75. [doi: [10.15288/jsas.1994.s12.70](https://doi.org/10.15288/jsas.1994.s12.70)] [Medline: [7723001](https://pubmed.ncbi.nlm.nih.gov/7723001/)]
34. Sobell L, Sobell M. Timeline Followback User's Guide: A Calendar Method for Assessing Alcohol and Drug Use. Toronto, Ontario, Canada: Addiction Research Foundation; 1996.
35. Radloff L. The CES-D scale: a self-report depression scale for research in the general population. *Appl Psychol Meas* 1977;1(3):385-401. [doi: [10.1177/014662167700100306](https://doi.org/10.1177/014662167700100306)]
36. Bova CA, Fennie KP, Knafl GJ, Dieckhaus KD, Watrous E, Williams AB. Use of electronic monitoring devices to measure antiretroviral adherence: practical considerations. *AIDS Behav* 2005 Mar;9(1):103-110. [doi: [10.1007/s10461-005-1685-0](https://doi.org/10.1007/s10461-005-1685-0)] [Medline: [15812617](https://pubmed.ncbi.nlm.nih.gov/15812617/)]
37. Deschamps AE, de Geest S, Vandamme A, Bobbaers H, Peetermans WE, van Wijngaerden E. Diagnostic value of different adherence measures using electronic monitoring and virologic failure as reference standards. *AIDS Patient Care STDS* 2008 Sep;22(9):735-743. [doi: [10.1089/apc.2007.0229](https://doi.org/10.1089/apc.2007.0229)] [Medline: [18754705](https://pubmed.ncbi.nlm.nih.gov/18754705/)]
38. Sorensen JL, Copeland AL. Drug abuse treatment as an HIV prevention strategy: a review. *Drug Alcohol Depend* 2000 Apr 1;59(1):17-31. [doi: [10.1016/s0376-8716\(99\)00104-0](https://doi.org/10.1016/s0376-8716(99)00104-0)] [Medline: [10706972](https://pubmed.ncbi.nlm.nih.gov/10706972/)]
39. Raiff B, Jarvis B, Dallery J. Text-message reminders plus incentives increase adherence to antidiabetic medication in adults with type 2 diabetes. *J Appl Behav Anal* 2016 Dec;49(4):947-953 [FREE Full text] [doi: [10.1002/jaba.337](https://doi.org/10.1002/jaba.337)] [Medline: [27417877](https://pubmed.ncbi.nlm.nih.gov/27417877/)]
40. Blashill AJ, Bedoya CA, Mayer KH, O'Cleirigh C, Pinkston MM, Remmert JE, et al. Psychosocial syndemics are additively associated with worse art adherence in HIV-infected individuals. *AIDS Behav* 2015 Jun;19(6):981-986 [FREE Full text] [doi: [10.1007/s10461-014-0925-6](https://doi.org/10.1007/s10461-014-0925-6)] [Medline: [25331267](https://pubmed.ncbi.nlm.nih.gov/25331267/)]
41. Chesney MA, Ickovics JR, Chambers DB, Gifford AL, Neidig J, Zwickl B, et al. Self-reported adherence to antiretroviral medications among participants in HIV clinical trials: the AACTG adherence instruments. Patient Care Committee & Adherence Working Group of the Outcomes Committee of the Adult AIDS Clinical Trials Group (AACTG). *AIDS Care* 2000 Jun;12(3):255-266. [doi: [10.1080/09540120050042891](https://doi.org/10.1080/09540120050042891)] [Medline: [10928201](https://pubmed.ncbi.nlm.nih.gov/10928201/)]
42. Wilson IB, Lee Y, Michaud J, Fowler FJ, Rogers WH. Validation of a new three-item self-report measure for medication adherence. *AIDS Behav* 2016 Nov;20(11):2700-2708 [FREE Full text] [doi: [10.1007/s10461-016-1406-x](https://doi.org/10.1007/s10461-016-1406-x)] [Medline: [27098408](https://pubmed.ncbi.nlm.nih.gov/27098408/)]

43. The LPT. The LifeWindows Information Motivation Behavioral Skills ART Adherence Questionnaire (LW-IMB-AAQ). University of Connecticut: Center for Health, Intervention, and Prevention 2006.
44. Johnson MO, Neilands TB, Dilworth SE, Morin SF, Remien RH, Chesney MA. The role of self-efficacy in HIV treatment adherence: validation of the HIV Treatment Adherence Self-Efficacy Scale (HIV-ASES). *J Behav Med* 2007 Oct;30(5):359-370 [FREE Full text] [doi: [10.1007/s10865-007-9118-3](https://doi.org/10.1007/s10865-007-9118-3)] [Medline: [17588200](https://pubmed.ncbi.nlm.nih.gov/17588200/)]
45. Blashill AJ, Perry N, Safren SA. Mental health: a focus on stress, coping, and mental illness as it relates to treatment retention, adherence, and other health outcomes. *Curr HIV/AIDS Rep* 2011 Dec;8(4):215-222 [FREE Full text] [doi: [10.1007/s11904-011-0089-1](https://doi.org/10.1007/s11904-011-0089-1)] [Medline: [21822626](https://pubmed.ncbi.nlm.nih.gov/21822626/)]
46. Gonzalez JS, Batchelder AW, Psaros C, Safren SA. Depression and HIV/AIDS treatment nonadherence: a review and meta-analysis. *J Acquir Immune Defic Syndr* 2011 Oct 1;58(2):181-187 [FREE Full text] [doi: [10.1097/QAI.0b013e31822d490a](https://doi.org/10.1097/QAI.0b013e31822d490a)] [Medline: [21857529](https://pubmed.ncbi.nlm.nih.gov/21857529/)]
47. Gonzalez A, Barinas J, O'Cleirigh C. Substance use: impact on adherence and HIV medical treatment. *Curr HIV/AIDS Rep* 2011 Dec;8(4):223-234. [doi: [10.1007/s11904-011-0093-5](https://doi.org/10.1007/s11904-011-0093-5)] [Medline: [21858414](https://pubmed.ncbi.nlm.nih.gov/21858414/)]
48. Sobell LC, Sobell MB. Validity of self-reports in three populations of alcoholics. *J Consult Clin Psychol* 1978 Oct;46(5):901-907. [doi: [10.1037//0022-006x.46.5.901](https://doi.org/10.1037//0022-006x.46.5.901)] [Medline: [701569](https://pubmed.ncbi.nlm.nih.gov/701569/)]
49. Sobell LC, Sobell MB. Convergent validity: an approach to increasing confidence in treatment outcome conclusions with alcohol and drug abusers. In: Sobell LC, Sobell MB, Ward E, editors. *Evaluating Alcohol and Drug Abuse Treatment Effectiveness: Recent Advances*. New York: Pergamon Press; 1980.
50. Sobell L, Maisto S, Sobell M, Cooper A. Reliability of alcohol abusers' self-reports of drinking behavior. *Behav Res Ther* 1979;17(2):157-160. [doi: [10.1016/0005-7967\(79\)90025-1](https://doi.org/10.1016/0005-7967(79)90025-1)] [Medline: [426744](https://pubmed.ncbi.nlm.nih.gov/426744/)]
51. Lewinsohn PM, Seeley JR, Roberts RE, Allen NB. Center for Epidemiologic Studies Depression Scale (CES-D) as a screening instrument for depression among community-residing older adults. *Psychol Aging* 1997 Jun;12(2):277-287. [doi: [10.1037//0882-7974.12.2.277](https://doi.org/10.1037//0882-7974.12.2.277)] [Medline: [9189988](https://pubmed.ncbi.nlm.nih.gov/9189988/)]
52. O'Cleirigh C, Valentine SE, Pinkston M, Herman D, Bedoya CA, Gordon JR, et al. The unique challenges facing HIV-positive patients who smoke cigarettes: HIV viremia, ART adherence, engagement in HIV care, and concurrent substance use. *AIDS Behav* 2015 Jan;19(1):178-185 [FREE Full text] [doi: [10.1007/s10461-014-0762-7](https://doi.org/10.1007/s10461-014-0762-7)] [Medline: [24770984](https://pubmed.ncbi.nlm.nih.gov/24770984/)]
53. Shuter J, Bernstein S. Cigarette smoking is an independent predictor of nonadherence in HIV-infected individuals receiving highly active antiretroviral therapy. *Nicotine Tob Res* 2008 Apr;10(4):731-736. [doi: [10.1080/14622200801908190](https://doi.org/10.1080/14622200801908190)] [Medline: [18418794](https://pubmed.ncbi.nlm.nih.gov/18418794/)]
54. Heatherton TF, Kozlowski LT, Frecker RC, Fagerström KO. The Fagerström Test for Nicotine Dependence: a revision of the Fagerström Tolerance Questionnaire. *Br J Addict* 1991 Sep;86(9):1119-1127. [doi: [10.1111/j.1360-0443.1991.tb01879.x](https://doi.org/10.1111/j.1360-0443.1991.tb01879.x)] [Medline: [1932883](https://pubmed.ncbi.nlm.nih.gov/1932883/)]
55. McLellan AT, Alterman AI, Cacciola J, Metzger D, O'Brien CP. A new measure of substance abuse treatment. Initial studies of the treatment services review. *J Nerv Ment Dis* 1992 Feb;180(2):101-110. [doi: [10.1097/00005053-199202000-00007](https://doi.org/10.1097/00005053-199202000-00007)] [Medline: [1737971](https://pubmed.ncbi.nlm.nih.gov/1737971/)]
56. Papke LE, Wooldridge JM. Panel data methods for fractional response variables with an application to test pass rates. *J Econ* 2008;145(1-2):121-133. [doi: [10.1016/j.jeconom.2008.05.009](https://doi.org/10.1016/j.jeconom.2008.05.009)]
57. Hall SM, Delucchi KL, Velicer WF, Kahler CW, Ranger-Moore J, Hedeker D, et al. Statistical analysis of randomized trials in tobacco treatment: longitudinal designs with dichotomous outcome. *Nicotine Tob Res* 2001 Aug;3(3):193-202. [doi: [10.1080/14622200110050411](https://doi.org/10.1080/14622200110050411)] [Medline: [11506764](https://pubmed.ncbi.nlm.nih.gov/11506764/)]
58. Liang K, Zeger SL. Longitudinal data analysis using generalized linear models. *Biometrika* 1986;73(1):13-22. [doi: [10.2307/2336267](https://doi.org/10.2307/2336267)]
59. Zeger SL, Liang K. Longitudinal data analysis for discrete and continuous outcomes. *Biometrics* 1986 Mar;42(1):121-130. [doi: [10.2307/2531248](https://doi.org/10.2307/2531248)] [Medline: [3719049](https://pubmed.ncbi.nlm.nih.gov/3719049/)]
60. Baron RM, Kenny DA. The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *J Pers Soc Psychol* 1986 Dec;51(6):1173-1182. [doi: [10.1037//0022-3514.51.6.1173](https://doi.org/10.1037//0022-3514.51.6.1173)] [Medline: [3806354](https://pubmed.ncbi.nlm.nih.gov/3806354/)]
61. Robins JM, Greenland S. Identifiability and exchangeability for direct and indirect effects. *Epidemiology* 1992 Mar;3(2):143-155. [doi: [10.1097/00001648-199203000-00013](https://doi.org/10.1097/00001648-199203000-00013)] [Medline: [1576220](https://pubmed.ncbi.nlm.nih.gov/1576220/)]
62. Pearl J. *Causality: Models, Reasoning, and Inference*. Cambridge, UK: Cambridge University Press; 2000.
63. UNICEF. *For Every Child, End AIDS: Seventh Stocktaking Report, 2016*. New York, NY: UNICEF; 2016.
64. Fisher JD, Amico KR, Fisher WA, Harman JJ. The information-motivation-behavioral skills model of antiretroviral adherence and its applications. *Curr HIV/AIDS Rep* 2008 Nov;5(4):193-203. [doi: [10.1007/s11904-008-0028-y](https://doi.org/10.1007/s11904-008-0028-y)] [Medline: [18838059](https://pubmed.ncbi.nlm.nih.gov/18838059/)]

Abbreviations

- ART:** antiretroviral therapy
- CBT:** cognitive behavioral therapy
- EPB:** electronic pill box

GEE: generalized estimating equation
HIV-ASES: HIV Treatment Adherence Self-Efficacy Scale
IMB: information-motivation-behavioral
LW-IMB-AAQ: LifeWindows IMB ART Adherence Questionnaire
mHealth: mobile health
MINI: Mini-International Neuropsychiatric Interview
PLWH: persons living with HIV
RCT: randomized controlled trial
SOC: standard of care
TLFB: Timeline Followback
TSR: Treatment Services Review

Edited by G Eysenbach; submitted 05.07.19; peer-reviewed by B Oh, D Finitsis; comments to author 30.08.19; accepted 31.08.19; published 13.11.19.

Please cite as:

Ramsey S, Ames E, Uber J, Habib S, Clark S

A Mobile Health App to Improve HIV Medication Adherence: Protocol for a Pilot Randomized Controlled Trial

JMIR Res Protoc 2019;8(11):e15356

URL: <http://www.researchprotocols.org/2019/11/e15356/>

doi: [10.2196/15356](https://doi.org/10.2196/15356)

PMID: [31719030](https://pubmed.ncbi.nlm.nih.gov/31719030/)

©Susan Ramsey, Evan Ames, Julia Uber, Samia Habib, Seth Clark. Originally published in JMIR Research Protocols (<http://www.researchprotocols.org>), 13.11.2019. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in JMIR Research Protocols, is properly cited. The complete bibliographic information, a link to the original publication on <http://www.researchprotocols.org>, as well as this copyright and license information must be included.

Protocol

Factors in Randomized Controlled Trials Reported to Impact the Implementation of Patient-Reported Outcome Measures Into Routine Care: Protocol for a Systematic Review

Natasha Anne Roberts^{1,2}, BN (Hons); Kimberly Alexander¹, PhD; David Wyld^{2,3}, MBBS; Monika Janda^{4,5}, PhD

¹School of Nursing, Queensland University of Technology, Kelvin Grove, Australia

²Cancer Care Services, Royal Brisbane and Women's Hospital, Herston, Australia

³School of Medicine, University of Queensland, St Lucia, Australia

⁴Centre for Health Services Research, University of Queensland, Woolloongabba, Australia

⁵Queensland University of Technology, Kelvin Grove, Australia

Corresponding Author:

Natasha Anne Roberts, BN (Hons)

School of Nursing

Queensland University of Technology

Musk Avenue

Kelvin Grove, 4059

Australia

Phone: 61 7 36468111

Email: n6.roberts@hdr.qut.edu.au

Abstract

Background: Patient-reported outcome measures (PROMs) are tools that enable patients to directly report their own assessments of well-being, or symptoms, in a structured and consistent way. Despite the usefulness of PROMs in optimizing health outcomes, their use in clinical practice is not routine. PROMs are complex to integrate into the clinical setting, with many elements potentially impacting on the success of implementation. For this reason, a protocol has been developed to guide a systematic review to collate information on implementation as presented in the randomized controlled trials (RCTs) to date.

Objective: The primary objective of this systematic review is to identify and synthesize factors available from RCT data about the fidelity of PROM interventions in clinical practice. The secondary objective will be an assessment of how implementation factors impact fidelity outcomes.

Methods: Preferred Reporting Items for Systematic Reviews and Meta-Analyses reporting standards will be followed. MEDLINE, EMBASE, and the Cumulative Index to Nursing and Allied Health Literature via OvidSP will be accessed using a defined search strategy. Grey literature and ClinicalTrials.gov will be reviewed for unpublished studies. Data extraction will be done to identify fidelity and factors impacting implementation, summarized using a narrative synthesis. An evidence-based implementation science framework will assist in identifying potential elements of importance and their effect on the process and outcomes of implementation. A meta-analysis to assess the impact of implementation factors will be attempted. A Cochrane risk of bias tool will be used.

Results: This protocol has received funding, and searches of databases will commence at the end of May 2019. It is planned that this systematic review will be finalized for publication in (December) 2019.

Conclusions: Applying an implementation science evidence-based framework to the published literature may identify factors present in the data that impact on the implementation of PROMs into routine clinical care. This systematic review aims to improve understanding of how these factors impact the fidelity of this intervention, so that PROMs can be more effectively used in the care of patients. This systematic review can also offer more detailed information about the process and outcomes of successful implementation of PROMs.

International Registered Report Identifier (IRRID): PRR1-10.2196/14579

(*JMIR Res Protoc* 2019;8(11):e14579) doi:[10.2196/14579](https://doi.org/10.2196/14579)

KEYWORDS

patient reported outcomes; PROs; PROMs; clinical practice; implementation; implementation science; iPARIHS

Introduction

Background

Patient-reported outcome measures (PROMs) offer the potential [1] to provide unique information that can be used by health professionals [2] to optimize both the health care pathway and outcomes for patients [3]. PROMs are valid and reliable assessment tools that collect information directly from patients and are defined by the Food and Drug Administration as “any report of the status of patient’s health condition that comes directly from the patient, without interpretation of the patient’s response by a clinician” (p. 508) [4]. The benefits that come from using PROMs are informed by the response to this information actioned by the health professionals, not by the completion of the report alone. With ever-increasing health care costs, the use of PROMs may optimize patient care, service delivery, and patient outcomes. They may also identify problems that have previously gone unnoticed and lead to increased service use [5]. Hospitals are moving to integrate PROMs into clinical settings, both for individual patient care and quality improvement activities as well as allocation of resources [5]. However, PROMs need to be successfully implemented in a health care setting so that patients and clinicians can use them as intended.

An understanding of what is impacting implementation can ensure the optimal use of a PROM intervention. This remains problematic, however, and despite the large body of research on the benefits of using PROMs for patient care [5-7], the uptake of these tools remains slow, indicating that their implementation may be ineffective if not done well, with a reason for poor implementation grounded in the complexity of health care systems [8].

The difficulties of implementation have been acknowledged in the literature. Guidelines developed by leading PROMs academics and published by the International Society of Quality of Life (ISOQOL) offer a tailored evidence-based approach to implementing PROMs into clinical practice by identifying the needs of the institution. In 2016, Porter et al [4] reviewed and evaluated the factors impacting on PROM implementation to develop a framework that specified the elements that should be considered in PROM implementation. The challenges identified in the study by Porter et al [4] focused largely on the disconnect between PROMs data and clinical pathways. Other systematic reviews of qualitative and nonrandomized research reported that the setting into which the PROMs were to be integrated had a significant effect on their implementation [4,9]. Antunes et al (2014) [10] conducted a systematic review on the use of PROMs in palliative care and identified that slow uptake was likely because of staff and setting-related elements. They proposed a need for ongoing coordination and education during implementation [10]. These are similar to the findings of the systematic review by Duncan et al [11] of the facilitators and barriers of PROMs use by allied health professionals. They attributed the contextual factors, such as organizational and peer

support, as having a significant impact on the success of PROM integration. Boyce et al [1] performed a systematic review of qualitative data describing staff experiences of PROM use and found that PROM usage was impacted if there was a lack of infrastructure to support staff in analyzing and acting on PROM data. What is consistently highlighted across these reviews is that the clinical setting and its stakeholders determine implementation success. A rapid scoping review of systematic reviews [12] was conducted to explore what evidence-based data were available regarding the implementation of PROMs. This scoping review demonstrated that there were some common factors impacting implementation of PROM, specifically, the engagement of staff, the use of technology, and pathways to respond to PROMs data.

None of the previous reviews, however, systematically extracted data about implementation issues from randomized controlled trials (RCTs) evaluating the use of PROMs. An RCT protocol design aims to ensure that the intervention is delivered as it is intended and also an outcome of successful implementation. Although not designed to measure implementation, RCTs have been purposefully designed to eliminate confounders and will report on these.

There is a lack of clear understanding of what influences successful PROM intervention implementation fidelity. This review may be useful to inform researchers on how to accurately measure implementation outcomes [13] and the implementation process [14].

Objective

The primary objective of this systematic review is to identify and synthesize factors available from RCT data about the fidelity of PROM interventions in clinical practice. These factors will then be structured around the Promoting Action on Research Implementation in Health Services (iPARIHS) implementation science framework, such as those relating to the context, participants, the intervention itself, or the study team facilitating the research.

The primary objective will be to assess intervention fidelity and if this has any influence on study outcomes. The secondary objective will be to describe any factors impacting fidelity and the processes and outcomes associated with these.

Research Question

This review will address the following research question:

What are the factors RCTs report that impact the implementation of PROMs into clinical practice?

Methods

Overview

This systematic review protocol has been registered in PROSPERO International Prospective Register of Systematic Reviews (CRD42017056138). It has been written according to the Preferred Reporting Items for Systematic Reviews and

Meta-Analyses (PRISMA) protocols [15]. The checklist is included as [Multimedia Appendix 1](#). The findings will be reported transparently [16,17] with a structured narrative synthesis [18]. If possible, a meta-analysis of implementation factors will be attempted.

Criteria for Considering Studies for This Review

Types of Studies

This systematic review will include RCTs that used PROMs with feedback provided to clinicians to support their decision making in the clinical setting. The control will be standard clinical practice or usual care. RCTs have been chosen because their design ascertains the enrollment of a relatively homogenous group of patients that are balanced between the intervention and control groups and control for the impact of confounders. A review of RCTs offers an opportunity to study the fidelity of implementing the PROM intervention and factors associated with better implementation in an optimized setting.

The focus of this review is the use of PROMs as an intervention for patient care in clinical practice, and any study that does not use a PROM intervention will be excluded. RCTs that use proxy PROM measures (ie, those completed by a carer) will also be excluded, as this review focuses only on reports collected directly from the patient.

Types of Participants

Participants will be any patients attending health care facilities, including hospital outpatients, specialist clinics, and health centers as well as the staff caring for them in these facilities, that is, patients completing PROMs reports and the clinicians responding to PROMs information.

Types of Interventions

The intervention will be the completion of PROMs by patients, with the results fed back to clinical staff to use in their ongoing clinical care.

Types of Outcome Measures

The primary outcome is intervention implementation fidelity, that is, whether the intervention was delivered as it was intended or not. Intervention fidelity will be assessed using the criteria described in the systematic review by Proctor et al [13]: (1) adherence to the program protocol, (2) dose or amount of program delivered, and (3) quality of the program delivery.

Search Methods for Identification of Studies

Electronic Searches

Searches of databases to be accessed for this step will include MEDLINE, EMBASE, and the Cumulative Index to Nursing and Allied Health Literature via the OvidSP website. All searches will be saved using an account established in each search database. Databases such as ClinicalTrials.gov will be searched for ongoing studies. Other sources of grey literature will be limited to clinical trial results reported in theses, dissertations, and conference papers. Field experts will be contacted.

Searching Other Resources

Field experts will be contacted for recommendations, and resources from the ISOQOL will be accessed. Reference lists of identified systematic reviews and studies will be searched to ensure a comprehensive list.

Data Collection

The findings will be reported listing all outcomes in tables [17], summarized using a structured narrative synthesis [18], and a quantitative meta-analysis using forest plots (if possible) to present the data will be performed [16].

Selection of Studies

Studies will be screened initially by retrieving abstracts to identify whether they meet the eligibility criteria. Screening will be done independently by NR and MJ. If a study is identified as eligible for inclusion, the full-text version will be retrieved. After review of the full text, if a study is subsequently decided as not eligible, it will be excluded. A PRISMA flowchart will be used to present this information [15].

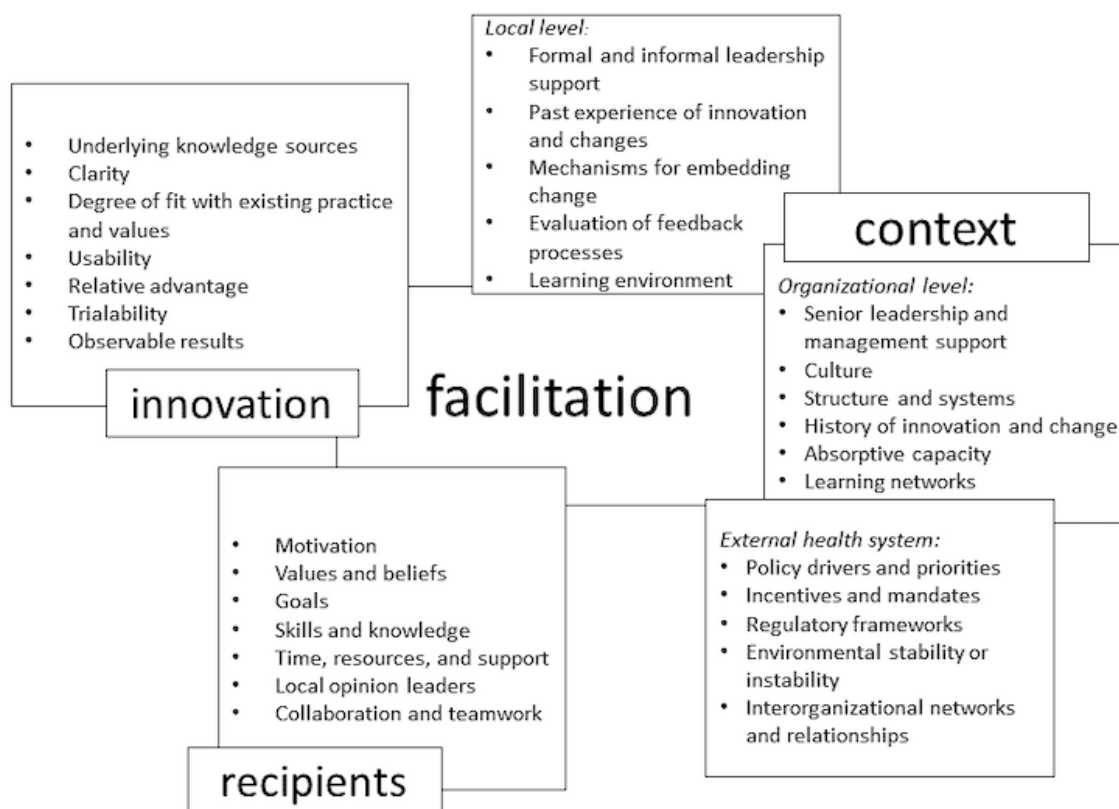
During the screening process, any discrepancies in the NR's and MJ's assessment of eligibility of the studies will be resolved by discussion. If this is not possible, the study will be referred to KA and DW for further input until a consensus is reached.

Data Extraction and Management

Endnote bibliographic software will be used to manage the literature by allocating studies using folders of *included*, *excluded*, and *for discussion*. Included studies will be entered for meta-analysis in RevMan 5.0. A database of the implementation data of included studies will be created during data extraction for narrative synthesis using Excel.

Data extraction will be done by NR and verified by MJ in 10% of studies. A data extraction table will be developed that, for each included study, states the research question, methodology, number of participants, primary outcome, secondary outcomes, tools used, and main findings to extract the demographics of the studies included.

Implementation data, including implementation strategies, process measurements, and outcome measurements will be extracted. The iPARIHS framework will be used to identify any implementation factors reported by study authors [19]. This information will be extracted using a content analysis approach. The key elements of iPARIHS are presented in [Figure 1](#). The framework identifies what is present in the context for those exposed to the intervention and within the intervention itself. This framework also acknowledges the role of a facilitator, which has been identified as important [1]. RCTs often have research staff facilitating the study, so the impact of this can also be measured. This framework has been successfully used in a number of clinical studies, such as the prevention of Methicillin-resistant *Staphylococcus aureus* [20] and the Eat Walk Engage protocol [21]. If reported, these factors will be defined as impacting outcomes [13] or processes of implementation [14].

Figure 1. Components of the integrated Promoting Action on Research Implementation in Health Services framework.

Assessment of Risk of Bias in Included Studies

Assessment of Methodological Quality and Risk of Bias

Other systematic reviews of efficacy have identified issues with study quality including attrition bias, performance bias, and a high risk of randomization bias for those health workers participating in the study [4,11]. Each study included will be assessed individually using the Cochrane risk of bias tool 2 (RoB 2.0).

This process will be carried out by the primary reviewers NR and MJ independently. If a consensus is needed, this will be addressed through discussion. If this is still not resolved, input will be sought from the other authors, KA and DW.

Analysis

Measures of Treatment Effect, Unit of Analysis Issues, and Dealing With Missing Data

All eligible studies will be included in the narrative synthesis irrespective of the dose, delivery, duration, or intensity of the intervention, that is, independent of how often the PROM is administered, how it is administered, the duration of the PROM intervention and follow-up, and the number of PROMs administered.

If a meta-analysis is possible, it will be performed through a standard approach, that is, dichotomous data effect sizes will be calculated as odds ratios with 95% confidence interval, continuous data will be converted into standardized mean differences (SMDs), and time to event data will be calculated as hazard ratios. SMDs will be used to accommodate differences

among PROM types reported by studies. If necessary, authors will be contacted if the report does not provide sufficient information. If the data cannot be obtained, the study will be excluded from the meta-analysis but still be included in the narrative synthesis. Similarly, studies with incomplete outcome data can still be included in the narrative synthesis if they report implementation factors.

Data Synthesis

A narrative data analysis approach [17,22] will be applied to the primary outcomes data collected based on the iPARIHS framework in Figure 1. This data will then be synthesized to describe intervention fidelity guided by the concepts presented in the study by Proctor et al [13]. The processes of implementation will be guided by the concepts described in the study by Powell et al [14]. Relationship within and between studies will be collated using mapping and tabulation of data [23]. The robustness of the synthesis will be assessed by comparing with previous systematic reviews, the scoping review, and study findings [18].

Meta-Analysis and Investigation of Heterogeneity

A meta-analysis will be performed to assess the impact of intervention fidelity on quality of life outcomes, provided there are sufficient data.

Stratified analysis of patient populations, for example, oncology, mental health, chronic diseases, will be attempted if there is heterogeneity in the data. Statistical heterogeneity will be assessed using I-square statistic to describe the variation across studies. There is likely to be heterogeneity in the evidence base because of enrolled patient populations or intervention design,

and for that reason, a random effects model will be needed. The variability in effect estimates because of heterogeneity, rather than sampling error, will be classified as the proportion of observed effects [23]. This process is expected to allow quantitative consolidation of findings across studies.

Sensitivity Analysis

A sensitivity analysis will be done by removing studies at high risk of bias as assessed by RoB 2.0, and the impact on study outcomes will be reported [23].

Results

This protocol has received funding. Searches of databases will commence at the end of May 2019. It is planned that this systematic review will be completed, and a paper will be finalized for publication in (December) 2019.

Discussion

This systematic review will have some limitations that will be addressed where possible. Limiting to RCTs may result in mainly positive studies, but this will be accounted for in the

final discussion of the systematic review. A search strategy confined to English language studies may result in a restricted assessment of health contexts and study findings. However, the search strategy is innovative, as the searches will extend beyond traditional databases and also include searches of clinical trial databases and consultation of experts in the field to capture any ongoing trials. The resulting systematic review can make a valuable contribution to the research knowledge.

PROMs have been shown to have the potential to improve both the processes of care and outcomes for patients. It is important to better understand how to translate these findings into clinical settings. This can ensure that the fidelity of future intervention can be improved, and outcomes can be achieved. An implementation science framework, such as iPARIHS, offers the opportunity in a systematic review to better identify the factors impacting on implementation. It is expected that the findings of this review can be used to describe the evidence available in RCTs investigating the use of PROMs in the clinical setting. This is important to rapidly progress PROMs in the clinical care of patients, as well as achieve better design and research studies in the future.

Acknowledgments

NR would like to acknowledge supervision and knowledge of her PhD supervisors MJ, KA, and DW. Appreciation also goes to the Metro North Research Unit and the Queensland University of Technology. She also thanks Cameron Rutter, liaison librarian at the Queensland University of Technology, for assistance in developing the search strategy and Lee Jones, statistician at the Queensland University of Technology, for helping her with the meta-analysis strategy. Funding has been provided through the Royal Brisbane and Women's Hospital Postgraduate Scholarship and Queensland University of Technology for an APA scholarship for periods of financial income support, as this review is completed as a part of PhD studies. This support has been reviewed and approved annually.

Authors' Contributions

This protocol has been developed as a part of postgraduate studies. NR collated this protocol with primary supervisory input from MJ and supervisory input from KA and DW.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Peer-reviewer report from the National Health and Medical Research Council, Australian Government.

[PDF File (Adobe PDF File), 52 KB - [resprot_v8i11e14579_app1.pdf](https://www.researchprotocols.org/2019/11/e14579_app1.pdf)]

References

1. Boyce MB, Browne JP, Greenhalgh J. The experiences of professionals with using information from patient-reported outcome measures to improve the quality of healthcare: a systematic review of qualitative research. *BMJ Qual Saf* 2014 Jun;23(6):508-518. [doi: [10.1136/bmjqs-2013-002524](https://doi.org/10.1136/bmjqs-2013-002524)] [Medline: [24505110](https://pubmed.ncbi.nlm.nih.gov/24505110/)]
2. Haywood KL, Garratt AM, Carrivick S, Mangnall J, Skevington SM. Continence specialists use of quality of life information in routine practice: a national survey of practitioners. *Qual Life Res* 2009 May;18(4):423-433. [doi: [10.1007/s11136-009-9459-1](https://doi.org/10.1007/s11136-009-9459-1)] [Medline: [19267220](https://pubmed.ncbi.nlm.nih.gov/19267220/)]
3. Spichiger E, Rieder E, Müller-Fröhlich C, Kesselring A. Fatigue in patients undergoing chemotherapy, their self-care and the role of health professionals: a qualitative study. *Eur J Oncol Nurs* 2012 Apr;16(2):165-171. [doi: [10.1016/j.ejon.2011.05.002](https://doi.org/10.1016/j.ejon.2011.05.002)] [Medline: [21624847](https://pubmed.ncbi.nlm.nih.gov/21624847/)]
4. 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](https://doi.org/10.2217/cer-2015-0014)] [Medline: [27427277](https://pubmed.ncbi.nlm.nih.gov/27427277/)]

5. Dawson J, Doll H, Fitzpatrick R, Jenkinson C, Carr AJ. The routine use of patient reported outcome measures in healthcare settings. *Br Med J* 2010 Jan 18;340:c186. [doi: [10.1136/bmj.c186](https://doi.org/10.1136/bmj.c186)] [Medline: [20083546](https://pubmed.ncbi.nlm.nih.gov/20083546/)]
6. Velikova G, Keding A, Harley C, Cocks K, Booth L, Smith AB, et al. Patients report improvements in continuity of care when quality of life assessments are used routinely in oncology practice: secondary outcomes of a randomised controlled trial. *Eur J Cancer* 2010 Sep;46(13):2381-2388. [doi: [10.1016/j.ejca.2010.04.030](https://doi.org/10.1016/j.ejca.2010.04.030)] [Medline: [20570138](https://pubmed.ncbi.nlm.nih.gov/20570138/)]
7. Basch E. Patient-reported outcomes - harnessing patients' voices to improve clinical care. *N Engl J Med* 2017 Jan 12;376(2):105-108. [doi: [10.1056/NEJMp1611252](https://doi.org/10.1056/NEJMp1611252)] [Medline: [28076708](https://pubmed.ncbi.nlm.nih.gov/28076708/)]
8. 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](https://doi.org/10.1007/s11136-011-0054-x)] [Medline: [22048932](https://pubmed.ncbi.nlm.nih.gov/22048932/)]
9. Wagle NW. NEJM Catalyst. 2017. Implementing Patient-Reported Outcome Measures URL: <https://catalyst.nejm.org/implementing-proms-patient-reported-outcome-measures/> [accessed 2019-10-10]
10. Antunes B, Harding R, Higginson IJ, EUROIMPACT. Implementing patient-reported outcome measures in palliative care clinical practice: a systematic review of facilitators and barriers. *Palliat Med* 2014 Feb;28(2):158-175. [doi: [10.1177/0269216313491619](https://doi.org/10.1177/0269216313491619)] [Medline: [23801463](https://pubmed.ncbi.nlm.nih.gov/23801463/)]
11. Duncan EA, Murray J. The barriers and facilitators to routine outcome measurement by allied health professionals in practice: a systematic review. *BMC Health Serv Res* 2012 May 22;12:96 [FREE Full text] [doi: [10.1186/1472-6963-12-96](https://doi.org/10.1186/1472-6963-12-96)] [Medline: [22506982](https://pubmed.ncbi.nlm.nih.gov/22506982/)]
12. Roberts N, Janda M, Alexander K, Wyld D. Implementing Patient Reported Outcomes into clinical practice: a scoping review, systematic review and meta-analysis. In: *Psycho-Oncology Supplement 3.: Psycho-oncology; 2017 Presented at: International Psychooncology Society Congress; August 14-18 2017; Berlin p. 811.*
13. 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;38(2):65-76 [FREE Full text] [doi: [10.1007/s10488-010-0319-7](https://doi.org/10.1007/s10488-010-0319-7)] [Medline: [20957426](https://pubmed.ncbi.nlm.nih.gov/20957426/)]
14. Powell BJ, McMillen JC, Proctor EK, Carpenter CR, Griffey RT, Bunger AC, et al. A compilation of strategies for implementing clinical innovations in health and mental health. *Med Care Res Rev* 2012 Apr;69(2):123-157 [FREE Full text] [doi: [10.1177/1077558711430690](https://doi.org/10.1177/1077558711430690)] [Medline: [22203646](https://pubmed.ncbi.nlm.nih.gov/22203646/)]
15. 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 2;350:g7647 [FREE Full text] [doi: [10.1136/bmj.g7647](https://doi.org/10.1136/bmj.g7647)] [Medline: [25555855](https://pubmed.ncbi.nlm.nih.gov/25555855/)]
16. Higgins J, Green S. Cochrane Training. 2011. Cochrane Handbook for Systematic Reviews of Interventions URL: <http://www.handbook.cochrane.org> [accessed 2017-09-01]
17. Anderson LM, Oliver SR, Michie S, Rehfuess E, Noyes J, Shemilt I. Investigating complexity in systematic reviews of interventions by using a spectrum of methods. *J Clin Epidemiol* 2013 Nov;66(11):1223-1229. [doi: [10.1016/j.jclinepi.2013.06.014](https://doi.org/10.1016/j.jclinepi.2013.06.014)] [Medline: [23953087](https://pubmed.ncbi.nlm.nih.gov/23953087/)]
18. Campbell M, Thomson H, Katikireddi SV, Sowden A. Reporting of narrative synthesis in systematic reviews of public health interventions: a methodological assessment. *The Lancet* 2016;388:S34. [doi: [10.1016/s0140-6736\(16\)32270-x](https://doi.org/10.1016/s0140-6736(16)32270-x)]
19. Harvey G, Kitson A. PARIHS revisited: from heuristic to integrated framework for the successful implementation of knowledge into practice. *Implement Sci* 2016 Mar 10;11:33 [FREE Full text] [doi: [10.1186/s13012-016-0398-2](https://doi.org/10.1186/s13012-016-0398-2)] [Medline: [27013464](https://pubmed.ncbi.nlm.nih.gov/27013464/)]
20. Balbale SN, Hill JN, Guihan M, Hogan TP, Cameron KA, Goldstein B, et al. Evaluating implementation of methicillin-resistant Staphylococcus aureus (MRSA) prevention guidelines in spinal cord injury centers using the PARIHS framework: a mixed methods study. *Implement Sci* 2015 Sep 09;10:130 [FREE Full text] [doi: [10.1186/s13012-015-0318-x](https://doi.org/10.1186/s13012-015-0318-x)] [Medline: [26353798](https://pubmed.ncbi.nlm.nih.gov/26353798/)]
21. Mudge AM, McRae P, Cruickshank M. Eat walk engage: an interdisciplinary collaborative model to improve care of hospitalized elders. *Am J Med Qual* 2015;30(1):5-13. [doi: [10.1177/1062860613510965](https://doi.org/10.1177/1062860613510965)] [Medline: [24270172](https://pubmed.ncbi.nlm.nih.gov/24270172/)]
22. Arai L, Britten N, Popay J, Roberts H, Petticrew M, Rodgers M, et al. Testing methodological developments in the conduct of narrative synthesis: a demonstration review of research on the implementation of smoke alarm interventions. *Evid Policy* 2007;3(3):361-383. [doi: [10.1332/174426407781738029](https://doi.org/10.1332/174426407781738029)]
23. Cochrane Effective Practice and Organisation of Care. URL: <http://epoc.cochrane.org> [accessed 2017-09-01]

Abbreviations

- iPARIHS:** Promoting Action on Research Implementation in Health Services
ISOQOL: International Society of Quality of Life
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROM: patient-reported outcome measurement
RCT: randomized controlled trial
ROB: risk of bias

SMD: standardized mean difference

Edited by G Eysenbach; submitted 03.05.19; peer-reviewed by J Walsh, M Barwick; comments to author 15.06.19; revised version received 26.06.19; accepted 27.06.19; published 26.11.19.

Please cite as:

Roberts NA, Alexander K, Wyld D, Janda M

Factors in Randomized Controlled Trials Reported to Impact the Implementation of Patient-Reported Outcome Measures Into Routine Care: Protocol for a Systematic Review

JMIR Res Protoc 2019;8(11):e14579

URL: <http://www.researchprotocols.org/2019/11/e14579/>

doi: [10.2196/14579](https://doi.org/10.2196/14579)

PMID: [31769763](https://pubmed.ncbi.nlm.nih.gov/31769763/)

©Natasha Anne Roberts, Kimberly Alexander, David Wyld, Monika Janda. Originally published in JMIR Research Protocols (<http://www.researchprotocols.org>), 26.11.2019. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in JMIR Research Protocols, is properly cited. The complete bibliographic information, a link to the original publication on <http://www.researchprotocols.org>, as well as this copyright and license information must be included.

Protocol

Prevalence of Malnutrition Among Elderly People in Iran: Protocol for a Systematic Review and Meta-Analysis

Homeira Khoddam^{1*}, MSc, PhD; Sepideh Eshkevarlaji^{2*}, MSc; Mahin Nomali^{3*}, MSc; Mahnaz Modanloo^{1*}, MSc, PhD; Abbas Ali Keshtkar^{4*}, MD, PhD

¹Nursing Research Center, Golestan University of Medical Sciences, Gorgan, Islamic Republic of Iran

²School of Nursing and Midwifery, Golestan University of Medical Sciences, Gorgan, Islamic Republic of Iran

³Department of Epidemiology & Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Islamic Republic of Iran

⁴Department of Health Sciences Education Development, School of Public Health, Tehran University of Medical Sciences, Tehran, Islamic Republic of Iran

* all authors contributed equally

Corresponding Author:

Mahnaz Modanloo, MSc, PhD

Nursing Research Center

Golestan University of Medical Sciences

Hirkan Boulevard

Gorgan, 4934174515

Islamic Republic of Iran

Phone: 98 9112739242

Email: modanloo.mahnaz@goums.ac.ir

Abstract

Background: Malnutrition occurs following a decrease or an imbalance in the absorption of energy, protein, vitamins, and minerals because of numerous factors. Thus, it has serious and life-threatening consequences. To plan for this issue, we need information on the burden of this problem.

Objective: The aim of this study is to determine the prevalence of malnutrition among elderly people in Iran.

Methods: For the purpose of this study, papers, including original articles, theses, and conference proceedings on the prevalence of malnutrition among people aged 60 years and above, and have been published in national and international journals until September 2018 will be included without any language limitation. The following keywords along with their synonyms in Persian will be used in the literature search: malnutrition, elderly, and Iran. At first, the screening process will be conducted based on our inclusion and exclusion criteria. Then, the full text of the remaining articles will be read carefully, and eligible articles will be selected according to the objectives of the study. Next, the methodological quality of the selected papers will be reviewed, and the required information will be extracted from those with acceptable quality. Finally, a meta-analysis will be performed using the Stata software (version 14) when optimum criteria are met. It should be noted that all stages of screening, selection, quality assessment of primary studies, and data extraction will be performed by two reviewers independently.

Results: This review is ongoing and will be completed at the end of 2019.

Conclusions: This review aims to provide comprehensive evidence about the prevalence of malnutrition among elderly people in Iran. This can help Iranian health managers and policy makers make informed decisions for preventing malnutrition and promoting the health status of elderly people.

Trial Registration: PROSPERO CRD42018115358; <https://tinyurl.com/y28su47m>

International Registered Report Identifier (IRRID): DERR1-10.2196/15334

(*JMIR Res Protoc* 2019;8(11):e15334) doi:[10.2196/15334](https://doi.org/10.2196/15334)

KEYWORDS

malnutrition; systematic review; aged; prevalence; Iran

Introduction

Description of the Condition

Rapid population growth is a result of positive social, economic, and health trends, which has not only changed the demographic pattern but has also significantly increased the life expectancy from about 48 years in the early 1950s to about 68 years in the early 21st century [1]. Therefore, both developed and developing countries have been faced with a growth in the aging population, which is considered as an important health challenge [2].

In most countries, the chronological age of 60 years has been considered as the beginning of old age [3]. According to the World Health Organization (WHO), the number of older people will reach 1.5 billion by 2050, and the majority of these people will be living in developing countries [1,4]. At the same time, the percentage of people aged over 60 years in Iran is expected to increase from 5.2% (in 2000) to 21.7% (in 2050) [5]. As one of the most important phases of life, old age is accompanied with a wide range of long-term conditions such as chronic illnesses, cognitive problems, physical weakness, anorexia, and chewing and swallowing problems that can disturb the nutritional balance and result in malnutrition [6-11]. Although any age group may suffer from malnutrition, it is most common among older people because of the comorbidities and changes in physiological and psychosocial characteristics of people in this age group [12].

Malnutrition has serious and life-threatening consequences that are known to be major causes of increased mortality among the elderly [13,14]. According to the WHO, nutritional disorders are one of the most common causes of death in the elderly [15]. In addition, complications of malnutrition, including osteoarthritis, osteoporosis, diabetes, cardiovascular disease, and hypertension, impose a significant social and economic burden on elderly people [10,16,17].

The prevalence of malnutrition in elderly people in different countries of the world varies between 10% and 60% [18-33]. Some of these differences are because of the variations in using the measurement tools, study setting, and demographic groups that have been studied [34-36].

Despite the high prevalence reported, it seems that the real prevalence is beyond the reports, as a significant proportion of malnourished individuals are not identified until nutritional deficiencies lead to significant physical changes [34]. On the basis of the issues mentioned above, it seems that the risk of malnutrition among elderly people is a major challenge to the health care systems around the world and needs a special and urgent attention [37].

Importance of This Review

Over the past decades, despite the scientific community's desire to conduct studies on the malnutrition of the elderly, there is a large knowledge gap in this area [38]. More importantly, research findings and health practices and policies on this issue are not interconnected, and therefore, informed strategies are not used [37]. In fact, all countries need to integrate the health care policies and researches on the prevention and treatment of malnutrition [35,37].

Iran, like many other countries, has been faced with a remarkable shift in population composition and needs to prepare to address this upcoming challenge. Although some actions such as revisiting the educational system and setting up new care settings for the elderly have been taking place, the role of research findings to inform decisions and policies is neglected.

Several studies have been conducted to determine the prevalence and risk factors of malnutrition in the elderly in Iran [39-50], and these studies have reported different and incomparable prevalence data. The wide discrepancy in the study results limits the use of such evidence for relevant national planning and policy making [29]. We need to synthesize and summarize the evidence on this issue, which would help us bridge the evidence-practice gap and promote the health care decisions and services to elderly people [35]. This aim can be achieved through systematic reviews and meta-analysis of context-based studies.

There are 3 published systematic reviews on malnutrition among elderly people; however, in one of them, hospitalized patients were the studied population [51], and another review had some significant shortcomings such as nonsystematic approach and incomprehensive search [52]. The third one is a systematic review and meta-analysis conducted in 2016 on the malnutrition outbreak among older people in Iran living with families or in nursing homes [26]. This study also had some limitations, including the lack of comprehensiveness in searching and a priori registration or publication of review protocol, using the reporting tool (Strengthening the Reporting of Observational Studies in Epidemiology) to evaluate the risk of bias, and failure to determine the source of heterogeneity. Thus, we designed this study to address the limitations of previous systematic reviews and provide a comprehensive evidence on the prevalence of malnutrition among aged people in Iran.

Objectives

Primary Objective

The primary objective is to assess the prevalence of malnutrition among aged people in Iran.

Secondary Objectives

The secondary objectives are (1) to evaluate the prevalence of malnutrition among elderly people in Iran according to the assessment tools, study setting, severity of the problem, and regional setting and (2) to evaluate the heterogeneity and determine its potential causes.

Methods

This protocol has been reported based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocol checklist [53].

Eligibility Criteria

Types of Studies

In this systematic review, we will include all studies that reported the prevalence of malnutrition among elderly people in Iran or provided main data to calculate this measure. These

may be included as descriptive and observational studies. We will include population-based prevention clinical trials, cohort studies, and case-control studies if the baseline data were available and consistent with the objectives of this systematic review.

Types of Participants

We will include studies conducted on people of both genders, aged 60 years and above, who live in elderly nursing homes or are community indwelling elders. Studies on hospitalized elderly people will be excluded. There will be no restriction in terms of race and ethnicity.

Type of Measuring Tools

We will include studies that measured and reported malnutrition by using standard and valid measuring tools (questionnaire, anthropometric, or biological indices).

Sample Size

We will include studies with a minimum sample size of 30.

Search Methods for the Identification of Studies

Electronic Searches

A comprehensive search will be conducted in local and international databases to obtain published and unpublished articles until September 30, 2018.

PubMed, Scopus, and Web of Science are the international databases that will be searched. In addition, the local databases that will be searched include Iranian Databases of Medical literature, Scientific Information Database, Magiran, Iran Medical Sciences Thesis Database and the Iranian Research Institute for Information Science and Technology.

Furthermore, relevant gray literature (eg, thesis or dissertations and conference papers) will be included by searching in the international and local databases and Google Scholar search engine. We will not consider any language limitation.

We will test the primary search strategy ([Multimedia Appendix 1](#)) in PubMed, the main database in the field of medical sciences. At first, we will find equivalent keywords from Medical Subject Headings database and will create appropriate syntaxes for PubMed. Then, we will adopt it for other databases.

Searching Other Resources

To ensure access to all relevant articles and to find those not previously found, the list of included articles, references, and the relevant national and international organizations' reports, such as WHO, will be searched manually.

Data Collection and Analysis

Selection of Studies

The study selection will be done in 2 stages. At first, the search results will be imported into the reference manager software (EndNote X7, Thomson Reuters) for storage and organization. After detecting and deleting duplicates, 2 researchers (SE and HKH) will screen the titles and abstracts of all retrieved documents based on the inclusion and exclusion criteria. Then, the full text of potentially eligible studies will be screened

independently by the same researchers to finalize the review and start data extraction. Any disagreement between reviewers will be resolved by discussing or consulting with a third person.

Irrelevant articles, which do not meet the inclusion criteria, will be deleted by providing reasons. All the mentioned steps will be presented on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram [54].

If there is a lack of access to the full text of some studies or if there is any unclear information, the researchers will contact the corresponding author thrice during a period of 7 to 14 days [55,56]. We will report all the missing data if we cannot find them. At the end, all other eligible articles retrieved from other sources will be added to the final list.

Data Extraction and Management

At this stage, the 2 researchers will independently extract data from the included articles using data extraction form. The data extraction form includes review information; bibliographic data such as authors, title, year, issue; and study data such as design, setting/context, year, sample size, sampling method, data gathering method, data collection period, participants, and main results. Data extraction will be done by 2 independent reviewers (MM and HKH), and any disagreement will be resolved by discussing or consulting with a third expert person.

Assessment of Risk of Bias in Included Studies

The quality assessment and risk of bias of the included studies will be assessed by 2 independent assessors (MN and SE), and the strategy of discussion or consulting with a third reviewer will be applied in case of disagreement. For assessing the observational studies, assessors will use a 10-item rating tool developed by Hoy et al [57] in 2012. This tool has been developed based on literature review, expert opinion, and the researchers' experiences and has a high interrater agreement in assessing the quality of prevalence studies. On the basis of this, each item scores 0 for the response *No* and 1 for *Yes*. The total score will be between 0 and 10 [57]. We will use the Cochrane Collaboration tool for assessing the clinical trials [58]. The result of risk of bias and quality assessment will be presented in a table.

Dealing With Missing Data

We will deal with missing data using 2 strategies. In case of missing the full text of studies from the review, or if there is any unclear information, the researchers will contact the corresponding author(s) thrice during a period of 7 to 14 days [55,56]. When outcome data are not reported, we will calculate the outcome data if there is additional information in the publications [59,60]. However, if these 2 strategies are not successful, we will analyze only the available data and report all missing data and discuss their impact on the findings [59].

Assessment of Heterogeneity

We will assess the heterogeneity among studies by using forest plot, I-square (I^2) test, and Cochran Q test [61-63]. The significance level of less than 0.05 and I^2 equal to or more than 50% will be assumed as a severe heterogeneity. In cases of severe heterogeneity, subgroup analysis considering age, gender,

elderly residency, and malnutrition severity will be performed to identify the potential source of heterogeneity.

Assessment of Reporting Bias

We will check the possibility of publication bias graphically (funnel plot) and statistically (Egger test) [61,64], using Stata software, version 12 (StataCorp LP). A *P* value of less than .05 will be considered as statistically significant or nonignorable publication bias.

Data Synthesis and Analysis of Outcomes

The main outcome of this review is malnutrition. If there are enough studies reporting the prevalence of malnutrition in elderly people, we will do a meta-analysis to calculate the pooled estimate of prevalence and subgroups analysis (gender, age, and residence place) 95% CIs using Stata software.

On the basis of the level of methodological heterogeneity, we will use fixed or random effects model to conduct meta-analyses [61].

Subgroup Analysis and Investigation of Heterogeneity

On the basis of the quality of heterogeneity, subgroup analysis will be conducted on the following variables: age, sex, geographical region, residency (nursing home/home), risk (at risk or affected), and severity of malnutrition. By this way, the potential sources of heterogeneity will be identified.

Sensitivity Analysis

Although the need for doing sensitivity analysis is not often specified before completing the systematic review and

meta-analysis [61], we will use it to determine the impact of the quality of the study, study design, sample size, and methods of analysis, if needed. In fact, this is a repeated meta-analysis to assess the robustness of the process of selection and inclusion of the studies [65].

Results

This protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) on December 23, 2018. We will report this systematic review and meta-analysis based on the PRISMA checklist. The flow diagram will be drawn to show the systematic search and selection process of articles. In addition, the table of excluded studies and the reasons for their exclusion will be presented.

Discussion

Systematic reviews and meta-analyses can synthesize and summarize the best knowledge available from health care studies for reducing gaps between evidence and practice [66]. This study presents a protocol for systematic review and meta-analysis targeted to provide comprehensive evidence about the prevalence of malnutrition among elderly people in Iran. The result of this review can provide a context-based evidence to help Iranian health managers and policy makers to make informed decisions for preventing malnutrition and promoting the health status of elderly people.

Acknowledgments

This protocol is the product of a thesis for the fulfillment of Master of Science degree in geriatric nursing at the School of Nursing and Midwifery, Golestan University of Medical Sciences (Gorgan, Iran). This project has been approved, and monetary aid was granted by the Research and Technology Department, Golestan University of Medical Sciences. The authors wish to thank the Golestan University of Medical Sciences.

Authors' Contributions

All authors contributed to design the systematic review, perform the preliminary search, and prepare and revise the full and PROSPERO versions of the protocol.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Search strategy developed for PubMed.

[DOCX File, 12 KB - [resprot_v8i11e15334_app1.docx](#)]

Multimedia Appendix 2

Peer-reviewer report from the Nursing Research Center, Golestan University of Medical Sciences.

[PDF File (Adobe PDF File), 504 KB - [resprot_v8i11e15334_app2.pdf](#)]

References

1. United Nation Population Fund. 2012. UNFPA Annual Report 2011 URL: <https://www.unfpa.org/publications/unfpa-annual-report-2011> [accessed 2019-04-04]

2. World Health Organization launches new initiative to address the health needs of a rapidly ageing population. *Cent Eur J Public Health* 2004 Dec;12(4):210, 216. [Medline: [15672498](#)]
3. World Health Organization. 2018. Proposed working definition of an older person in Africa for the MDS Project URL: <http://www.who.int/healthinfo/survey/ageingdefolder/en/> [accessed 2019-04-04]
4. World Health Organization. Health situation and trend assessment: Elderly population URL: http://www.searo.who.int/entity/health_situation_trends/data/chi/elderly-population/en/ [accessed 2019-04-04]
5. Statistical Center of Iran. 2015. General population and housing census 2014 URL: <http://www.amar.org.ir/> [accessed 2019-04-04]
6. Mastronuzzi T, Grattagliano I. Nutrition as a health determinant in elderly patients. *Curr Med Chem* 2019;26(19):3652-3661. [doi: [10.2174/0929867324666170523125806](#)] [Medline: [28545376](#)]
7. Saka B, Kaya O, Ozturk GB, Erten N, Karan MA. Malnutrition in the elderly and its relationship with other geriatric syndromes. *Clin Nutr* 2010 Dec;29(6):745-748. [doi: [10.1016/j.clnu.2010.04.006](#)] [Medline: [20627486](#)]
8. Shlisky J, Bloom DE, Beaudreault AR, Tucker KL, Keller HH, Freund-Levi Y, et al. Nutritional considerations for healthy aging and reduction in age-related chronic disease. *Adv Nutr* 2017 Jan;8(1):17-26 [FREE Full text] [doi: [10.3945/an.116.013474](#)] [Medline: [28096124](#)]
9. van der Schueren MA, Guaitoli PR, Jansma EP, de Vet HC. A systematic review of malnutrition screening tools for the nursing home setting. *J Am Med Dir Assoc* 2014 Mar;15(3):171-184. [doi: [10.1016/j.jamda.2013.10.006](#)] [Medline: [24290910](#)]
10. Vega A. Nutritional issues in older adults. *Top Clin Nutr* 2015;30(3):247-263. [doi: [10.1097/tin.0000000000000038](#)]
11. Wada H. [Problems and strategies in the treatment of mental disorders in elderly patients with physical illness]. *Nihon Ronen Igakkai Zasshi* 2000 Nov;37(11):885-888 [FREE Full text] [doi: [10.3143/geriatrics.37.885](#)] [Medline: [11193361](#)]
12. Marshall S, van der Meij BS, Milte R, Collins CE, de van der Schueren MA, Banbury M, et al. Family in rehabilitation, empowering carers for improved malnutrition outcomes: protocol for the freer pilot study. *JMIR Res Protoc* 2019 Apr 30;8(4):e12647 [FREE Full text] [doi: [10.2196/12647](#)] [Medline: [31038466](#)]
13. Pirlich M, Lochs H. Nutrition in the elderly. *Best Pract Res Clin Gastroenterol* 2001 Dec;15(6):869-884. [doi: [10.1053/bega.2001.0246](#)] [Medline: [11866482](#)]
14. Ülger Z, Halil M, Kalan I, Yavuz BB, Cankurtaran M, Güngör E, et al. Comprehensive assessment of malnutrition risk and related factors in a large group of community-dwelling older adults. *Clin Nutr* 2010 Aug;29(4):507-511. [doi: [10.1016/j.clnu.2010.01.006](#)] [Medline: [20117863](#)]
15. World Health Organization. 2011. Global Health and Aging URL: https://www.who.int/ageing/publications/global_health.pdf [accessed 2019-04-04]
16. Bernstein M. Nutritional needs of the older adult. *Phys Med Rehabil Clin N Am* 2017 Nov;28(4):747-766. [doi: [10.1016/j.pmr.2017.06.008](#)] [Medline: [29031341](#)]
17. van der Schueren MA, Lonterman-Monach S, de Vries OJ, Danner SA, Kramer MH, Muller M. Prevalence and determinants for malnutrition in geriatric outpatients. *Clin Nutr* 2013 Dec;32(6):1007-1011. [doi: [10.1016/j.clnu.2013.05.007](#)] [Medline: [23755842](#)]
18. Cabrera MA, Mesas AE, Garcia AR, de Andrade SM. Malnutrition and depression among community-dwelling elderly people. *J Am Med Dir Assoc* 2007 Nov;8(9):582-584. [doi: [10.1016/j.jamda.2007.07.008](#)] [Medline: [17998114](#)]
19. Cuervo M, García A, Ansorena D, Sánchez-Villegas A, Martínez-González MA, Astiasarán I, et al. Nutritional assessment interpretation on 22,007 Spanish community-dwelling elders through the Mini Nutritional Assessment test. *Public Health Nutr* 2009 Jan;12(1):82-90. [doi: [10.1017/S136898000800195X](#)] [Medline: [18413012](#)]
20. Harris D, Haboubi N. Malnutrition screening in the elderly population. *J R Soc Med* 2005 Sep;98(9):411-414 [FREE Full text] [doi: [10.1258/jrsm.98.9.411](#)] [Medline: [16140852](#)]
21. Ramon JM, Subirà C. [Prevalence of malnutrition in the elderly Spanish population]. *Med Clin (Barc)* 2001 Dec 15;117(20):766-770. [doi: [10.1016/s0025-7753\(01\)72252-x](#)] [Medline: [11784503](#)]
22. Smoliner C, Norman K, Wagner K, Hartig W, Lochs H, Pirlich M. Malnutrition and depression in the institutionalised elderly. *Br J Nutr* 2009 Dec;102(11):1663-1667. [doi: [10.1017/S0007114509990900](#)] [Medline: [19622192](#)]
23. Vedantam A, Subramanian V, Rao NV, John KR. Malnutrition in free-living elderly in rural south India: prevalence and risk factors. *Public Health Nutr* 2010 Sep;13(9):1328-1332. [doi: [10.1017/S1368980009991674](#)] [Medline: [19807935](#)]
24. Verbrugge M, Beeckman D, van Hecke A, Vanderwee K, van Herck K, Clays E, et al. Malnutrition and associated factors in nursing home residents: a cross-sectional, multi-centre study. *Clin Nutr* 2013 Jun;32(3):438-443. [doi: [10.1016/j.clnu.2012.09.008](#)] [Medline: [23089280](#)]
25. Ribeiro RS, Rosa MI, Bozzetti MC. Malnutrition and associated variables in an elderly population of Criciúma, SC. *Rev Assoc Med Bras (1992)* 2011;57(1):56-61 [FREE Full text] [doi: [10.1016/s0104-4230\(11\)70017-3](#)] [Medline: [21390461](#)]
26. Abolghasem Gorji H, Alikhani M, Mohseni M, Moradi-Joo M, Ziaifar H, Moosavi A. The prevalence of malnutrition in Iranian elderly: a review article. *Iran J Public Health* 2017 Dec;46(12):1603-1610 [FREE Full text] [Medline: [29259934](#)]
27. Banks M, Ash S, Bauer J, Gaskill D. Prevalence of malnutrition in adults in Queensland public hospitals and residential aged care facilities. *Nutri Diet* 2007 Sep;64(3):172-178. [doi: [10.1111/j.1747-0080.2007.00179.x](#)]

28. Gaskill D, Black LJ, Isenring EA, Hassall S, Sanders F, Bauer JD. Malnutrition prevalence and nutrition issues in residential aged care facilities. *Australas J Ageing* 2008 Dec;27(4):189-194. [doi: [10.1111/j.1741-6612.2008.00324.x](https://doi.org/10.1111/j.1741-6612.2008.00324.x)] [Medline: [19032620](https://pubmed.ncbi.nlm.nih.gov/19032620/)]
29. Huang YC, Wueng SL, Ou CC, Cheng CH, Su KH. Nutritional status of functionally dependent and nonfunctionally dependent elderly in Taiwan. *J Am Coll Nutr* 2001 Apr;20(2 Suppl):135-142. [doi: [10.1080/07315724.2001.10719025](https://doi.org/10.1080/07315724.2001.10719025)] [Medline: [11349936](https://pubmed.ncbi.nlm.nih.gov/11349936/)]
30. Kabir ZN, Ferdous T, Cederholm T, Khanam MA, Streatfield K, Wahlin A. Mini Nutritional Assessment of rural elderly people in Bangladesh: the impact of demographic, socio-economic and health factors. *Public Health Nutr* 2006 Dec;9(8):968-974. [doi: [10.1017/phn2006990](https://doi.org/10.1017/phn2006990)] [Medline: [17125558](https://pubmed.ncbi.nlm.nih.gov/17125558/)]
31. Kikafunda JK, Lukwago FB. Nutritional status and functional ability of the elderly aged 60 to 90 years in the Mpigi district of central Uganda. *Nutrition* 2005 Jan;21(1):59-66. [doi: [10.1016/j.nut.2004.09.009](https://doi.org/10.1016/j.nut.2004.09.009)] [Medline: [15661479](https://pubmed.ncbi.nlm.nih.gov/15661479/)]
32. Lahiri S, Biswas A, Santra S, Lahiri S. Assessment of nutritional status among elderly population in a rural area of West Bengal, India. *Int J Med Sci Public Health* 2015;4(4):569-572. [doi: [10.5455/ijmsph.2015.20122014117](https://doi.org/10.5455/ijmsph.2015.20122014117)]
33. Wei JM, Li S, Claytor L, Partridge J, Goates S. Prevalence and predictors of malnutrition in elderly Chinese adults: results from the China Health and Retirement Longitudinal Study. *Public Health Nutr* 2018 Dec;21(17):3129-3134 [FREE Full text] [doi: [10.1017/S1368980018002227](https://doi.org/10.1017/S1368980018002227)] [Medline: [30282567](https://pubmed.ncbi.nlm.nih.gov/30282567/)]
34. Elia M, Zelloppour L, Stratton RJ. To screen or not to screen for adult malnutrition? *Clin Nutr* 2005 Dec;24(6):867-884. [doi: [10.1016/j.clnu.2005.03.004](https://doi.org/10.1016/j.clnu.2005.03.004)] [Medline: [15893857](https://pubmed.ncbi.nlm.nih.gov/15893857/)]
35. Visser M, Volkert D, Corish C, Geisler C, de Groot LC, Cruz-Jentoft AJ, et al. Tackling the increasing problem of malnutrition in older persons: The Malnutrition in the Elderly (MaNuEL) Knowledge Hub. *Nutr Bull* 2017;42(2):178-186. [doi: [10.1111/nbu.12268](https://doi.org/10.1111/nbu.12268)]
36. Poulia K, Yannakoulia M, Karageorgou D, Gamaletsou M, Panagiotakos DB, Sipsas NV, et al. Evaluation of the efficacy of six nutritional screening tools to predict malnutrition in the elderly. *Clin Nutr* 2012 Jun;31(3):378-385. [doi: [10.1016/j.clnu.2011.11.017](https://doi.org/10.1016/j.clnu.2011.11.017)] [Medline: [22182948](https://pubmed.ncbi.nlm.nih.gov/22182948/)]
37. Volkert D. Malnutrition in older adults - urgent need for action: a plea for improving the nutritional situation of older adults. *Gerontology* 2013;59(4):328-333. [doi: [10.1159/000346142](https://doi.org/10.1159/000346142)] [Medline: [23406648](https://pubmed.ncbi.nlm.nih.gov/23406648/)]
38. Craven DL, Pelly FE, Isenring E, Lovell GP. Barriers and enablers to malnutrition screening of community-living older adults: a content analysis of survey data by Australian dietitians. *Aust J Prim Health* 2017 May;23(2):196-201. [doi: [10.1071/PY16054](https://doi.org/10.1071/PY16054)] [Medline: [27784507](https://pubmed.ncbi.nlm.nih.gov/27784507/)]
39. Abdollahzade SM, Eftekhari MH, Almasi-Hashiani A. The prevalence of malnutrition in elderly members of Jahandidegan Council, Shiraz, Iran. *Int J Nutri Sci* 2018;3(2):86-91 [FREE Full text]
40. Ahmadi SM, Mohammadi MR, Mostafavi S, Keshavarzi S, Kooshesh S, Joulaei H, et al. Dependence of the geriatric depression on nutritional status and anthropometric indices in elderly population. *Iran J Psychiatry* 2013 Jun;8(2):92-96 [FREE Full text] [Medline: [24130608](https://pubmed.ncbi.nlm.nih.gov/24130608/)]
41. Aliabadi M, Kimiagar M, Ghayoor MM, Faizabadi M. Prevalence of malnutrition and factors related to it in the elderly subjects in Khorasan Razavi province, Iran. *Iranian J Nutri Sci Food Technol* 2007;2(3):45-56 [FREE Full text]
42. Aliabadi M, Kimiagar M, Ghayour-Mobarhan M, Shakeri MT, Nematy M, Ilaty AA, et al. Prevalence of malnutrition in free living elderly people in Iran: a cross-sectional study. *Asia Pac J Clin Nutr* 2008;17(2):285-289 [FREE Full text] [Medline: [18586650](https://pubmed.ncbi.nlm.nih.gov/18586650/)]
43. Bostani Khalesi Z, Bokaie M. Nutritional status and related factors in elderly nursing home residents. *Elderly Health J* 2015;1(1):16-21 [FREE Full text]
44. Eshaghi S, Babak A, Manzori L, Marasi M. The nutritional status of the elderly and their associated factors in Isfahan. *Iranian J Age* 2007;2(3):340-345 [FREE Full text]
45. Keshavarzi S, Ahmadi SM, Lankarani KB. The impact of depression and malnutrition on health-related quality of life among the elderly Iranians. *Glob J Health Sci* 2014 Nov 26;7(3):161-170 [FREE Full text] [doi: [10.5539/gjhs.v7n3p161](https://doi.org/10.5539/gjhs.v7n3p161)] [Medline: [25948441](https://pubmed.ncbi.nlm.nih.gov/25948441/)]
46. Mokhber N, Majdi MR, Ali-Abadi M, Shakeri M, Kimiagar M, Salek R, et al. Association between malnutrition and depression in elderly people in Razavi Khorasan: a population based-study in Iran. *Iran J Public Health* 2011;40(2):67-74 [FREE Full text] [Medline: [23113074](https://pubmed.ncbi.nlm.nih.gov/23113074/)]
47. Nabavi SH, Aslani T, Ghorbani S, Mortazavi SH, Taherpour M, Sajadi S. The prevalence of malnutrition and its related factors among the elderly of Bojnourd, 2014. *J Kermanshah Univ Med Sci* 2015;19(1):32-36 [FREE Full text]
48. Naghibi SA, Mohammadi A, Yusefi A, Cherati J. The study of the nutritive condition of the elderly resident of Sari Sanatorium. *Iran J Health Sci* 2014;2(2):58-62. [doi: [10.18869/acadpub.jhs.2.2.58](https://doi.org/10.18869/acadpub.jhs.2.2.58)]
49. Nazemi L, Skoog I, Karlsson I, Hosseini S, Mohammadi MR, Hosseini M, et al. Malnutrition, prevalence and relation to some risk factors among elderly residents of nursing homes in Tehran, Iran. *Iran J Public Health* 2015 Feb;44(2):218-227 [FREE Full text] [Medline: [25905056](https://pubmed.ncbi.nlm.nih.gov/25905056/)]
50. Nouri Saeidlou S, Merdol TK, Mikaili P, Bektas Y. Assessment of the nutritional status of elderly people living at nursing homes in Northwest Iran. *Int J Acad Res* 2011;3(1):463-472 [FREE Full text]

51. Haghghian Roudsari A, Baygi F, Shokouhi M, Bazhan M, Rashidi A. Assessment of malnutrition prevalence and its related factors in the referred patients to the medical centers in Iran and some countries in the world. *Iranian J Nutri Sci Food Technol* 2013;7(5):591-597 [FREE Full text]
52. Amraee M, Shamsi A, Asadifard S, Momeni Z. Civilica. Systematic review of malnutrition in Iranian elderly URL: https://www.civilica.com/Paper-NSSC01-NSSC01_204.html [accessed 2109-04-04]
53. 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 2;350:g7647 [FREE Full text] [doi: [10.1136/bmj.g7647](https://doi.org/10.1136/bmj.g7647)] [Medline: [2555855](https://pubmed.ncbi.nlm.nih.gov/2555855/)]
54. 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](https://doi.org/10.1371/journal.pmed.1000097)] [Medline: [19621072](https://pubmed.ncbi.nlm.nih.gov/19621072/)]
55. Meursing Reynders R, Ladu L, di Girolamo N. Contacting of authors by systematic reviewers: protocol for a cross-sectional study and a survey. *Syst Rev* 2017 Dec 8;6(1):249 [FREE Full text] [doi: [10.1186/s13643-017-0643-z](https://doi.org/10.1186/s13643-017-0643-z)] [Medline: [29216930](https://pubmed.ncbi.nlm.nih.gov/29216930/)]
56. Cooper C, Bou JT, Varley-Campbell J. Evaluating the effectiveness, efficiency, cost and value of contacting study authors in a systematic review: a case study and worked example. *BMC Med Res Methodol* 2019 Mar 5;19(1):45 [FREE Full text] [doi: [10.1186/s12874-019-0685-0](https://doi.org/10.1186/s12874-019-0685-0)] [Medline: [30836935](https://pubmed.ncbi.nlm.nih.gov/30836935/)]
57. Hoy D, Brooks P, Woolf A, Blyth F, March L, Bain C, et al. Assessing risk of bias in prevalence studies: modification of an existing tool and evidence of interrater agreement. *J Clin Epidemiol* 2012 Sep;65(9):934-939. [doi: [10.1016/j.jclinepi.2011.11.014](https://doi.org/10.1016/j.jclinepi.2011.11.014)] [Medline: [22742910](https://pubmed.ncbi.nlm.nih.gov/22742910/)]
58. Cochrane Training. 2017. Cochrane Handbook for Systematic Reviews of Interventions URL: <https://training.cochrane.org/handbook> [accessed 2019-04-04]
59. Lipsey M, Wilson D. *Practical Meta-analysis*. Thousand Oaks: Sage Publications Inc; 2001.
60. Barendregt JJ, Doi SA, Lee YY, Norman RE, Vos T. Meta-analysis of prevalence. *J Epidemiol Community Health* 2013 Nov 1;67(11):974-978. [doi: [10.1136/jech-2013-203104](https://doi.org/10.1136/jech-2013-203104)] [Medline: [23963506](https://pubmed.ncbi.nlm.nih.gov/23963506/)]
61. Hanji MB. *Meta-analysis In Psychiatry Research: Fundamental And Advanced Methods*. USA: Apple Academic Press; 2017.
62. Böhning D, Lerdsuwansri R, Holling H. Some general points on the measure of heterogeneity in meta-analysis. *Metrika* 2017;80(6-8):685-695. [doi: [10.1007/s00184-017-0622-3](https://doi.org/10.1007/s00184-017-0622-3)]
63. 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](https://doi.org/10.1136/bmj.327.7414.557)] [Medline: [12958120](https://pubmed.ncbi.nlm.nih.gov/12958120/)]
64. Shi X, Nie C, Shi S, Wang T, Yang H, Zhou Y, et al. Effect comparison between Egger's test and Begg's test in publication bias diagnosis in meta-analyses: evidence from a pilot survey. *Int J Res Stud Biosci* 2017;5(5):14-20. [doi: [10.20431/2349-0365.0505003](https://doi.org/10.20431/2349-0365.0505003)]
65. Higgins JP, Green S. *Cochrane Handbook for Systematic Reviews of Interventions*. 2011. Cochrane handbook for systematic reviews of interventions. Version 5.1.0: The Cochrane Collaboration URL: <https://handbook-5-1.cochrane.org/> [accessed 2019-10-15]
66. Higgins JP, Green S. *Cochrane Handbook for Systematic Reviews of Interventions*. England: John Wiley & Sons; 2011.

Abbreviations

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

PROSPERO: International Prospective Register of Systematic Reviews

WHO: World Health Organization

Edited by G Eysenbach; submitted 02.07.19; peer-reviewed by M Alikhani, E Andrikopoulou, M Behzadifar; comments to author 24.07.19; revised version received 07.08.19; accepted 13.08.19; published 12.11.19.

Please cite as:

Khoddam H, Eshkevarlaji S, Nomali M, Modanloo M, Keshtkar AA

Prevalence of Malnutrition Among Elderly People in Iran: Protocol for a Systematic Review and Meta-Analysis

JMIR Res Protoc 2019;8(11):e15334

URL: <https://www.researchprotocols.org/2019/11/e15334>

doi: [10.2196/15334](https://doi.org/10.2196/15334)

PMID: [31582361](https://pubmed.ncbi.nlm.nih.gov/31582361/)

©Homeira Khoddam, Sepideh Eshkevarlaji, Mahin Nomali, Mahnaz Modanloo, Abbas Ali Keshtkar. Originally published in *JMIR Research Protocols* (<http://www.researchprotocols.org>), 12.11.2019. This is an open-access article distributed under the

terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in JMIR Research Protocols, is properly cited. The complete bibliographic information, a link to the original publication on <http://www.researchprotocols.org>, as well as this copyright and license information must be included.

Protocol

Allegiance Bias and Treatment Quality as Moderators of the Effectiveness of Humanistic Psychotherapy: Protocol for a Systematic Review and Meta-Analysis

Olivia Schünemann¹, PhD; Alessa Jansen², PhD; Ulrike Willutzki³, PhD; Nina Heinrichs¹, PhD

¹University of Bremen, Bremen, Germany

²Bundespsychotherapeutenkammer Germany, Berlin, Germany

³Witten/Herdecke University, Witten, Germany

Corresponding Author:

Olivia Schünemann, PhD

University of Bremen

Grazer Strasse 2

Bremen

Germany

Phone: 49 421 218 68541

Email: oschuene@uni-bremen.de

Abstract

Background: In many countries, humanistic psychotherapy (HPT) is viewed as a broad psychotherapeutic approach and is accepted in health care systems. To qualify for reimbursement by health insurance in Germany, psychotherapy approaches have to be evaluated positively by the German Scientific Board of Psychotherapy (GSBP). The GSBP examined HPT and its subapproaches based on an application by a number of professional organizations affiliated with HPT (Work Group Humanistic Psychotherapy, WGHP). The GSBP came to the decision that none of the HPT subapproaches provided sufficient evidence to be evaluated as evidence based. Potential reasons for the discrepancy between international recognition of HPT and GSBP's decision will be explored: researchers' allegiance may have led to a risk of bias disadvantaging HPT. Furthermore, the evaluation criteria of the GSBP did not systematically consider whether HPT was conceptualized bona fide and implemented with sufficient treatment integrity in the studies.

Objective: This systematic review will re-examine the studies included in the review of the GSBP. Within 2 comparisons (HPT vs control and HPT vs other psychotherapeutic interventions), we will examine moderating effects of treatment quality (bona fide and treatment integrity) and allegiance on the effectiveness of HPT.

Methods: This review is based on the prior systematic review by the GSBP. The GSBP examined randomized controlled trials (RCTs) and studies with non-RCTs of HPT interventions for individuals with mental disorders. All studies suggested by the WGHP were included; moreover, the GSBP conducted searches in standard electronic databases (Cochrane Central Register of Controlled Trials, MEDLINE, PsycINFO, and PSYINDEX) and handsearches in relevant systematic reviews and contacted experts. A total of 2 independent GSBP reviewers performed study screening using a structured form. On the basis of the prior work of the GSBP, all studies that were positively screened by the GSBP will be included in this review. Data will be extracted independently by 4 authors. Standardized mean difference will be calculated, and possible publication bias will be tested using funnel plots and Egger test. A priori defined subgroup or meta-regression analyses will be performed for treatment quality, allegiance, type of nonactive control, study quality, type of subapproach, and target population (children and adolescents or adults).

Results: The GSBP identified 115 eligible studies that will be reanalyzed in this systematic review.

Conclusions: Results about moderator effects of treatment quality and allegiance will provide important information about their impact on the evaluation of HPT and other psychotherapy approaches and can be used for further evaluation methods.

Trial Registration: PROSPERO CRD42019128983; https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=128983

International Registered Report Identifier (IRRID): PRR1-10.2196/15140

(*JMIR Res Protoc* 2019;8(11):e15140) doi:[10.2196/15140](https://doi.org/10.2196/15140)

KEYWORDS

bona fide; systematic review; meta-analysis

Introduction**Background**

Humanistic psychotherapy (HPT) is often viewed as a broad psychotherapeutic approach next to psychodynamic, cognitive behavioral, and systemic psychotherapeutic approaches [1], and HPT is largely accepted worldwide. However, in Germany, as yet, HPT is not approved within the German health care system—in contrast to psychodynamic, cognitive behavioral, and systemic therapy. To become established in the German health care system and for service providers (eg, psychotherapists) to be reimbursed by health insurances, the procedure is as follows: the German Scientific Board of Psychotherapy (GSBP) in a first step evaluates the concept and evidence of psychotherapeutic approaches or subapproach methods. Only if the GSBP recognizes an approach as scientifically sound, further steps to integrate the approach into the German health care system are taken. In 2012, a number of professional organizations affiliated with HPT, the Work Group Humanistic Psychotherapy (WGHP), submitted an application for scientific recognition of HPT (Humanistic Psychotherapy Application, HPT-A) to the GSBP [2]. On the basis of the GSBP's method paper 2.8 [3] that defines criteria and procedures for the evaluation process, the GSBP examined HPT, including its subapproaches as defined by the HPT-A [2].

The general evaluation process within the GSBP includes 2 steps. First, it is evaluated whether the concept of an intervention can be judged as a psychotherapy approach (an overall concept) or as a subapproach according to the criteria of the GSBP. Second, the evidence for the approach or its subapproaches is evaluated. The GSBP concluded in 2018 that HPT may not be considered as a psychotherapy approach according to its criteria [4]. This was mainly decided because of the heterogeneity of the HPT subapproaches and the lack of a common concept of indications and contraindications; furthermore, a general training concept for HPT as a broad concept including knowledge about all subapproaches was not sufficiently elaborated. As a consequence, GSBP evaluated the evidence on the level of HPT subapproaches but not as an overall approach [4]. None of these subapproaches provided enough evidence to be evaluated as evidence based according to the criteria of the GSBP [4]. Moreover, even when considering all subapproaches together, there was not sufficient evidence for the treatment of anxiety disorders with HPT; this is a mandatory requirement for the recognition of a psychotherapy approach by the GSBP [4].

This conclusion was much debated within the German professional public. In light of the widespread recognition of HPT worldwide, this outcome seems puzzling: other reviews on HPT [5] and the meta-analysis by Elliott et al [1] mainly demonstrated positive effects of HPT. Elliott et al [1] analyzed about 191 studies on the effectiveness (including both efficacy and effectiveness studies) of HPT involving person-centered psychotherapy, supportive or nondirective psychotherapy, task-focused psychotherapy, integrative emotion-focused

psychotherapy, existentially oriented supportive-expressive group therapy for medical populations (eg, cancer), and other subapproaches (such as gestalt psychotherapy or psychodrama) with results demonstrating large pre-post and pre-follow-up effect sizes. Results comparing only HPT with cognitive behavioral therapy (CBT) indicated that CBT seems to be slightly superior to HPT [1].

Reasons for the discrepancy between the meta-analysis by Elliott et al [1] and the result of the review process by the GSBP [4] are multifold. A central point is the nonidentical selection of subapproaches included by the WGHP [2] versus 2 meta-analyses by Elliott et al [1,6]. Moreover, although there is some overlap between the diagnostic groups examined by Elliott et al [1] and defined by the GSBP [3], the GSBP follows the diagnostic system, for example, of the International Statistical Classification of Diseases, Tenth Revision (ICD-10), more stringently. Furthermore, the meta-analysis by Elliott et al [1] included studies applying motivational interviewing but did not examine child and adolescent psychotherapy in contrast to the GSBP [4].

Furthermore, according to the GSBP's method paper 2.8 [3], the body of evidence is evaluated in a 2-step process: (1) does the particular study fulfill specified inclusion criteria? (see section *Criteria for Selecting Studies for This Review*) and (2) does the study provide evidence for the efficacy of the approach or subapproach: yes or no? In contrast to this categorical approach, Elliott et al [1] also accounted for the size of effects by summarizing effect sizes across studies.

When evaluating the evidence of HPT according to the GSBP procedures [4], the humanistic subapproaches were often designed as a control group in comparison with other psychotherapeutic approaches, such as CBT, in the studies that were included. As researchers' allegiance is often associated with therapy outcomes [7], this design may have led to a risk of bias diminishing possible effects of HPT. Elliott et al [1] controlled allegiance in their comparison of HPT with CBT. This led to a reduction of the difference in pre-post effect sizes between HPT and CBT, resulting in similar pre-post effect sizes for both CBT and HPT.

In addition, the evaluation process of the GSBP [4] does not systematically evaluate the effects of treatment quality, including bona fide psychotherapy and treatment integrity. Bona fide psychotherapy may be defined by mentioning or describing an established psychological approach, psychological treatment principles, a treatment manual, or active treatment ingredients [8]. Moreover, bona fide psychotherapy is usually implemented by a trained therapist (in this case in HPT) [9]. Bona fide thus targets the *conceptual quality* of a treatment. An additional quality feature of psychotherapy is treatment integrity “[...] conceptualized broadly including adherence to specific treatment procedures (e.g., the importance of exposure in psychotherapy for post-traumatic stress disorder), common factors (e.g., therapeutic alliance), and therapist effects (i.e., differences in the effects due to individual therapists)” (pg 8 [10]). Treatment

integrity thus targets the *process quality* of treatment and psychotherapy. We assume that process quality and conceptual quality are closely associated. Treatment quality seems to be relevant for research on HPT, as Elliott et al [1] found that only nondirective supportive (non-bona fide) HPT showed worse outcomes in comparison with CBT.

Thus, both allegiance and treatment quality may have had effects on the evaluation of the evidence of the humanistic subapproaches by the GSBP.

Objectives

This systematic review will re-examine the studies identified within the systematic review of the GSBP [4] to analyze the relevance of allegiance and treatment quality (bona fide psychotherapy and treatment integrity) for the effectiveness of HPT (including both efficacy and effectiveness studies). Therefore, 2 comparisons will be conducted: (1) comparison of humanistic subapproaches versus control and (2) comparison of humanistic subapproaches versus other psychotherapeutic interventions. Within both comparisons, we will analyze the moderating effects of treatment quality. In addition, allegiance to HPT in the first comparison and allegiance to the comparator psychotherapeutic intervention in the second comparison will be analyzed as moderators.

Methods

Design and Procedure

This study is a secondary moderator analysis based on a systematic review conducted by the GSBP [4]. The following tasks were completed by the GSBP [4]: (1) development of a search strategy with defining criteria for the study selection (see section *Criteria for Selecting Studies for This Review*) including the types of studies, participants, interventions, and comparators (see corresponding paragraphs below); (2) search of studies (see sections *Search Methods for Identification of Studies* and *Bibliographic Database Search*); and (3) study screening (see section *Criteria for Selecting Studies for This Review*). Thus, the criteria for selecting studies and the search methods for identifying studies were defined by the methods underlying the evaluation process of the GSBP [3]. Randomized controlled trials (RCTs) and non-RCTs with control groups were included.

On the basis of the prior work of the GSBP [4], this study will pursue the following tasks: (1) data extraction according to a coding protocol developed specifically for this study (see sections *Types of Outcome Measures* and *Data Extraction*), (2) assessment of methodological quality, and (3) data synthesis (see the corresponding paragraphs below) to estimate effect sizes and potential moderators (allegiance and treatment quality).

Criteria for Selecting Studies for This Review

This systematic review will be based exactly on the set of studies previously identified by the GSBP. The research questions of this study focus on determining whether the evaluation of psychotherapy studies by the GSBP is biased by allegiance or treatment quality. As the board's decisions have far-reaching consequences for psychotherapeutic approaches and their implementation in the German health care system, it is an

extremely important question to evaluate whether researcher allegiance and treatment quality are to be considered or can be neglected in this context. To be able to compare the present result with the original result of the GSBP and to evaluate whether the GSBP review should be supplemented by an analysis of effect sizes and potential moderators (allegiance and treatment quality), the body of studies to be included has to be identical. There will be no additional study search to identify more recently published literature. The criteria for study selection and the search strategy of the GSBP [4] were as follows: the GSBP included and excluded studies based on a 2-step screening process. First, titles and abstracts were screened independently by 2 reviewers. Second, potentially relevant German or English publications were screened by 2 independent reviewers using a structured form [3]. Disagreement was resolved by a consensus discussion by members of the GSBP.

Types of Studies

The GSBP [4] examined RCTs and non-RCTs. Studies without any control group were excluded. All studies had to include pre- and postassessments regardless of follow-up assessments. Studies were excluded in case of clear indication of data manipulation.

Types of Participants

Studies examining participants without any mental disorder or studies assessing mental disorders without objective and reliable diagnosis process via standard operationalized diagnostic interviews were excluded. Only studies applying interventions to individuals with clinically significant mental disorders were analyzed. All diagnoses had to be made on the basis of either the ICD [11] or the Diagnostic and Statistical Manual of Mental Disorders [12]. Participants were adults or children and adolescents suffering from any of the following mental disorders (diagnostic groups according to GSBP [3]): (1) mood and affective disorders (F3, F94.1, and F53 according to ICD-10); (2) anxiety disorders and obsessive-compulsive disorders (F40-F42, F93, and F94.0); (3) dissociative and conversion disorders (F44-F48); (4) substance abuse and dependence (F1 and F55); (5) personality and behavior disorders (F6); (6) reaction to severe stress and adjustment disorders (F43); (7) eating disorders (F50); (8) nonorganic sleep disorders (F51); (9) sexual dysfunction (F52); (10) psychological and behavioral factors associated with disorders or diseases classified elsewhere (F54); (11) schizophrenia, schizotypal, and delusional disorders (F2); (12) organic, including symptomatic, mental disorders (F0); (13) mental retardation (F7) and pervasive developmental disorders (F84); (14) hyperkinetic disorders (F90) and conduct disorders (F91 and F94.2-F94.9); (15) disorders of psychological development (F80-F83); (16) nonorganic enuresis (F98.0) and nonorganic encopresis (F98.1); (17) feeding disorder of infancy and childhood (F98.2); and (18) tic disorders (F95) and stereotyped movement disorders (F98.4).

Types of Interventions

The following HPT subapproaches were examined according to the definitions by the WGHPT [2]: (1) client or person-centered therapy, (2) gestalt therapy, (3) emotion-focused individual and couple therapy, (4) psychodrama, (5) logotherapy,

(6) existential analysis, (7) body psychotherapy (including bioenergetic, biodynamic, biosynthesis psychotherapy, and Hakomi; excluding Reiki, Alexander Technique, Feldenkrais, and breathing therapy), (8) Pesso Boyden System Psychomotor, (9) integrative therapy, and (10) transactional analysis. A manual, a treatment guideline, or the name of the psychotherapeutic subapproach had to be mentioned for the study to be included.

Types of Comparators

Both controlled and comparative effectiveness studies were included. Active control groups were other evidence-based psychotherapeutic interventions previously considered to be effective by the GSBP (CBT, psychodynamic psychotherapy, and systemic therapy). Nonactive comparators were no-treatment control (patients are administered only assessments); wait-list control (patients received treatment following the study period); attention-placebo, nonspecific control, sham treatment (patients received treatment that involves nonspecific psychotherapeutic factors), and treatment as usual. In addition to the GSBP [4], this review will extract *other* active and nonactive control conditions (eg, medication).

Types of Outcome Measures

The primary efficacy outcome of this review for the planned moderator analyses will be symptom severity at the end of treatment measured on a metric symptom-specific scale. If studies report more than 1 symptom-specific metric outcome, outcomes on self-rating scales (eg, Beck Depression Inventory) will be given priority over observer-rated scales (eg, Hamilton Depression Rating Scale). As studies on multiple populations quite likely using a broad variety of symptom-specific scales are included, it is not possible to specify a list of relevant outcomes or define a hierarchy of symptom scales before the extraction process. Therefore, first, all outcome measures from all studies will be extracted. In a second step, a sequence for all used self-rating (as well as observer-rated) scales will be determined that will be applied to all studies. In this sequence, more commonly used symptom scales and more reliable scales will be given priority over seldom used respectively less reliable scales. The sequence of scales will be documented to rule out selective outcome reporting.

Secondary efficacy outcomes will include assessment of impairment and consequences, such as interpersonal outcomes (eg, Dyadic Adjustment Scale), general assessment of functioning (eg, General Assessment of Functioning), or quality of life (eg, WHO Quality of Life).

The primary efficacy outcome will be analyzed separately for short term (end of intervention) and follow-up if available (6 months after the end of intervention). If multiple follow-up measures are reported, the one closest to 6 months will be used.

The primary safety outcome will be dropping out of the study because of any reason.

All outcomes that are likely to be meaningful to people making a decision about the target condition (clinicians, patients or consumers, the general public, administrators, and policy makers) will be addressed independently of the frequency of

their reporting in primary studies. Owing to the long tradition of psychotherapy research, most instruments used in clinical trials are usually psychometrically sound. Such measures will be preferred throughout the review (if referenced or sufficient psychometric quality reported).

In accordance with the GSBP's method paper 2.8 [3], studies that do not use any reliable or valid outcome measure (at least for primary outcomes) or that use only primary outcomes not representing relevant variables for participants or mental disorders (eg, severity of symptoms, psychological strain, impairment in daily life, quality of life, and utilization of health services) will be excluded. In addition, studies with incomplete reporting of intervention effects or changes in primary and secondary outcomes compared with the control group will be excluded.

Search Methods for Identification of Studies

This systematic review will be based on all studies identified within the systematic review of the GSBP [4]. First, the GSBP included all studies suggested by the WGHPT [2]. Second, the GSBP used several methods to retrieve further potentially relevant articles. In addition to standard electronic databases, handsearch in relevant systematic reviews was performed. In addition, experts were contacted once in the beginning of the process and after each electronic database research to name relevant studies to add relevant missing studies.

Bibliographic Database Search

The following databases were searched: Cochrane Central Register of Controlled Trials, MEDLINE, PsycINFO, and PSYINDEX. No language restrictions were applied. All databases were searched using both standard vocabulary (eg, Medical Subject Headings) and keywords (freetext). The full search strategy is presented in [Multimedia Appendix 1](#). Both English and German keywords were used. First Bibliographic database search was conducted in December 2013, and a search update was performed in July 2016. As described above, a further update of the GSBP search is not feasible as answering the primary research questions necessitates exactly the identical study pool of the GSBP [4].

Data Collection and Assessment of Methodological Quality

Data Extraction

For each study, study characteristics and results for the planned moderator analyses will be extracted by 1 of 2 authors (OS or AJ) using a structured form and assessing the full text. Methodological quality for each study will be assessed independently by 2 authors (OS and NH or AJ and UW). Disagreement will be recorded and resolved by discussion either within the author pair or within whole author team if necessary. Extracted data will include information on participant characteristics (eg, age, gender, and diagnostic group), study characteristics (eg, sample sizes, study design, allocation, and dropout rates), intervention characteristics (eg, HPT subapproach, type of control group, therapist characteristics, and setting), primary and secondary outcomes, risk of bias, allegiance, and treatment quality (bona fide and treatment

integrity). Outcomes will be extracted from publications with estimation and substitution of missing data according to the guidelines of the Cochrane Collaboration [13], for example, calculating standard errors from exactly reported *t* test values. Data will be managed using Microsoft Excel (Microsoft Corporation).

Assessment of Methodological Quality

Internal validity will be assessed with the second version of Cochrane's risk of bias tool (RoB 2.0; [14]) adapted according to suggestions made by Munder and Barth [10] for its use in psychotherapy outcome research. The risk of bias tool provided by Cochrane is a widely used measure to assess internal validity in controlled trials, yet its application on psychotherapeutic studies has been criticized [10]. Munder and Barth [10] have therefore provided suggestions for its use in the context of psychotherapy research. Accordingly, the following 4 domains will be assessed in accordance with RoB 2.0: (1) bias arising from the randomization process (sequence generation, allocation concealment, and baseline differences), (2) bias because of missing outcome data (availability of outcome data), (3) bias in outcome measurement (appropriate measuring and differences between groups), and (4) bias in selection of the reported result (accordance with specified plan, multiple measurement, and multiple analyses). The domain "bias due to deviations from intended interventions" (pg 17 [14]; effect of adhering to intervention) of the RoB 2.0 tool will be adapted as suggested by Munder and Barth [10] (concomitant treatments, implementation of treatment, and adherence to intervention). In case of non-RCTs, risk of bias will be assessed with the ROBINS-I tool provided by Cochrane for non-RCTs comparing different interventions [15]. Allegiance will be assessed according to the multilevel allegiance rating scale provided by Steinert et al [16]. Both bona fide psychotherapy and treatment integrity will be rated using the definition by Benish et al [8] and Munder and Barth [10].

External validity (generalizability) will be addressed by documenting study setting, patient selection criteria, patient characteristics, applicability of the intervention in routine care, clinical relevance of outcomes, efficacy at follow-up, and discontinuation rates.

If considerable methodological heterogeneity is present, subgroup analyses will be performed by comparing the findings between studies of low, some, and high risk of bias (according to Munder and Barth [10]). The strength of the body of evidence will be provided by presenting and discussing results of the methodological quality of all included studies.

Data Synthesis

Planned Treatment Comparisons

Overall, 2 comparisons will be conducted. First, HPT subapproaches will be compared with nonactive controls. Second, HPT subapproaches will be compared with other psychotherapeutic interventions that have previously been scientifically recognized by the GSBP (CBT, psychodynamic psychotherapy, and systemic psychotherapy).

Meta-Analysis

The statistical analysis will follow actual guidelines [13,17,18]. For metric measures (eg, symptom severity and quality of life), standardized mean difference will be calculated, as it is unlikely that all studies administer the same measures. For rare outcomes (dropout rates) with highly varying baseline rates, odds ratios will be calculated. For all studies, effect sizes will be calculated using the intention-to-treat principle, that is, analyzing all subjects allocated to a study arm. For all metric outcomes, the definition of the intention-to-treat sample provided by the authors will be followed if available. All analyses will be performed by applying a random effects model with inverse variance weights [19]. We plan to use a random effects model rather than fixed effects one because we assume that the included studies will not be functionally equivalent and will show considerable clinical (concerning population and intervention) and methodological (eg, design and quality) heterogeneity. Statistical heterogeneity between study results will be tested for significance using Cochran Q test and quantified using the I^2 statistic [20]. Results will be visually displayed as forest plots. Possible publication bias will be tested using visual examination of funnel plots and applying Egger test [21].

Subgroup and Meta-Regression Analysis

A priori defined subgroup (in case of categorical predictors) or meta-regression (in case of metric predictors) analyses will be performed according to treatment quality, allegiance, type of nonactive control (wait-list vs all others including treatment as usual), study quality, type of HPT subapproach, and population (children and adolescents vs adults). Differences between subgroups will be tested formally [22-24]. All meta-regression analyses will be performed using the restricted maximum likelihood estimate method, a recommended random effect approach that accounts for residual between-trial heterogeneity [25]. In case of considerable heterogeneity between study results that cannot be explained by the a priori defined subgroup and meta-regression analyses, a series of a posteriori (explorative) meta-regression analyses will be performed to identify sources of heterogeneity. A priori and a posteriori analyses will be clearly labeled as such.

Sensitivity Analysis

Sensitivity analyses will be performed for the primary efficacy outcome using results from all trials in contrast to results from RCTs only.

Qualitative Summary

If clinical or methodological heterogeneity of the included studies proves to be extremely high, a qualitative rather than quantitative synthesis of the evidence will be performed.

Results

This systematic review and meta-analysis was submitted for registration in the PROSPERO International prospective register of systematic reviews (CRD42019128983). As this review and meta-analysis is a reexamination of the previous review process by the GSBP, preliminary searches, piloting of the study

selection process, and formal screening of search results against eligibility criteria were completed. In the context of their screening process, the GSBP identified 115 eligible studies that will be reanalyzed in the following systematic review and meta-analysis. The next step will be final data extraction.

Discussion

The examination of the moderating effects of treatment quality and allegiance will provide important information concerning

their effects on the evaluation of psychotherapy approaches. This information is crucial for the further development of the evaluation methods of the GSBP and for other stakeholders that need to assess the efficacy and effectiveness of psychotherapeutic approaches within health care systems. The examination of treatment quality and allegiance within the evaluation of humanistic subapproaches may further highlight the role of implementation of interventions when new innovative concepts are compared with well-established interventions.

Acknowledgments

The authors would like to thank all members of the GSBP in the period from 2014 to 2018 for their openness to have UW and NH follow up on these research objectives that are based on the joint work done in the GSBP. This study was not financially supported by external funding.

Conflicts of Interest

AJ is an employee of the Federal Chamber of Psychotherapists. NH and UW are members of the GSBP. All authors are trained in CBT.

Multimedia Appendix 1

Full search strategy.

[PDF File (Adobe PDF File), 462 KB - [resprot_v8i11e15140_app1.pdf](#)]

References

1. Elliott R, Greenberg L, Watson J, Timulak L, Freire E. Research on humanistic- experiential psychotherapies. In: Lambert M, editor. *Bergin & Garfield's Handbook of Psychotherapy and Behavior Change*. New York: Wiley; 2013:495-538.
2. Work Group Humanistic Psychotherapy (WGHP). Humanistic Psychotherapy Application (HPT-A). Arbeitsgemeinschaft Humanistische Psychotherapie (AGHPT) URL: [http://www.aghpt.de/texte/aghpt-antrag_an_den_wbp_\(1\)_antragstext_2012-10-12.pdf](http://www.aghpt.de/texte/aghpt-antrag_an_den_wbp_(1)_antragstext_2012-10-12.pdf) [accessed 2019-09-30]
3. German Scientific Board of Psychotherapy (GSBP) Wissenschaftlicher Beirat Psychotherapie. 8 Methodenpapier des Wissenschaftlichen Beirats Psychotherapie nach § 11 PsychTh: Version 2. Method paper of the German Scientific Board of Psychotherapy version 2 URL: https://www.wbpsychotherapie.de/fileadmin/user_upload/downloads/pdf-Ordner/WBP/Methodenpapier28.pdf [accessed 2019-09-30]
4. German Scientific Board of Psychotherapy (GSBP) Wissenschaftlicher Beirat Psychotherapie. Scientific advisory board psychotherapy according to § 11 psychthg: report on the scientific recognition of humanistic psychotherapy. *Dtsch Arztebl* 2018;115(110):1-14 [FREE Full text] [doi: [10.3238/arztebl.2018.gut_hpt01](https://doi.org/10.3238/arztebl.2018.gut_hpt01)]
5. Cooper M, Watson J, Höllendampf D. *Person-Centered and Experiential Therapies Work: A Review of the Research on Counselling, Psychotherapy and Related Practices*. Ross-on-Wye: PCCS Books; 2010.
6. Elliott R, Greenberg L, Lietaer G. Research on experiential therapies. In: Lambert M, editor. *Bergin & Garfield's Handbook of Psychotherapy and Behavior Change*. New York: Wiley; 2004:493-539.
7. Munder T, Brüttsch O, Leonhart R, Gerger H, Barth J. Researcher allegiance in psychotherapy outcome research: an overview of reviews. *Clin Psychol Rev* 2013 Jun;33(4):501-511. [doi: [10.1016/j.cpr.2013.02.002](https://doi.org/10.1016/j.cpr.2013.02.002)] [Medline: [23500154](https://pubmed.ncbi.nlm.nih.gov/23500154/)]
8. Benish SG, Imel ZE, Wampold BE. The relative efficacy of bona fide psychotherapies for treating post-traumatic stress disorder: a meta-analysis of direct comparisons. *Clin Psychol Rev* 2008 Jun;28(5):746-758. [doi: [10.1016/j.cpr.2007.10.005](https://doi.org/10.1016/j.cpr.2007.10.005)] [Medline: [18055080](https://pubmed.ncbi.nlm.nih.gov/18055080/)]
9. Wampold BE, Mondin GW, Moody M, Stich F, Benson K, Ahn H. A meta-analysis of outcome studies comparing bona fide psychotherapies: empirically, 'all must have prizes.'. *Psychol Bull* 1997;122(3):203-215. [doi: [10.1037//0033-2909.122.3.203](https://doi.org/10.1037//0033-2909.122.3.203)]
10. Munder T, Barth J. Cochrane's risk of bias tool in the context of psychotherapy outcome research. *Psychother Res* 2018 May;28(3):347-355. [doi: [10.1080/10503307.2017.1411628](https://doi.org/10.1080/10503307.2017.1411628)] [Medline: [29224503](https://pubmed.ncbi.nlm.nih.gov/29224503/)]
11. World Health Organization. *The International Statistical Classification Of Diseases And Health Related Problems: ICD-10*. Geneva: World Health Organization; 1992.
12. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders - DSM-IV-TR*. Washington, DC: American Psychiatric Association; 2000.
13. Higgins J, Greenberg L. *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1*. Chichester: The Cochrane Collaboration; 2011.

14. Higgins JP, Savović J, Page MJ, Sterne JA. Google Sites. 2018. Revised Cochrane Risk-of-Bias Tool for Randomized Trials (RoB 2) URL: <https://sites.google.com/site/riskofbiastool/welcome/rob-2-0-tool/current-version-of-rob-2> [accessed 2019-09-30]
15. Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *Br Med J* 2016 Oct 12;355:i4919 [FREE Full text] [doi: [10.1136/bmj.i4919](https://doi.org/10.1136/bmj.i4919)] [Medline: [27733354](https://pubmed.ncbi.nlm.nih.gov/27733354/)]
16. Steinert C, Munder T, Rabung S, Hoyer J, Leichsenring F. Psychodynamic therapy: as efficacious as other empirically supported treatments? A meta-analysis testing equivalence of outcomes. *Am J Psychiatry* 2017 Oct 01;174(10):943-953. [doi: [10.1176/appi.ajp.2017.17010057](https://doi.org/10.1176/appi.ajp.2017.17010057)] [Medline: [28541091](https://pubmed.ncbi.nlm.nih.gov/28541091/)]
17. Khan K, Ter RG, Glanville J, Sowden A, Kleijnen J, Prospero - University of York. 2009. Undertaking Systematic Reviews of Research on Effectiveness: CRD's Guidance for Those Carrying out or Commissioning Reviews URL: <http://www.crd.york.ac.uk/CRDWeb/ShowRecord.asp?AccessionNumber=32001000984> [accessed 2019-09-30]
18. Egger M, Davey-Smith G, Altman D. Systematic Reviews in Health Care: Meta-Analysis in Context. London: BMJ Publishing Group; 2001.
19. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986 Sep;7(3):177-188. [doi: [10.1016/0197-2456\(86\)90046-2](https://doi.org/10.1016/0197-2456(86)90046-2)] [Medline: [3802833](https://pubmed.ncbi.nlm.nih.gov/3802833/)]
20. 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](https://doi.org/10.1136/bmj.327.7414.557)] [Medline: [12958120](https://pubmed.ncbi.nlm.nih.gov/12958120/)]
21. Sterne JA, Egger M, Smith GD. Investigating and dealing with publication and other biases. In: Egger M, Smith GD, Altman DG, editors. Systematic Reviews in Health Care: Meta-Analysis in Context. London: BMJ Publishing Group; 2016:248-282.
22. Bucher HC, Guyatt GH, Griffith LE, Walter SD. The results of direct and indirect treatment comparisons in meta-analysis of randomized controlled trials. *J Clin Epidemiol* 1997 Jun;50(6):683-691. [doi: [10.1016/s0895-4356\(97\)00049-8](https://doi.org/10.1016/s0895-4356(97)00049-8)] [Medline: [9250266](https://pubmed.ncbi.nlm.nih.gov/9250266/)]
23. Deeks J, Altman D, Bradburn J. Statistical methods for examining heterogeneity and combining results from several studies in meta-analysis. In: Egger M, Smith GD, Altman DG, editors. Systematic Reviews in Health Care: Meta-Analysis in Context. London: BMJ Publishing Group; 2003:313-335.
24. Song F, Altman DG, Glenny A, Deeks JJ. Validity of indirect comparison for estimating efficacy of competing interventions: empirical evidence from published meta-analyses. *Br Med J* 2003 Mar 1;326(7387):472 [FREE Full text] [doi: [10.1136/bmj.326.7387.472](https://doi.org/10.1136/bmj.326.7387.472)] [Medline: [12609941](https://pubmed.ncbi.nlm.nih.gov/12609941/)]
25. Thompson SG, Sharp SJ. Explaining heterogeneity in meta-analysis: a comparison of methods. *Stat Med* 1999 Oct 30;18(20):2693-2708. [doi: [10.1002/\(sici\)1097-0258\(19991030\)18:20<2693::aid-sim235>3.0.co;2-v](https://doi.org/10.1002/(sici)1097-0258(19991030)18:20<2693::aid-sim235>3.0.co;2-v)] [Medline: [10521860](https://pubmed.ncbi.nlm.nih.gov/10521860/)]

Abbreviations

CBT: cognitive behavioral therapy

GSBP: German Scientific Board of Psychotherapy

HPT: humanistic psychotherapy

HPT-A: Humanistic Psychotherapy Application

ICD-10: International Statistical Classification of Diseases, Tenth Revision

RCT: randomized controlled trial

WGHP: Work Group Humanistic Psychotherapy

Edited by G Eysenbach; submitted 26.06.19; peer-reviewed by T Munder, L Hess; comments to author 10.08.19; revised version received 15.08.19; accepted 17.08.19; published 25.11.19.

Please cite as:

Schünemann O, Jansen A, Willutzki U, Heinrichs N

Allegiance Bias and Treatment Quality as Moderators of the Effectiveness of Humanistic Psychotherapy: Protocol for a Systematic Review and Meta-Analysis

JMIR Res Protoc 2019;8(11):e15140

URL: <http://www.researchprotocols.org/2019/11/e15140/>

doi: [10.2196/15140](https://doi.org/10.2196/15140)

PMID: [31763989](https://pubmed.ncbi.nlm.nih.gov/31763989/)

©Olivia Schünemann, Alessa Jansen, Ulrike Willutzki, Nina Heinrichs. Originally published in JMIR Research Protocols (<http://www.researchprotocols.org>), 25.11.2019. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction

in any medium, provided the original work, first published in JMIR Research Protocols, is properly cited. The complete bibliographic information, a link to the original publication on <http://www.researchprotocols.org>, as well as this copyright and license information must be included.

Protocol

Time-Limited Trials Among Critically Ill Patients With Advanced Medical Illnesses to Reduce Nonbeneficial Intensive Care Unit Treatments: Protocol for a Multicenter Quality Improvement Study

Dong Chang¹, MD, MSc; Jennifer Parrish¹, DO; Nader Kamangar², MD; Janice Liebler³, MD; May Lee³, MD; Thanh Neville⁴, MD, MS

¹Los Angeles BioMedical Research Institute, Harbor-University of California Los Angeles Medical Center, Torrance, CA, United States

²Olive View Medical Center, Sylmar, CA, United States

³Los Angeles County-University of Southern California Medical Center, Los Angeles, CA, United States

⁴Division of Pulmonary and Critical Care Medicine, University of California Los Angeles School of Medicine, Los Angeles, CA, United States

Corresponding Author:

Dong Chang, MD, MSc

Los Angeles BioMedical Research Institute

Harbor-University of California Los Angeles Medical Center

1000 W Carson St Box 405

Torrance, CA, 90509

United States

Phone: 1 310 974 9529

Email: dchang@labiomed.org

Abstract

Background: Invasive intensive care unit (ICU) treatments for patients with advanced medical illnesses and poor prognoses may prolong suffering with minimal benefit. Unfortunately, the quality of care planning and communication between clinicians and critically ill patients and their families in these situations are highly variable, frequently leading to overutilization of invasive ICU treatments. Time-limited trials (TLTs) are agreements between the clinicians and the patients and decision makers to use certain medical therapies over defined periods of time and to evaluate whether patients improve or worsen according to predetermined clinical parameters. For patients with advanced medical illnesses receiving aggressive ICU treatments, TLTs can promote effective dialogue, develop consensus in decision making, and set rational boundaries to treatments based on patients' goals of care.

Objective: The aim of this study will be to examine whether a multicomponent quality-improvement strategy that uses protocolized TLTs as the default ICU care-planning approach for critically ill patients with advanced medical illnesses will decrease duration and intensity of nonbeneficial ICU care without changing hospital mortality.

Methods: This study will be conducted in medical ICUs of three public teaching hospitals in Los Angeles County. In Aim 1, we will conduct focus groups and semistructured interviews with key stakeholders to identify facilitators and barriers to implementing TLTs among ICU patients with advanced medical illnesses. In Aim 2, we will train clinicians to use protocol-enhanced TLTs as the default communication and care-planning approach in patients with advanced medical illnesses who receive invasive ICU treatments. Eligible patients will be those who the treating ICU physicians consider to be at high risk for nonbeneficial treatments according to guidelines from the Society of Critical Care Medicine. ICU physicians will be trained to use the TLT protocol through a curriculum of didactic lectures, case discussions, and simulations utilizing actors as family members in role-playing scenarios. Family meetings will be scheduled by trained care managers. The improvement strategy will be implemented sequentially in the three participating hospitals, and outcomes will be evaluated using a before-and-after study design. Key process outcomes will include frequency, timing, and content of family meetings. The primary clinical outcome will be ICU length of stay. Secondary outcomes will include hospital length of stay, days receiving life-sustaining treatments (eg, mechanical ventilation, vasopressors, and renal replacement therapy), number of attempts at cardiopulmonary resuscitation, frequency of invasive ICU procedures, and disposition from hospitalization.

Results: The study began in August 2017. The implementation of interventions and data collection were completed at two of the three hospitals. As of September 2019, the study was at the postintervention stage at the third hospital. We have completed

focus groups with physicians at each medical center (N=29) and interviews of family members and surrogate decision makers (N=18). The study is expected to be completed in the first quarter of 2020, and results are expected to be available in mid-2020.

Conclusions: The successful completion of the aims in this proposal may identify a systematic approach to improve communication and shared decision making and to reduce nonbeneficial invasive treatments for ICU patients with advanced medical illnesses.

International Registered Report Identifier (IRRID): DERR1-10.2196/16301

(*JMIR Res Protoc* 2019;8(11):e16301) doi:[10.2196/16301](https://doi.org/10.2196/16301)

KEYWORDS

intensive care; critical care; prognosis; outcome; prediction; medical uncertainty; medical futility; palliative care; communication

Introduction

Background

Clinical Significance of Intensive Care Unit Overutilization Among Patients With Advanced Medical Illnesses

In the United States, 1 in 5 people die using intensive care unit (ICU) services, frequently receiving invasive treatments despite minimal anticipated benefit [1,2]. Investigators in our research group found that 20% of ICU patients in the University of California Los Angeles (UCLA) health care system were perceived by physicians to be receiving futile care [3]. A recent study from our research group [4] and previous work from others [5-7] also showed that hospitals that utilize ICUs more frequently were more likely to perform invasive procedures and have higher costs with no improvement in hospital mortality. Interestingly, most patients with advanced medical illnesses prefer not to receive such aggressive care at the end of life [1,8-12] but ICU care in this population is increasing [2,13]. This trend represents an important health care problem; a multicenter controlled study estimated that patients with advanced medical illnesses who died in ICUs spent an average of 8 days in undesirable states, such as being comatose or receiving mechanical ventilation [14]. Among conscious ICU patients who died, 50% experienced significant pain for more than half the time during the final week of life [14]. Furthermore, terminal hospitalizations account for 7.5% of total inpatient costs in the United States, with ICU care accounting for nearly 80% of these costs [1,15]. Overall, these findings show that optimizing ICU utilization among patients with advanced medical illnesses is an opportunity to improve the quality and efficiency of care in this high-risk, high-cost population.

Intensive Care Unit Overutilization in the Los Angeles County Department of Health Services

Like many health care systems, ICU overutilization is highly prevalent in the hospitals of the Los Angeles County (LAC) Department of Health Services (DHS), the second-largest public health care system in the United States. A recent study from our group showed that among 808 medical ICU patients at Harbor-UCLA Medical Center (HUMC), over 20% had reduced likelihoods of benefit from ICU care due to advanced medical illnesses, such as advanced dementia and metastatic cancer (see [Table 1](#)) [16]. Of these patients, 86% died or were discharged in severely compromised health states and only 6% were discharged home. This subset of patients is at the highest risk to have invasive treatments that prolong suffering without improving outcomes. As such, we focus this proposal on improving ICU utilization on these critically ill patients with advanced medical illnesses.

In order to understand why patients with advanced medical illnesses received ICU care so frequently, we conducted semistructured interviews of ICU physicians and nurses at LAC DHS hospitals. Key themes that emerged from these interviews were that health care providers do not comprehensively discuss prognoses, risks and benefits, and patient preferences for ICU treatments, which lead to inaccurate expectations from ICU care and unrealistic fears of prematurely forgoing potentially beneficial treatments. Barriers to effective shared decision making included (1) underappreciation of the value of ICU care planning, (2) lack of institutional standards and tools for ICU care planning, and (3) difficulty in scheduling meetings between providers and families.

Table 1. Priority levels of medical intensive care unit (ICU) admissions at Harbor-University of California Los Angeles Medical Center.

| Priority | Description | Percentage, % |
|----------|--|---------------|
| 1 | Critically ill, needing intensive treatment and monitoring that cannot be provided outside of ICUs | 46.9 |
| 2 | Not critically ill, but requiring close monitoring and potentially immediate intervention | 23.4 |
| 3 | Critically ill, but reduced likelihood of recovery because of underlying diseases or severity of acute illness | 20.9 |
| 4 | Not appropriate for ICU; equivalent outcomes achievable with non-ICU care | 8.8 |

Facilitating Shared Decision Making Using Time-Limited Trials

Prior work has shown that developing ICU interventions that change physician behaviors, facilitate communication between

providers and families, and improve patient care is challenging [14,17,18]. A large multicenter clinical trial—the Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatment (SUPPORT)—did not improve the quality of end-of-life care by providing physicians with patients’

prognostic information and nurse-facilitated advanced-care planning [14]. A hypothesis for why SUPPORT failed to change outcomes is that it did not use a multifaceted, systems approach to changing physicians' behaviors [19,20]. Furthermore, even when prognoses are understood and risks and benefits of ICU care are discussed, it is likely that clinicians, patients, and families frequently remain uncertain about the appropriateness of ICU care [21-23]. In such situations, the default decision in most ICUs is to pursue aggressive ICU treatments, often without reassessment of that decision [24].

For patients with advanced illnesses, this approach places them at risk for prolonged suffering with minimal anticipated benefit [3,4]. Time-limited trials (TLTs) are agreements between the clinicians and the patients and decision makers to use certain medical therapies over a defined period of time and evaluate whether patients improve or worsen according to predetermined clinical parameters [24]. TLTs involve detailed discussions of patients' preferences for care, prognosis, and what would constitute clinical improvement based on patients' values and preferences. Follow-up meetings are held to see if patients improve or worsen according to predetermined clinical parameters and next steps in care are negotiated based on these results [24]. TLTs promote regular structured dialogue between providers and patients and their families, promote consensus in decision making through iterative assessments of clinical trajectory, and set rational boundaries to treatments based on patients' goals of care. TLTs have been used effectively for outpatient advanced-care planning in patients with end-stage kidney disease, stroke, cancer, and chronic obstructive pulmonary disease [25-30]. However, to our knowledge there have been no studies that examined their effectiveness in ICU patients. Schenker et al examined audio-recordings of ICU family meetings for 72 patients at high risk for death or severe impairment and found that TLTs were offered only 13% of the time [31]. When TLTs were offered, clinicians frequently did

not discuss key elements, such as outcomes used to determine improvement, worsening, or possible next steps after the trial [31].

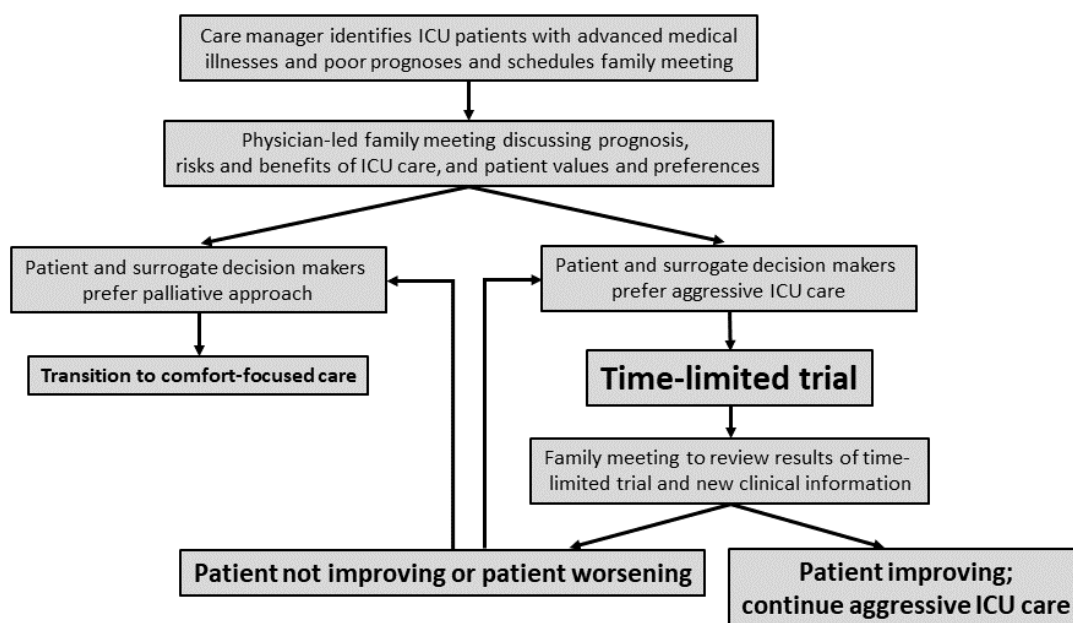
In summary, nonbeneficial treatments are frequently delivered in medical ICUs to patients with advanced medical illnesses. Although the appropriateness of ICU care in this population is subject to varying opinions, there is general consensus that intensity of ICU treatments should align with patients' prognoses, preferences, and values [32]. Previous studies suggest that most patients with advanced medical illnesses, when informed of their therapeutic options, would forgo invasive treatments and would prefer palliative approaches [1,8-12]. Unfortunately, structured care planning between clinicians and critically ill patients and their families is infrequent [33,34]. TLTs are a promising, but underutilized, care-planning approach for ICU patients with advanced medical illnesses. An intervention utilizing TLTs as a default care-planning approach for ICU patients with advanced medical illnesses has the potential to address key barriers to shared decision making identified in our preliminary studies [35]. However, given the paucity of studies on their use in critically ill patients and the complexity of ICU communication, input from key stakeholders on how best to implement TLTs in this group is crucial.

Objectives

Overview

The objective of this proposal is to test an intervention that seeks to reduce invasive and nonbeneficial ICU treatments by improving communication between providers, surrogate decision makers, and critically ill patients with advanced medical illnesses. We propose to implement an intervention that facilitates communication and shared decision making between providers and patients and their families by using protocolized TLTs for ICU patients with advanced medical illnesses who receive aggressive care (see Figure 1).

Figure 1. Implementation strategy for time-limited trials. ICU: intensive care unit.



We hypothesize that a multicomponent quality-improvement intervention, informed by stakeholder input and that uses protocolized TLTs as the default ICU care-planning approach for critically ill patients with advanced medical illnesses, will decrease the duration and intensity of nonbeneficial ICU care without changing hospital mortality. We will examine our hypothesis with the specific aims discussed in the following sections.

Aim 1

Aim 1 consists of identifying barriers and facilitators to performing TLTs in ICU patients with advanced medical illnesses using focus groups of physicians and semistructured interviews of patients and their families.

Aim 2

Aim 2 consists of examining whether a multicomponent quality-improvement intervention using TLTs as the default care-planning approach for ICU patients with advanced medical illnesses reduces duration and intensity of nonbeneficial ICU treatments

Methods

Overview

This proposal will be conducted in the medical ICUs of three public hospitals in LAC DHS: HUMC, Olive View Medical Center (OVMC), and Los Angeles County-University of Southern California (LAC-USC) Medical Center. We will implement the aims sequentially across the medical centers. The sequential implementation strategy will be used to identify ways to improve training and uptake of the interventions with each iteration. For Aim 1, we will conduct focus groups and interviews with key stakeholders to identify facilitators and barriers to implementing TLTs among ICU patients with advanced medical illnesses. This will be performed prior to implementing quality-improvement interventions in Aim 2 (see [Multimedia Appendix 1](#)). The information obtained from these qualitative evaluations will be used to enhance our implementation strategy for Aim 2, in which we will examine the effectiveness of our intervention using a before-and-after study design (see [Multimedia Appendix 1](#)).

Aim 1

Rationale and Overview

In the first phase of the proposed study, we will conduct focus groups with ICU physicians and interviews with patients and/or surrogate decision makers to explore attitudes toward ICU care among patients with advanced medical illnesses and strategies to optimally implement TLTs. We anticipate that themes from these sessions will include perceived barriers to conducting family meetings, knowledge and skill deficits among clinicians in conducting meetings, clinical outcomes most effective in decision making, optimal timing and frequency of meetings, optimal duration of TLTs, and communicating sensitive medical topics to lay populations.

Experimental Approach

Structure of Focus Groups With Intensive Care Unit Physicians

In-person focus groups with medical ICU physicians will be conducted at HUMC, OVMC, and LAC-USC Medical Center. We will invite all ICU attendings and fellows from each institution; we anticipate that 10-30 people will be invited and that 6-15 will participate per institution. Informed consent will be obtained for audio-recording. The meetings will be held at each medical center, will last approximately 90 minutes, and will be led by two of the study investigators.

Content of Focus Groups With Intensive Care Unit Physicians

Moderators will lead discussions in each group. Discussions will begin with an explanation of the risks and benefits of aggressive ICU care for patients with advanced medical illnesses and of the goal of delivering care that aligns with patients' values and preferences. We will explain the concept of TLTs and elicit responses to a prespecified set of open-ended questions.

Sample questions include the following: (1) How are decisions regarding ICU care currently made? (2) Do you believe that TLTs are appropriate interventions? Why or why not? (3) What information is needed to effectively make decisions about continuing aggressive ICU care? (4) What is the best way to communicate that information? (5) Should care providers make recommendations regarding the next steps in care after TLTs? (6) What are barriers to having meetings with patients and their families? (7) What information do you typically provide in family meetings? (8) How do you feel about using a protocol and checklist during family meetings? (9) How comfortable are you with making recommendations for end-of-life care? and (10) How much variability do you perceive between physicians regarding prognoses and goals of care?

Structure of Semistructured Interviews With Patients and Surrogate Decision Makers

In-person interviews with patients and/or surrogate decision makers will be conducted at HUMC, OVMC, and LAC-USC Medical Center. We will invite English-speaking patients or family members and surrogate decision makers who are available to participate in interviews; we anticipate that 20 people will be invited and that 10 will participate per institution. Patients and family members will be invited for interviews after at least 72 hours of ICU hospitalization to provide adequate opportunities for communication and care planning with ICU clinicians. Informed consent will be obtained for audio-recording. The interviews will be held at each medical center, will last approximately 45 minutes, and will be led by one of the study investigators.

Content of Semistructured Interviews With Patients and Surrogate Decision Makers

An investigator will lead semistructured interviews of patients and/or family members, which will explore decision making in the ICU. We will explore factors that played key roles in

decision making during ICU hospitalization with a prespecified set of open-ended questions.

Sample questions will include the following: (1) Describe the most difficult decision you had to make during this hospitalization, (2) What decision did you make and how did you come to that decision? (3) What did the ICU care providers do that made that decision harder or easier? (4) What clinical events resonated with you regarding whether you or your family member was improving or worsening? (5) What other factors besides those discussed in family meetings affect your decision regarding ICU care? (6) How often were you confused about information that was presented to you during hospitalization? (7) What information was difficult to understand and why? and (8) What can the care providers do to better support you during this time?

Analysis of Focus Groups and Interviews

Analysis of data from focus groups and interviews will be descriptive, summarizing the range of issues that ICU physicians, patients, and surrogate decision makers discuss.

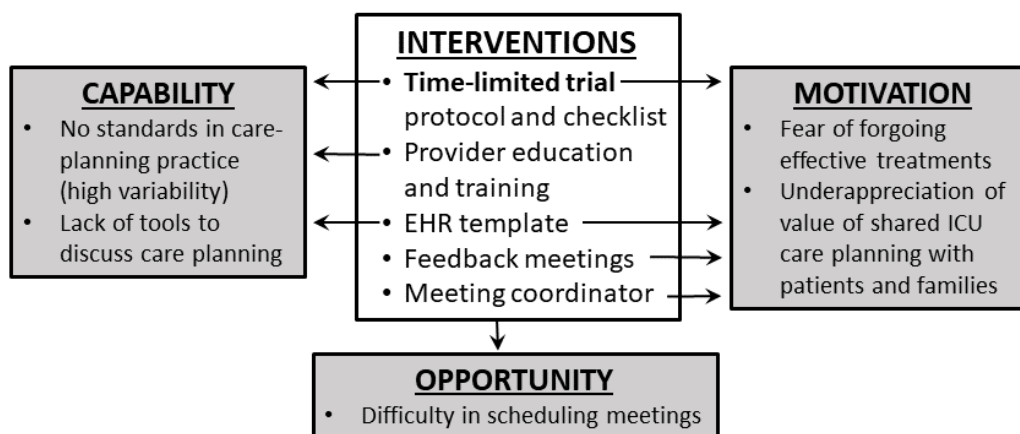
Using the audio-recordings and moderators' notes, content analysis of the group discussions and interviews will be performed to systematically define themes, emphasizing those that represent facilitators and barriers to implementation of our intervention [36-39]. These themes will be used to modify the implementation of the quality-improvement intervention in Aim 2.

Aim 2

Rationale and Overview

In the second phase of the proposed study, we will implement an intervention that facilitates family meetings using serial TLTs as the default care-planning approach for ICU patients with advanced medical illnesses. The multicomponent intervention is based on the *capability, opportunity, motivation to perform a behavior* (COM-B) framework by Michie and colleagues [40-42]; the intervention will address barriers identified in our preliminary studies that inhibit capabilities, opportunities, and motivation for effective shared decision making (see [Figure 2](#)).

Figure 2. Conceptual framework for interventions. EHR: electronic health record; ICU: intensive care unit.



Experimental Approach

Study Population

Patients with a low likelihood of benefitting from ICU care due to advanced medical illnesses will be identified by assigning patients to priority levels from the Society of Critical Care Medicine guidelines for ICU admissions (see [Table 1](#)) [43-45]. This system prioritizes ICU admissions based on the projected likelihood of benefit. For this proposal, we will train all ICU physicians—attending and fellows—to perform daily priority-level assessments for ICU patients. We have previously published our experience with training ICU teams to classify patients using this system [16]. Each day, case managers will ask ICU physicians to assign priority levels to each patient after ICU rounds. Our intervention will be implemented on all new ICU admissions who are assigned to priority levels 3 or 4. We will exclude patients who were assigned to different priority levels on admission but who are assigned to priority levels 3 or 4 during their ICU stay. If patients cannot communicate for themselves and do not have surrogate decision makers, they will be excluded.

Setting and Study Design

The study will be conducted in medical ICUs of three LAC DHS hospitals using a before-and-after study design. The study will be conducted sequentially among the three hospitals to allow investigators to modify and improve the implementation strategy over the course of the study based on clinician feedback (see [Multimedia Appendix 1](#)). For each hospital, we will collect preintervention data during the first 4 months and examine outcomes for a 4-month period after implementing the study intervention (see [Multimedia Appendix 1](#)). There are 52 medical ICU beds among the three hospitals. We anticipate that 960 patients will be admitted and screened in both the pre- and postintervention periods across the three medical ICUs. Based on our preliminary data, we estimate that 15% will be priority 3 and 4 patients who are candidates for intervention and 10% will be excluded due to lack of surrogate decision makers. As such, we estimate studying 130 patients during each 4-month period. Using $\alpha=.05$ (two-sided), $\beta=.20$ (80% power), and mean ICU stay of 6.5 days (SD 3.7) from our previous study [16], we expect to be able to detect a difference of 1.3 ICU days between time periods.

Time-Limited Trial Protocol

Physician-led family meetings will be conducted using a standardized protocol, which includes: (1) introductions, (2) summary of ICU course, (3) discussion of short- and long-term prognosis, (4) risks and benefits of aggressive ICU care, and (5) eliciting patients' preferences for care during critical illness and/or at the end of life (see [Multimedia Appendix 2](#) and [Figure 1](#)). Based on discussion of these elements, if patients and surrogate decision makers wish for a palliative approach, the patient will be transitioned to comfort-focused care. If patients and surrogate decision makers prefer aggressive ICU care, a TLT will be performed. For the TLT, care providers and surrogate decision makers will identify specific clinical parameters that will be used to determine whether patients are improving or worsening. Care providers will recommend a time period for which these parameters will be followed and likely actions to be taken at the end of the trial based on improvement or worsening. In the follow-up meeting, care providers will review trends in clinical parameters; they will also redefine prognoses based on these trends and additional clinical information obtained since the last meeting. Based on this information, recommendations regarding the next steps for care will be made. If the patients and surrogate decision makers opt for a palliative approach, comfort-focused care will be provided. If they prefer continuation of aggressive care, another TLT will be negotiated. This iterative process will be continued, with sequential meetings performed at the discretion of the ICU team (see [Figure 1](#)).

Multicomponent Implementation Strategy

Additional components to the implementation strategy are shown in [Figures 1](#) and [2](#). ICU physicians—attending and fellows—will be trained to use the TLT protocol in educational sessions utilizing actors as family members in role-playing scenarios (see [Figure 2](#)). Case managers will identify eligible patients each day by asking ICU physicians which admissions are ranked priority 3 or 4 and will schedule family meetings between care providers and patients and their families within 24 hours of admission. Family meetings will be conducted using checklists to improve compliance with the protocol (see [Multimedia Appendix 2](#)). A standardized electronic health record (EHR) template will be created to encourage documentation of important outcomes from meetings and to facilitate data collection. Each medical ICU will have a physician champion who will direct implementation of study protocols at each medical center and conduct monthly feedback sessions with ICU teams to discuss opportunities for improvement. Physician champions and research team members will meet every month to discuss strategies to improve family meetings, patient enrollment, and data collection.

Outcomes and Measurements

All outcomes will be collected in both the pre- and postintervention periods. The primary outcome will be ICU length of stay. Secondary outcomes will include hospital length of stay, days receiving life-sustaining treatments (eg, mechanical ventilation, use of vasopressor medications, and renal replacement therapy), number of attempts at cardiopulmonary resuscitation (CPR), number of invasive procedures (eg, central

venous or arterial catheterization, thoracentesis, paracentesis, lumbar puncture, and endoscopy), and outcomes of hospitalization (eg, death, discharge to hospice, skilled nursing facility, or home). These data will be collected from retrospective chart review by trained case managers using standardized data abstraction forms.

Analysis Plan

Primary and secondary outcomes will be compared before and after the intervention [46-48]. Days in ICU, days in hospital, and days receiving life-sustaining treatments will be compared using Wilcoxon rank-sum tests [49,50]. ICU and hospital mortality rates will be compared using χ^2 tests. Other continuous and categorical outcomes will be compared between groups using t tests or χ^2 tests, respectively, or equivalent nonparametric approaches for variables that are nonnormally distributed. Multivariable regression models will be used to examine the effects of covariates, such as patient demographics, comorbid conditions, severity of illness, and hospitals, on study outcomes [49,50]. Primary and secondary outcomes before and after the intervention will also be analyzed and will be stratified by ICU survivors and nonsurvivors. Days receiving ICU care, days receiving life-sustaining treatments, number of invasive procedures, and number of CPR attempts among patients who did not survive hospitalization will be considered nonbeneficial treatment and will be compared before and after the intervention.

Expected Results

We expect to find fewer ICU days, hospital days, and days of life-sustaining treatments after the TLT intervention. We also expect a fewer number of attempts at CPR and other invasive procedures. We expect mortality rates to remain unchanged before and after the intervention. We expect reductions in ICU days, days receiving life-sustaining treatments, and number of invasive procedures after the intervention to be greater among patients who died during hospitalization than among survivors.

Limitations

We recognize that priority levels used to identify patients are subjective. However, we believe that using clinicians' general impressions on the likelihood of benefit from ICU care, rather than more objective measures such as prognostic scoring systems or predefined lists of medical conditions, emulates clinical practice and will be more informative regarding the effectiveness of this intervention. If there are fewer priority 3 and 4 patients than anticipated, we will expand the study criteria to include patients who were initially categorized into a different priority level on ICU admission but were assigned priority level 3 or 4 during the ICU hospitalization. Based on our preliminary data, this will make an additional 10% of ICU patients eligible for the study.

Ethical Considerations

Our project was approved by the Institutional Review Board (IRB) at the Los Angeles BioMedical Research Institute at HUMC (project number: 043544) with approval at the other two medical centers using a reliance agreement. For Aim 1, informed consent was obtained for participants in focus groups and interviews. For Aim 2, the IRB waived the need for informed consent. There were several key factors involved in

the waiver of consent. First, communication between ICU physicians and families is an expected practice; as well, the aim of the quality-improvement intervention was to encourage physicians to discuss elements that are vital to effective shared decision making, such as patient values and preferences, prognosis, and expectations for ICU treatments. As such, the intervention posed minimal risk to participants beyond usual ICU practice. Second, TLTs were not coercive or prescriptive, and maintained patient and family autonomy in decision making: at the end of the TLTs, patients and family members could choose to continue invasive treatments. Third, the quality-improvement intervention created a new default communication approach that applied to all ICU patients with advanced medical illnesses, regardless of participation in the study. Finally, implementation of the quality-improvement program was approved by the LAC DHS. Given these factors, the IRB determined that there was minimal risk to participants, waiver of consent would not adversely affect the rights and welfare of the participants, and the project could not be feasibly performed without the waiver.

Results

The study began in August 2017. The implementation of interventions and data collection were completed at HUMC and OVMC. As of September 2019, the study was at the postintervention stage at the LAC-USC Medical Center. We have completed focus groups with physicians at each medical

center (N=29) and interviews of family members and surrogate decision makers (N=18). The study is expected to be completed in the first quarter of 2020, and results are expected to be available in mid-2020.

Discussion

Overutilization of ICU treatments among critically ill patients with advanced medical illnesses leads to medical care that is invasive, costly, and potentially misaligned with patient preferences. The successful completion of the aims in this proposal will improve the quality and efficiency of care by reducing unnecessary invasive treatments and decreasing ICU care that does not achieve its intended goals and prolongs suffering. This will be achieved through better communication and alignment of ICU care with patients' values and preferences. Additionally, these studies will generate preliminary data and a track record of collaboration between researchers, clinicians, and hospital leaders, which will be foundational for future applications that attempt large-scale implementation of interventions that improve ICU communication and care planning. Thus, this proposal has the potential to catalyze the development of an ICU research program that addresses complex challenges in health care systems; this could be done through partnerships between academicians in health services research and frontline physicians and hospital administrators with experience in operationalizing health care improvements.

Acknowledgments

The study outlined in this manuscript was funded through the LAC DHS/UCLA Clinical and Translational Research Institute (CTSI) Implementation Science Award (grant number: UL1TR001881). The content is solely the responsibility of the authors and does not necessarily represent the views of the DHS and UCLA CTSI. The funding institutions had no role in the design of the study, data collection or interpretation, or writing and approval of the final manuscript. The authors also gratefully acknowledge the contributions of the care providers and champions at each of the hospitals participating in this study.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Study timeline.

[[XLSX File \(Microsoft Excel File\), 14 KB - resprot_v8i11e16301_app1.xlsx](#)]

Multimedia Appendix 2

Time-limited trial (TLT) family meeting protocol and checklist.

[[PDF File \(Adobe PDF File\), 161 KB - resprot_v8i11e16301_app2.pdf](#)]

Multimedia Appendix 3

Peer-reviewer report from the UCLA Clinical and Translational Science Institute.

[[PDF File \(Adobe PDF File\), 169 KB - resprot_v8i11e16301_app3.pdf](#)]

References

1. Angus DC, Barnato AE, Linde-Zwirble WT, Weissfeld LA, Watson RS, Rickert T, Robert Wood Johnson Foundation ICU End-Of-Life Peer Group. Use of intensive care at the end of life in the United States: An epidemiologic study. *Crit Care Med* 2004 Mar;32(3):638-643. [doi: [10.1097/01.ccm.0000114816.62331.08](https://doi.org/10.1097/01.ccm.0000114816.62331.08)] [Medline: [15090940](https://pubmed.ncbi.nlm.nih.gov/15090940/)]

2. Morden NE, Chang C, Jacobson JO, Berke EM, Bynum JP, Murray KM, et al. End-of-life care for Medicare beneficiaries with cancer is highly intensive overall and varies widely. *Health Aff (Millwood)* 2012 Apr;31(4):786-796 [FREE Full text] [doi: [10.1377/hlthaff.2011.0650](https://doi.org/10.1377/hlthaff.2011.0650)] [Medline: [22492896](https://pubmed.ncbi.nlm.nih.gov/22492896/)]
3. Huynh TN, Kleerup EC, Wiley JF, Savitsky TD, Guse D, Garber BJ, et al. The frequency and cost of treatment perceived to be futile in critical care. *JAMA Intern Med* 2013 Nov 11;173(20):1887-1894. [doi: [10.1001/jamainternmed.2013.10261](https://doi.org/10.1001/jamainternmed.2013.10261)] [Medline: [24018712](https://pubmed.ncbi.nlm.nih.gov/24018712/)]
4. Chang DW, Shapiro MF. Association between intensive care unit utilization during hospitalization and costs, use of invasive procedures, and mortality. *JAMA Intern Med* 2016 Oct 01;176(10):1492-1499. [doi: [10.1001/jamainternmed.2016.4298](https://doi.org/10.1001/jamainternmed.2016.4298)] [Medline: [27532500](https://pubmed.ncbi.nlm.nih.gov/27532500/)]
5. Admon AJ, Seymour CW, Gershengorn HB, Wunsch H, Cooke CR. Hospital-level variation in ICU admission and critical care procedures for patients hospitalized for pulmonary embolism. *Chest* 2014 Dec;146(6):1452-1461 [FREE Full text] [doi: [10.1378/chest.14-0059](https://doi.org/10.1378/chest.14-0059)] [Medline: [24992579](https://pubmed.ncbi.nlm.nih.gov/24992579/)]
6. Gershengorn HB, Iwashyna TJ, Cooke CR, Scales DC, Kahn JM, Wunsch H. Variation in use of intensive care for adults with diabetic ketoacidosis. *Crit Care Med* 2012 Jul;40(7):2009-2015 [FREE Full text] [doi: [10.1097/CCM.0b013e31824e9eae](https://doi.org/10.1097/CCM.0b013e31824e9eae)] [Medline: [22564962](https://pubmed.ncbi.nlm.nih.gov/22564962/)]
7. Safavi KC, Dharmarajan K, Kim N, Strait KM, Li S, Chen SI, et al. Variation exists in rates of admission to intensive care units for heart failure patients across hospitals in the United States. *Circulation* 2013 Feb 26;127(8):923-929 [FREE Full text] [doi: [10.1161/CIRCULATIONAHA.112.001088](https://doi.org/10.1161/CIRCULATIONAHA.112.001088)] [Medline: [23355624](https://pubmed.ncbi.nlm.nih.gov/23355624/)]
8. Institute of Medicine. In: Field MJ, Cassel CK, editors. *Approaching Death: Improving Care at the End of Life*. Washington, DC: The National Academies Press; 1997.
9. Pritchard R, Fisher E, Teno J, Sharp S, Reding D, Knaus W, et al. Influence of patient preferences and local health system characteristics on the place of death. SUPPORT Investigators. Study to Understand Prognoses and Preferences for Risks and Outcomes of Treatment. *J Am Geriatr Soc* 1998 Oct;46(10):1242-1250. [doi: [10.1111/j.1532-5415.1998.tb04540.x](https://doi.org/10.1111/j.1532-5415.1998.tb04540.x)] [Medline: [9777906](https://pubmed.ncbi.nlm.nih.gov/9777906/)]
10. Barnato AE, Anthony DL, Skinner J, Gallagher PM, Fisher ES. Racial and ethnic differences in preferences for end-of-life treatment. *J Gen Intern Med* 2009 Jun;24(6):695-701 [FREE Full text] [doi: [10.1007/s11606-009-0952-6](https://doi.org/10.1007/s11606-009-0952-6)] [Medline: [19387750](https://pubmed.ncbi.nlm.nih.gov/19387750/)]
11. Barnato AE, Herndon MB, Anthony DL, Gallagher PM, Skinner JS, Bynum JP, et al. Are regional variations in end-of-life care intensity explained by patient preferences?: A study of the US Medicare population. *Med Care* 2007 May;45(5):386-393 [FREE Full text] [doi: [10.1097/01.mlr.0000255248.79308.41](https://doi.org/10.1097/01.mlr.0000255248.79308.41)] [Medline: [17446824](https://pubmed.ncbi.nlm.nih.gov/17446824/)]
12. Frankl D, Oye RK, Bellamy PE. Attitudes of hospitalized patients toward life support: A survey of 200 medical inpatients. *Am J Med* 1989 Jun;86(6):645-648. [Medline: [11659207](https://pubmed.ncbi.nlm.nih.gov/11659207/)]
13. Earle CC, Neville BA, Landrum MB, Ayanian JZ, Block SD, Weeks JC. Trends in the aggressiveness of cancer care near the end of life. *J Clin Oncol* 2004 Jan 15;22(2):315-321. [doi: [10.1200/JCO.2004.08.136](https://doi.org/10.1200/JCO.2004.08.136)] [Medline: [14722041](https://pubmed.ncbi.nlm.nih.gov/14722041/)]
14. The SUPPORT Principal Investigators. A controlled trial to improve care for seriously ill hospitalized patients. The Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments (SUPPORT). *JAMA* 1995;274(20):1591-1598. [Medline: [7474243](https://pubmed.ncbi.nlm.nih.gov/7474243/)]
15. Halpern NA, Pastores SM. Critical care medicine in the United States 2000-2005: An analysis of bed numbers, occupancy rates, payer mix, and costs. *Crit Care Med* 2010 Jan;38(1):65-71. [doi: [10.1097/CCM.0b013e3181b090d0](https://doi.org/10.1097/CCM.0b013e3181b090d0)] [Medline: [19730257](https://pubmed.ncbi.nlm.nih.gov/19730257/)]
16. Chang DW, Dacosta D, Shapiro MF. Priority levels in medical intensive care at an academic public hospital. *JAMA Intern Med* 2017 Feb 01;177(2):280-281. [doi: [10.1001/jamainternmed.2016.8060](https://doi.org/10.1001/jamainternmed.2016.8060)] [Medline: [28027383](https://pubmed.ncbi.nlm.nih.gov/28027383/)]
17. Grol R, Wensing M. What drives change? Barriers to and incentives for achieving evidence-based practice. *Med J Aust* 2004 Mar 15;180(S6):S57-S60. [Medline: [15012583](https://pubmed.ncbi.nlm.nih.gov/15012583/)]
18. Scheunemann LP, McDevitt M, Carson SS, Hanson LC. Randomized, controlled trials of interventions to improve communication in intensive care: A systematic review. *Chest* 2011 Mar;139(3):543-554. [doi: [10.1378/chest.10-0595](https://doi.org/10.1378/chest.10-0595)] [Medline: [21106660](https://pubmed.ncbi.nlm.nih.gov/21106660/)]
19. Lynn J, Arkes H, Stevens M, Cohn F, Koenig B, Fox E, et al. Rethinking fundamental assumptions: SUPPORT's implications for future reform. Study to Understand Prognoses and Preferences and Risks of Treatment. *J Am Geriatr Soc* 2000 May;48(S1):S214-S221. [doi: [10.1111/j.1532-5415.2000.tb03135.x](https://doi.org/10.1111/j.1532-5415.2000.tb03135.x)] [Medline: [10809478](https://pubmed.ncbi.nlm.nih.gov/10809478/)]
20. Lynn J, De Vries KO, Arkes HR, Stevens M, Cohn F, Murphy P, et al. Ineffectiveness of the SUPPORT intervention: Review of explanations. *J Am Geriatr Soc* 2000 May;48(S1):S206-S213. [doi: [10.1111/j.1532-5415.2000.tb03134.x](https://doi.org/10.1111/j.1532-5415.2000.tb03134.x)] [Medline: [10809477](https://pubmed.ncbi.nlm.nih.gov/10809477/)]
21. Elpern EH, Patterson PA, Gloskey D, Bone RC. Patients' preferences for intensive care. *Crit Care Med* 1992 Jan;20(1):43-47. [doi: [10.1097/00003246-199201000-00014](https://doi.org/10.1097/00003246-199201000-00014)] [Medline: [1729042](https://pubmed.ncbi.nlm.nih.gov/1729042/)]
22. Wu C, Melnikow J, Dinh T, Holmes J, Gaona S, Bottyan T, et al. Patient admission preferences and perceptions. *West J Emerg Med* 2015 Sep;16(5):707-714 [FREE Full text] [doi: [10.5811/westjem.2015.7.27458](https://doi.org/10.5811/westjem.2015.7.27458)] [Medline: [26587095](https://pubmed.ncbi.nlm.nih.gov/26587095/)]

23. Goodlin SJ, Zhong Z, Lynn J, Teno JM, Fago JP, Desbiens N, et al. Factors associated with use of cardiopulmonary resuscitation in seriously ill hospitalized adults. *JAMA* 1999;282(24):2333-2339. [doi: [10.1001/jama.282.24.2333](https://doi.org/10.1001/jama.282.24.2333)] [Medline: [10612321](https://pubmed.ncbi.nlm.nih.gov/10612321/)]
24. Quill TE, Holloway R. Time-limited trials near the end of life. *JAMA* 2011 Oct 05;306(13):1483-1484. [doi: [10.1001/jama.2011.1413](https://doi.org/10.1001/jama.2011.1413)] [Medline: [21972312](https://pubmed.ncbi.nlm.nih.gov/21972312/)]
25. Rinehart A. Beyond the futility argument: The fair process approach and time-limited trials for managing dialysis conflict. *Clin J Am Soc Nephrol* 2013 Nov;8(11):2000-2006 [FREE Full text] [doi: [10.2215/CJN.12191212](https://doi.org/10.2215/CJN.12191212)] [Medline: [23868900](https://pubmed.ncbi.nlm.nih.gov/23868900/)]
26. Fried TR, Vaz Fragoso CA, Rabow MW. Caring for the older person with chronic obstructive pulmonary disease. *JAMA* 2012 Sep 26;308(12):1254-1263 [FREE Full text] [doi: [10.1001/jama.2012.12422](https://doi.org/10.1001/jama.2012.12422)] [Medline: [23011715](https://pubmed.ncbi.nlm.nih.gov/23011715/)]
27. Neuman MD, Allen S, Schwarze ML, Uy J. Using time-limited trials to improve surgical care for frail older adults. *Ann Surg* 2015 Apr;261(4):639-641 [FREE Full text] [doi: [10.1097/SLA.0000000000000939](https://doi.org/10.1097/SLA.0000000000000939)] [Medline: [25211275](https://pubmed.ncbi.nlm.nih.gov/25211275/)]
28. Holloway RG, Arnold RM, Creutzfeldt CJ, Lewis EF, Lutz BJ, McCann RM, American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology. Palliative and end-of-life care in stroke: A statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2014 Jun;45(6):1887-1916. [doi: [10.1161/STR.0000000000000015](https://doi.org/10.1161/STR.0000000000000015)] [Medline: [24676781](https://pubmed.ncbi.nlm.nih.gov/24676781/)]
29. Shrimel MG, Ferket BS, Scott DJ, Lee J, Barragan-Bradford D, Pollard T, et al. Time-limited trials of intensive care for critically ill patients with cancer: How long is long enough? *JAMA Oncol* 2016 Jan;2(1):76-83 [FREE Full text] [doi: [10.1001/jamaoncol.2015.3336](https://doi.org/10.1001/jamaoncol.2015.3336)] [Medline: [26469222](https://pubmed.ncbi.nlm.nih.gov/26469222/)]
30. Scherer JS, Holley JL. The role of time-limited trials in dialysis decision making in critically ill patients. *Clin J Am Soc Nephrol* 2016 Feb 05;11(2):344-353 [FREE Full text] [doi: [10.2215/CJN.03550315](https://doi.org/10.2215/CJN.03550315)] [Medline: [26450932](https://pubmed.ncbi.nlm.nih.gov/26450932/)]
31. Schenker Y, Tiver GA, Hong SY, White DB. Discussion of treatment trials in intensive care. *J Crit Care* 2013 Oct;28(5):862-869 [FREE Full text] [doi: [10.1016/j.jcrc.2013.04.015](https://doi.org/10.1016/j.jcrc.2013.04.015)] [Medline: [23768446](https://pubmed.ncbi.nlm.nih.gov/23768446/)]
32. Curtis JR, Engelberg RA, Bensink ME, Ramsey SD. End-of-life care in the intensive care unit: Can we simultaneously increase quality and reduce costs? *Am J Respir Crit Care Med* 2012 Oct 01;186(7):587-592 [FREE Full text] [doi: [10.1164/rccm.201206-1020CP](https://doi.org/10.1164/rccm.201206-1020CP)] [Medline: [22859524](https://pubmed.ncbi.nlm.nih.gov/22859524/)]
33. Curtis J, Engelberg R, Nielsen E, Au D, Patrick D. Patient-physician communication about end-of-life care for patients with severe COPD. *Eur Respir J* 2004 Aug;24(2):200-205 [FREE Full text] [doi: [10.1183/09031936.04.00010104](https://doi.org/10.1183/09031936.04.00010104)] [Medline: [15332385](https://pubmed.ncbi.nlm.nih.gov/15332385/)]
34. McNeely PD, Hébert PC, Dales RE, O'Connor AM, Wells G, McKim D, et al. Deciding about mechanical ventilation in end-stage chronic obstructive pulmonary disease: How respirologists perceive their role. *CMAJ* 1997 Jan 15;156(2):177-183 [FREE Full text] [Medline: [9012718](https://pubmed.ncbi.nlm.nih.gov/9012718/)]
35. Bruce CR, Liang C, Blumenthal-Barby JS, Zimmerman J, Downey A, Pham L, et al. Barriers and facilitators to initiating and completing time-limited trials in critical care. *Crit Care Med* 2015 Dec;43(12):2535-2543. [doi: [10.1097/CCM.0000000000001307](https://doi.org/10.1097/CCM.0000000000001307)] [Medline: [26465223](https://pubmed.ncbi.nlm.nih.gov/26465223/)]
36. Rabiee F. Focus-group interview and data analysis. *Proc Nutr Soc* 2004 Nov;63(4):655-660. [doi: [10.1079/pns2004399](https://doi.org/10.1079/pns2004399)] [Medline: [15831139](https://pubmed.ncbi.nlm.nih.gov/15831139/)]
37. Sim J. Collecting and analysing qualitative data: Issues raised by the focus group. *J Adv Nurs* 1998 Aug;28(2):345-352. [doi: [10.1046/j.1365-2648.1998.00692.x](https://doi.org/10.1046/j.1365-2648.1998.00692.x)] [Medline: [9725732](https://pubmed.ncbi.nlm.nih.gov/9725732/)]
38. Joseph DH, Griffin M, Sullivan ED. Videotaped focus groups: Transforming a therapeutic strategy into a research tool. *Nurs Forum* 2000;35(1):15-20. [doi: [10.1111/j.1744-6198.2000.tb01173.x](https://doi.org/10.1111/j.1744-6198.2000.tb01173.x)] [Medline: [10847061](https://pubmed.ncbi.nlm.nih.gov/10847061/)]
39. Huynh TN, Kleerup EC, Wiley JF, Savitsky TD, Guse D, Garber BJ, et al. The frequency and cost of treatment perceived to be futile in critical care. *JAMA Intern Med* 2013 Nov 11;173(20):1887-1894. [doi: [10.1001/jamainternmed.2013.10261](https://doi.org/10.1001/jamainternmed.2013.10261)] [Medline: [24018712](https://pubmed.ncbi.nlm.nih.gov/24018712/)]
40. Michie S, van Stralen MM, West R. The behaviour change wheel: A new method for characterising and designing behaviour change interventions. *Implement Sci* 2011 Apr 23;6:42 [FREE Full text] [doi: [10.1186/1748-5908-6-42](https://doi.org/10.1186/1748-5908-6-42)] [Medline: [21513547](https://pubmed.ncbi.nlm.nih.gov/21513547/)]
41. Weiss CH, Krishnan JA, Au DH, Bender BG, Carson SS, Cattamanchi A, ATS Ad Hoc Committee on Implementation Science. An official American Thoracic Society Research Statement: Implementation science in pulmonary, critical care, and sleep medicine. *Am J Respir Crit Care Med* 2016 Oct 15;194(8):1015-1025 [FREE Full text] [doi: [10.1164/rccm.201608-1690ST](https://doi.org/10.1164/rccm.201608-1690ST)] [Medline: [27739895](https://pubmed.ncbi.nlm.nih.gov/27739895/)]
42. Nilsen P. Making sense of implementation theories, models and frameworks. *Implement Sci* 2015 Apr 21;10:53 [FREE Full text] [doi: [10.1186/s13012-015-0242-0](https://doi.org/10.1186/s13012-015-0242-0)] [Medline: [25895742](https://pubmed.ncbi.nlm.nih.gov/25895742/)]
43. Task Force of the American College of Critical Care Medicine, Society of Critical Care Medicine. Guidelines for intensive care unit admission, discharge, and triage. *Crit Care Med* 1999 Mar;27(3):633-638. [Medline: [10199547](https://pubmed.ncbi.nlm.nih.gov/10199547/)]
44. Nates JL, Nunnally M, Kleinpell R, Blosser S, Goldner J, Birriel B, et al. ICU admission, discharge, and triage guidelines: A framework to enhance clinical operations, development of institutional policies, and further research. *Crit Care Med* 2016 Aug;44(8):1553-1602. [doi: [10.1097/CCM.0000000000001856](https://doi.org/10.1097/CCM.0000000000001856)] [Medline: [27428118](https://pubmed.ncbi.nlm.nih.gov/27428118/)]
45. Sprung CL, Danis M, Iapichino G, Artigas A, Kesecioglu J, Moreno R, et al. Triage of intensive care patients: Identifying agreement and controversy. *Intensive Care Med* 2013 Nov;39(11):1916-1924 [FREE Full text] [doi: [10.1007/s00134-013-3033-6](https://doi.org/10.1007/s00134-013-3033-6)] [Medline: [23925544](https://pubmed.ncbi.nlm.nih.gov/23925544/)]

46. Sedgwick P. Before and after study designs. *BMJ* 2014 Aug 08;349:g5074. [doi: [10.1136/bmj.g5074](https://doi.org/10.1136/bmj.g5074)] [Medline: [25106742](https://pubmed.ncbi.nlm.nih.gov/25106742/)]
47. Eccles M, Grimshaw J, Campbell M, Ramsay C. Research designs for studies evaluating the effectiveness of change and improvement strategies. *Qual Saf Health Care* 2003 Feb;12(1):47-52 [FREE Full text] [doi: [10.1136/qhc.12.1.47](https://doi.org/10.1136/qhc.12.1.47)] [Medline: [12571345](https://pubmed.ncbi.nlm.nih.gov/12571345/)]
48. Mason J, Wood J, Freemantle N. Designing evaluations of interventions to change professional practice. *J Health Serv Res Policy* 1999 Apr;4(2):106-111. [doi: [10.1177/135581969900400209](https://doi.org/10.1177/135581969900400209)] [Medline: [10387402](https://pubmed.ncbi.nlm.nih.gov/10387402/)]
49. Skovlund E, Fenstad GU. Should we always choose a nonparametric test when comparing two apparently nonnormal distributions? *J Clin Epidemiol* 2001 Jan;54(1):86-92. [doi: [10.1016/s0895-4356\(00\)00264-x](https://doi.org/10.1016/s0895-4356(00)00264-x)] [Medline: [11165471](https://pubmed.ncbi.nlm.nih.gov/11165471/)]
50. Vickers AJ. Parametric versus non-parametric statistics in the analysis of randomized trials with non-normally distributed data. *BMC Med Res Methodol* 2005 Nov 03;5:35 [FREE Full text] [doi: [10.1186/1471-2288-5-35](https://doi.org/10.1186/1471-2288-5-35)] [Medline: [16269081](https://pubmed.ncbi.nlm.nih.gov/16269081/)]

Abbreviations

COM-B: capability, opportunity, motivation to perform a behavior

CPR: cardiopulmonary resuscitation

CTSI: Clinical and Translational Research Institute

DHS: Department of Health Services

EHR: electronic health record

HUMC: Harbor-UCLA Medical Center

ICU: intensive care unit

IRB: Institutional Review Board

LAC: Los Angeles County

LAC-USC: Los Angeles County-University of Southern California

OVMC: Olive View Medical Center

SUPPORT: Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatment

TLT: time-limited trial

UCLA: University of California Los Angeles

Edited by G Eysenbach; submitted 17.09.19; peer-reviewed by T Aslanidis, A Davoudi, S Joebges, D Peña; comments to author 09.10.19; revised version received 21.10.19; accepted 22.10.19; published 25.11.19.

Please cite as:

Chang D, Parrish J, Kamangar N, Liebler J, Lee M, Neville T

Time-Limited Trials Among Critically Ill Patients With Advanced Medical Illnesses to Reduce Nonbeneficial Intensive Care Unit Treatments: Protocol for a Multicenter Quality Improvement Study

JMIR Res Protoc 2019;8(11):e16301

URL: <http://www.researchprotocols.org/2019/11/e16301/>

doi: [10.2196/16301](https://doi.org/10.2196/16301)

PMID: [31763988](https://pubmed.ncbi.nlm.nih.gov/31763988/)

©Dong Chang, Jennifer Parrish, Nader Kamangar, Janice Liebler, May Lee, Thanh Neville. Originally published in *JMIR Research Protocols* (<http://www.researchprotocols.org>), 25.11.2019. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in *JMIR Research Protocols*, is properly cited. The complete bibliographic information, a link to the original publication on <http://www.researchprotocols.org>, as well as this copyright and license information must be included.

Protocol

Improving Team-Based Decision Making Using Data Analytics and Informatics: Protocol for a Collaborative Decision Support Design

Don Roosan¹, PharmD, PhD; Anandi V Law¹, PhD; Mazharul Karim¹, BPharm; Moom Roosan², PharmD, PhD

¹Western University of Health Sciences, College of Pharmacy, Pomona, CA, United States

²Chapman University, School of Pharmacy, Irvine, CA, United States

Corresponding Author:

Don Roosan, PharmD, PhD

Western University of Health Sciences

College of Pharmacy

309 E 2nd St

Pomona, CA, 91766

United States

Phone: 1 9094698778

Email: droosan@westernu.edu

Abstract

Background: According to the September 2015 Institute of Medicine report, Improving Diagnosis in Health Care, each of us is likely to experience one diagnostic error in our lifetime, often with devastating consequences. Traditionally, diagnostic decision making has been the sole responsibility of an individual clinician. However, diagnosis involves an interaction among interprofessional team members with different training, skills, cultures, knowledge, and backgrounds. Moreover, diagnostic error is prevalent in the interruption-prone environment, such as the emergency department, where the loss of information may hinder a correct diagnosis.

Objective: The overall purpose of this protocol is to improve team-based diagnostic decision making by focusing on data analytics and informatics tools that improve collective information management.

Methods: To achieve this goal, we will identify the factors contributing to failures in team-based diagnostic decision making (aim 1), understand the barriers of using current health information technology tools for team collaboration (aim 2), and develop and evaluate a collaborative decision-making prototype that can improve team-based diagnostic decision making (aim 3).

Results: Between 2019 to 2020, we are collecting data for this study. The results are anticipated to be published between 2020 and 2021.

Conclusions: The results from this study can shed light on improving diagnostic decision making by incorporating diagnostics rationale from team members. We believe a positive direction to move forward in solving diagnostic errors is by incorporating all team members, and using informatics.

International Registered Report Identifier (IRRID): DERR1-10.2196/16047

(*JMIR Res Protoc* 2019;8(11):e16047) doi:[10.2196/16047](https://doi.org/10.2196/16047)

KEYWORDS

informatics; health care team; data science; decision support techniques; decision-making, computer-assisted; data display; diagnosis, computer-assisted

Introduction

Background

Americans experience at least one diagnostic error in their lifetime, sometimes with devastating consequences (Institute of Medicine [IOM] report 2015). Lack of timely attention to

diagnostic error can have dire implications for public health, as exemplified by the widely reported diagnostic error regarding Ebola virus infection in a Dallas hospital emergency department (ED) [1]. Diagnostic error is likely to be one of the most common types of errors in ED settings [2]. The high-paced, high-volume, low-certainty, multiagent, dynamic, and complex

environment may lead to diagnostic errors and adverse events [3-6]. Thus, in an environment prone to interruptions, vital patient information and cues to make a diagnosis are often lost during information collection and integration among physicians, residents, nurses, and other health care providers.

The team-based diagnostic approach has the potential to reduce errors. Although the current diagnostic process is often the responsibility of an individual clinician, ideally the diagnostic process involves collaboration among multiple health care professionals [7]. To manage the increasing complexity, clinicians will need to collaborate effectively and draw upon the knowledge and expertise of other health care professionals. Collaborative problem solving has been found to have a positive impact on diagnostic performance for team members to combine, sort, and filter new information [8-11]. Current diagnostic decision support tools do not support team-based decision making. These tools can generate diagnostic hypotheses based on the information already entered into the electronic health record (EHR) [12-15]. However, information loss in ED is more common during team communication among health care professionals [16,17]. Therefore, the recent IOM report calls for research into the process of how, where, when, and who is responsible for the entry of the vital information into the system to understand the etiology of failures in the team-based diagnostic decision-making process [18].

Research has shown that technology can positively impact provider interactions and coordination, helping group dynamics and efficiency [19]. Various computer supported cooperative work studies in health care have shown that clinicians deploy working records or provisional information to facilitate team collaboration, mostly in paper environments during case discussions to exchange key information [20-22]. These working records are essentially summaries of patients' situations or important information cues that providers write down during patient interviews or during the information-gathering stage. Currently, the information documented on these working records is not transferred to the EHR and often is discarded after knowledge sharing sessions. Moreover, the decision support tools in the EHR do not support such computerized transitional documentation [23]. For example, nurses in ED collect patient medical history into transitional documents. Clinicians enter patient interview information related to diagnosis on paper or sticky notes [23]. However, the informal information, if shared with the team, can help to achieve shared team situation awareness to reach the correct diagnosis [24]. Research on collaborative environments has shown that sharing a physical workspace to communicate information can provide benefits such as improved activity awareness and coordination [25-28]. For example, Defense Collaboration Services (developed by the US Department of Defense) have shared Web-based platforms that can be accessed by different team members, and they can raise information need as well as input vital information cues related to mission planning [29,30]. Such real-time platforms in health care can provide an overview of the patient's situation from different information-gathering agents (eg, nurses, residents, students, and physicians) to reach the correct diagnosis.

Objective

The informal information in a real-time workspace can help the team to communicate and interpret vital information with each other, which can improve team-based diagnostic decision making in the ED by reducing the loss of information. The objective of our study is to develop a collaborative prototype for improving team diagnostic decision making using an informatics approach.

Methods

Overview

We want to focus on all types of diagnosis for adult patients who come to the ED in both the trauma and medicine units. This will ensure that we can generalize the future prototype for all ED patients. The overall methodology is described in the following 3 aims.

- Aim 1: identify factors contributing to failures in team-based diagnostic decision making
- Aim 2: understand the barriers in using health information technology (IT) tools for team collaboration
- Aim 3: design and evaluate a collaborative decision-making prototype

Aim 1: Identify Factors Contributing to Failures in Team-Based Diagnostic Decision Making

The research questions are as follows: (1) What are the specific diagnostic workflow processes that are vulnerable to failures in information gathering, integrating, interpreting, and establishing an explanation of the correct diagnosis? and (2) What specific information cues do teams share with each other to reach a diagnosis collaboratively?

Aim 1 Methods Overview

We will use the combination of direct observation, hierarchical task analysis (HTA), and health care failure mode and effect analysis (HFMEA) to analyze team tasks in the diagnosis process [31-33]. HTA involves describing the task being analyzed through the breakdown of the task into a hierarchy of goals, subgoals, operations, and plans [31]. The HFMEA technique will help us detect possible failure modes of each of the subprocesses and identify potential causes, effects, and solutions for the failure in the team diagnostic process [32]. A research assistant with qualitative coding background will analyze the data. The steps involved in this method are as follows:

- Step 1: observe scenarios in ED settings and transcribe the scenarios from audio recordings
- Step 2: use data from the transcription to create HTA process maps
- Step 3: conduct HFMEA to identify failures and improvement strategies

Step 1: Observe Scenarios

The observation will start once the patient is admitted in the ED. A total of 2 research assistants will simultaneously observe the ED nurse and the attending physician. The observations will be nonintrusive, and researchers will turn on audio recorders

only when the team is discussing or communicating with each other regarding the patient case [34-40]. We will take notes and audio record the conversation, interactions, and case discussion among the ED team members. We will transcribe the audio recordings and collect the transitional information that the nurse and the attending physicians record on paper.

Step 2: Construct Hierarchical Task Analysis Process Maps

The research team will analyze the observation transcript independently and construct HTA process maps for each case until there are no more tasks related to reach the diagnosis. We will merge the goals and tasks for the physician and the nurse to construct the process maps. For example, if the highest goal is *finding diagnosis*, we will merge nursing goal of *finding patients home medication history* as a subgoal under *finding*

diagnosis. We will focus on the main goals associated with finding the correct diagnosis and represent the associated task steps to accomplish those goals in a hierarchical decision tree (Figure 1) [31,41,42]. After we have developed the HTA process maps for each of the 40 patient cases, we will validate the HTA process maps with 2 ED physicians [41,43]. Finally, we will map the failure-prone tasks' steps from the decision tree, based on the list for detecting failures across the diagnostic process developed by the IOM committee, as described in Table 1 [44]. For example, if *consultation with other clinical team was not possible* (Figure 1, subtask 2.2), we will code that as information integration 4 (information from other team not available), or if *past medical conditions get missed* (Figure 1, subtask 3.2), then we will code that as information interpretation 1 (inaccurate interpretation of history). After mapping with failure-prone subtasks, we will start the HFMEA process.

Figure 1. Hierarchical task analysis diagram: tasks and subtasks are designated by numbers. EHR: electronic health record.

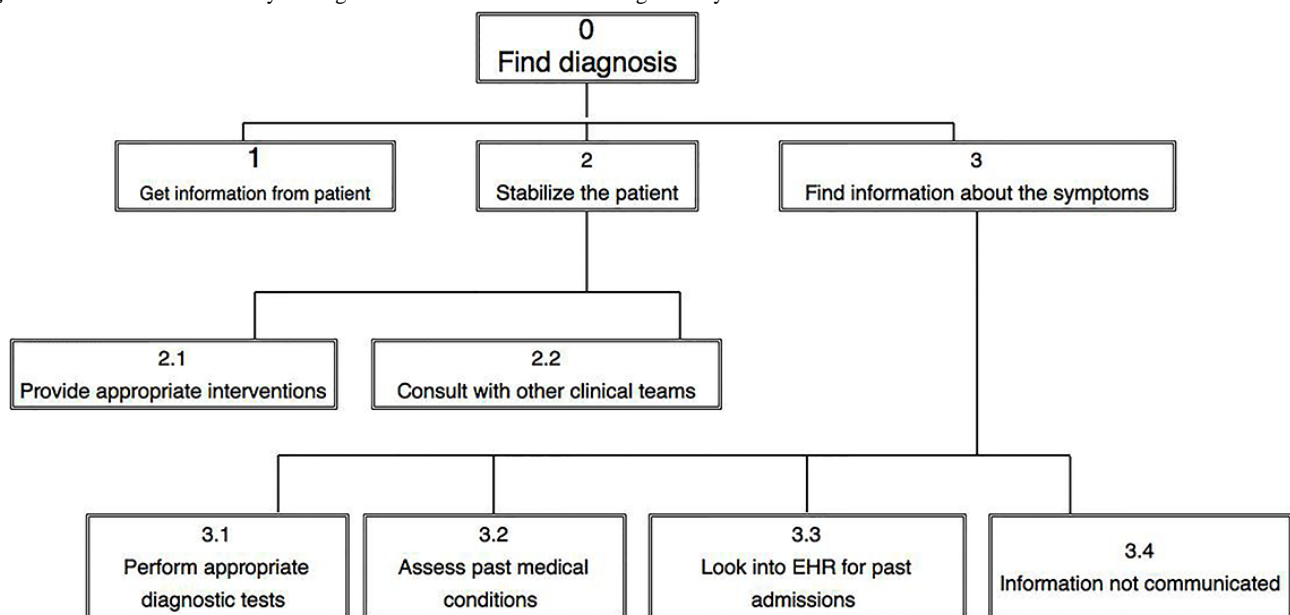


Table 1. Nature of failures and description derived from the Institute of Medicine's report.

| Nature of failure | Failure description |
|--------------------------------------|--|
| Information gathering 1 | Unable to elicit key information |
| Information gathering 2 | Unable to get key history |
| Information gathering 3 | Missed key physical findings |
| Information gathering 4 | Failed to order or perform needed tests |
| Information gathering 5 | Inappropriate review of test results |
| Information gathering 6 | Wrong tests ordered |
| Information gathering 7 | Tests ordered in wrong sequence |
| Information gathering 8 | Technical errors in handling, labeling, and processing of tests |
| Information integration 1 | Wrong hypothesis generation |
| Information integration 2 | Inaccurate suboptimal weighing and prioritization |
| Information integration 3 | Unable to recognize or weigh urgency |
| Information integration 4 | Information from other teams not available |
| Information interpretation 1 | Inaccurate interpretation of history |
| Information interpretation 2 | Inaccurate interpretation of physical findings |
| Information interpretation 3 | Inaccurate interpretation of test results |
| Establish explanation of diagnosis 1 | Delay in considering diagnosis |
| Establish explanation of diagnosis 2 | Patient develops infections or other complications |
| Establish explanation of diagnosis 3 | Information missed to form hypothesis because of health information technology |
| Establish explanation of diagnosis 4 | Signs and symptoms not recognized for specific disease |
| Establish explanation of diagnosis 5 | Delay or missed follow-up |

Step 3: Conduct Health Care Failure Mode and Effect Analysis

We will form a multidisciplinary ED team including 1 ED physician, 1 ED resident, and 1 ED nurse. We will then ask the team to conduct a brainstorming session with each HTA process map and discuss the vulnerable junctions (task steps) for patient safety, information loss, misinterpretation, group conflict, and factors associated with poor communication. The team will also discuss additional failure-prone task steps found in step 2 to find potential solutions. The team will rate the severity score (scale of 1 to 4) for each failure-prone task step as minor (score 1), moderate, major, and catastrophic (score 4). Then, the team will also rate the probability of the occurrence of such incidents on a scale of 1 to 4 as remote (score 1: happening rarely in 2

years), uncommon (once a year), occasional (every 3-6 months), or frequent (score 4: every month). We will combine the severity and probability scores to obtain a hazard score. We will focus only on subtasks with hazard scores of 5 or greater to identify potential solutions. Finally, the team will be asked to find potential solutions, including health IT interventions, that can improve the team communication and team diagnostic decision-making process. The final results will be shown as in [Table 2](#) for each of the 40 patient cases.

Each brainstorming session will be limited to 50 min, will be audio recorded and transcribed, and will occur over multiple sessions. The principal investigator will conduct a final data analysis of the transcripts to identify the high failure-prone task steps and possible solutions.

Table 2. Factors contributing to failure in team-based diagnostic decision-making process.

| Hazard score | Subtasks | Failure mode | Failure description | Causes | Effects | Remedial strategy |
|--------------|---|--------------------------------------|--|--|----------------------------|---|
| 5 | Subtask 2.2: consult with clinical teams | Information gathering 4 | Information from other teams not available | Radiology is overwhelmed with tasks | Delay in patient diagnosis | Update radiology team to send urgent patient results first |
| 7 | Subtask 3.3: information overlooked in EHR ^a for past admissions | Establish explanation of diagnosis 3 | Information missed to form hypothesis because of health information technology | Information lost because of interruption | Wrong diagnosis | Actively engage different team members to focus on multiple data sources in EHR |

^aEHR: electronic health record.

Study Subjects and Recruitment Methods

We will recruit 4 ED physicians and 4 ED nurses for the observation study to increase provider diversity. For the HFMEA part of the study, we will recruit 2 ED physicians, 2 ED nurse, and 2 ED residents. A total of 14 providers will be recruited from 3 hospital sites by email and telephone, and a US \$50 gift card will be provided for participation.

Sample Size Justification

On the basis of our pilot study sample size, we will observe 40 patient cases. We will include only adults (aged >18 years) for selecting cases. We will observe each scenario until the team reaches a consensus about the diagnosis. Previous studies have observed 32 to 50 cases for reaching data saturation [43,45-47].

Team Members Makeup

For this aim, we will assume the ED team includes the attending physician and the attending nurse. However, we will include senior and junior-level residents, radiology physicians, other nursing staff, pharmacists, and support staff based on the makeup of that current team on that particular shift.

Limitations

The HTA and HFMEA methods are time consuming, specifically observation, construction of the HTA, and data analysis. However, a 3-year timeline is reasonable. In addition, there may be concern that step 2 (HTA process maps) may not generate adequate failure-prone steps. However, step 3 (HFMEA) brainstorming session by the group will also identify failure-prone steps in addition to discussing failure-prone steps found in the HTA process maps and will complement each other.

Aim 2: Understand the Barriers in Using Health Information Technology Tools for Team Collaboration

The research questions are as follows: (1) *What are the barriers to sharing information using current health IT tools?* and (2) *What are the leverage points (ie, critical pieces of information that lead to a useful decision path [48]) for the team during complex diagnostic decision-making tasks and negotiating conflict [49]?*

Aim 2 Methods Overview

We will conduct a Critical Incident Technique (CIT)-based team Cognitive Task Analysis (CTA) interview [50-53]. CTA is a process of understanding cognition while performing complex tasks. It provides a mechanism for eliciting and representing general and specific knowledge [54-56]. Team CTA is an extension of CTA that considers a team as a single cognitive entity (eg, more than a collection of individuals) [57,58]. CIT comprises a set of procedures for gathering facts on human behavior in a recent complex situation. In this study, team CTA will help us identify the barriers that ED team members face while gathering, integrating, interpreting information and forming hypotheses about the diagnosis using current health IT tools. Effective teamwork includes motivating and gathering information from each discipline, regardless of interdisciplinary conflicts [59].

Procedure

We will ask the team members to describe a recent complex case that was challenging to solve as a team for an admitted patient. Experiences related to critical incidents in interprofessional teamwork will be evoked by asking open-ended questions: "Are there any difficulties or challenges involved in working together using the current health IT tools?" followed by "Can you describe a situation that you remember in detail when you experienced such a difficulty?" Once the situation is established with time-specific detail, follow-up questions and probes will be asked to elicit the team's dynamic decision-making strategies to negotiate conflicts, the specific actions by each team member, and the process by which the problem was solved. We will focus on how team members prioritize and rank patient information to negotiate conflict to reach consensus.

Study Subjects and Recruitment Methods

We will recruit 5 ED teams by email and telephone. Each team will consist of 4 clinicians, including 1 attending ED physician, 1 ED nurse, 1 ED resident, and 1 ED pharmacist. Inclusion criteria will be at least 1-year experience as a team member and a recent (within last 3 months) experience in working in the ED. Each clinician will receive a US \$50 gift card for participation.

Data Collection

We will use the transcripts from the audio recordings of the interviews for data analysis. All patient identifiers will be removed.

Study Measures

The study measures are as follows: (1) cues and patterns of the team members' preferences for using current health IT tools, (2) leverage points (cues related to shared and complementary cognition), (3) common sources of conflict and resolution strategies [60], and (4) complementary knowledge and skills to synthesize task elements.

Data Analysis

A total of 2 investigators will independently code the transcripts from the team CTA interviews and merge the individual codes into subthemes and later into broader themes through a process of negotiated consensus. We will code based on a qualitative content analysis process [61-63]. We will use ATLAS.ti software for data analysis.

Sample Size Justification

We will interview 20 providers for the team CTA interviews. Previous studies used a range of 6 to 30 providers for successfully conducting similar team CTA interviews [64-67].

Limitations

CTA studies are based on memories. It can be difficult to explore past information, as key pieces of information may not be stored properly in the memory [68]. Therefore, we conducted a pilot study to prepare the questions that can evoke the response needed for data analysis [55].

Aim 3: Design and Evaluate a Collaborative Decision-Making Prototype

Aim 3 Methods Overview

We will develop complex case vignettes, design the prototype, and conduct the usability study.

Complex Team-Based Diagnostic Case Vignette Design

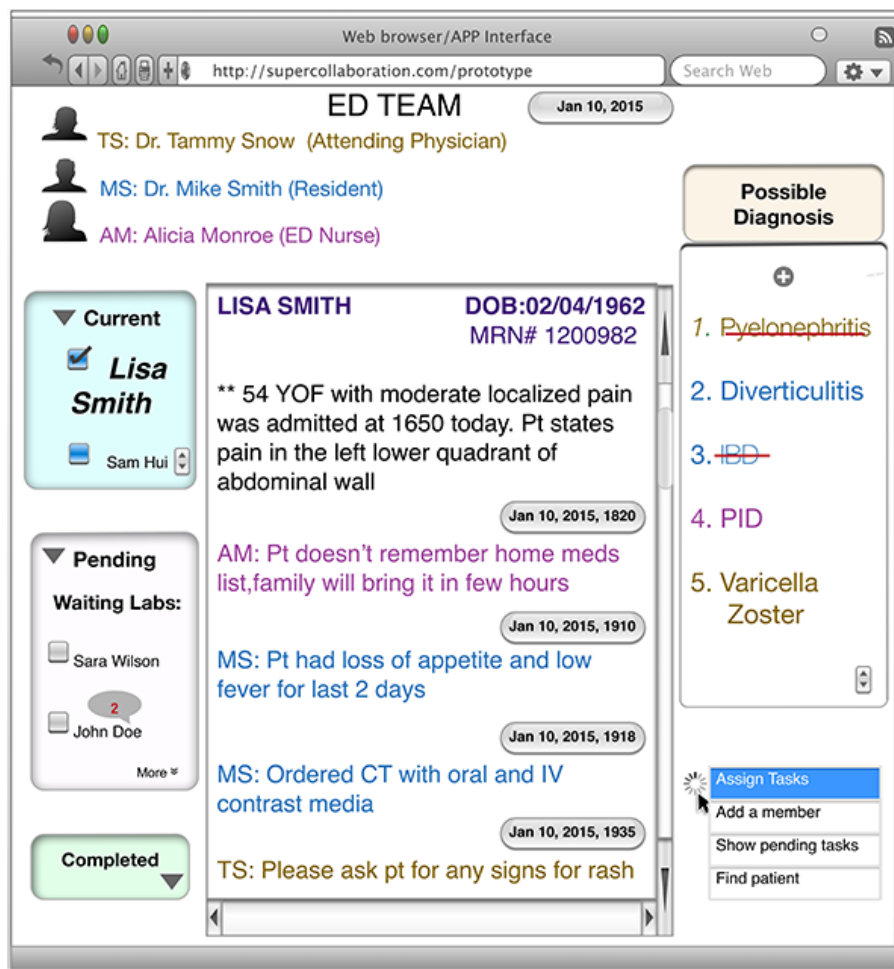
We will design 8 complex clinical vignettes based on team-based diagnostic problems from our findings from aims 1 and 2 [69]. We will validate the complexity of cases with 3 ED physicians. These cases will be presented to participants in a mock electronic EHR.

Prototype Design: Preliminary Design Concept

The purpose of this prototype is to gather, integrate, and collect vital patient information from different team members to rank and filter information for making an informed diagnostic decision collaboratively. The results from aim 1 will inform design by allocating failure-prone task steps as the main focus

in the interface (ie, if *unable to get key history* becomes a major failure-prone task, then a separate tab should be created in the interface as *pending information for patients*). The results from aim 2 will provide specific design allocation for features such as knowledge characteristics (ie, team should be able to see updates of all patients in 1 screen) or expertise process requirements (ie, comments from each team member based on medical expertise should be grouped to improve trust in the information) and so on. For example, in this shared platform (Figure 2), all team members can enter relevant information regarding the patient (color coded as mocha for ED physicians, blue for residents, and magenta for nurses). Everyone can also add possible hypotheses about the diagnosis in the *possible diagnosis* tab. Only the ED physician will be able to delete a diagnosis (shown as red strike-through in the diagnosis tab). Physicians and other team members can also assign tasks and group patients by *waiting labs* or *completed* (left side of the interface). This is an initial version only. The design will be refined based on aim 1, aim 2, and iterative design in aim 3 to ensure patient safety.

Figure 2. Screenshot of the mock-up user interface for the collaborative decision-making prototype.



Iterative Design

To facilitate rapid development, initial low-fidelity mock-ups and storyboarding will be iteratively created to illustrate the design and functionality of the tool and load it in a laptop. We will use the usability inquiry approach for the iterative design

to understand user's likes, dislikes, and needs [70]. The interprofessional research team (including 9 clinicians with diverse clinical background and 6 researchers) will then iteratively review and revise the mock-up based on the written and verbal feedback related to usability (think-aloud methods), efficiency, and ease of use for 3 months or until no further

revisions are identified. Think-aloud methods will provide rich verbal data about specific changes and functionalities of the initial mock-up [71-73]. We will audio record and screen record (using Camtasia Studio) the sessions to analyze verbal feedback and measure the mouse movements. We will analyze the data using think-aloud methods and screen recordings to identify design issues and iterate interface functionalities accordingly.

Usability Testing of the Prototype

We will conduct the study in the Emanate Health System. We will provide initial training to each provider about the scope of the research, the prototype tool, and the 3 steps of usability testing that will reveal the prototype's ease of use, familiarity, effectiveness, and user satisfaction. Each session will last less than 60 min. We will conduct the usability testing of the prototype in the following 3 steps:

- Step 1: evaluate ease of use and familiarity
- Step 2: test prototype effectiveness
- Step 3: conduct prototype evaluation

Step 1: Evaluate Ease of Use and Familiarity (10-12 Min)

We will use the *cognitive walkthrough* evaluation method to understand the user's background and the level of mental effort [74-76]. First, we will ask each provider about his or her initial perception and what action each of the interface components (eg, buttons and checkboxes) is expected to perform when interacted with. Then we will ask each provider to complete a sequence of tasks and subtasks while using the prototype and will provide assistance when asked. An example of a potential task is as follows: "Please use the interface to add a potential diagnosis" or "Please assign a task to your colleague." Providers will then be given 5 min to use the tool on their own to gain familiarity, and any questions asked will be answered. Finally, we will ask the providers to conduct similar tasks without assistance to understand familiarity and ease of use. The number of times assistance is needed will be audio recorded and will serve as a descriptive measure of ease of use for data analysis. The ability of providers to accomplish tasks without assistance will serve as a marker of high ease of use. The principal investigator will conduct the final data analysis from the audio transcripts to find the number of times assistance was required before and after demonstration.

Step 2: Test Prototype Effectiveness (36 Min)

To measure the effectiveness of decision making using the prototype, we will use a 2 randomized between (presence/absence of the prototype) \times 2 between (expertise) \times 2 within (time pressure) factorial design. Each team will receive 8 vignettes presented in random order. The main effect of the presence or absence of the prototype tests the experimental question. With this design, we are also able to test for the interaction between the impact of the interface and the domain of expertise under time pressure. For example, the interface could change the interaction between time pressure and domain expertise (a 3-way interaction), eliminate the influence of time pressure overall for both ED expert and non-ED expert teams (2-way interaction), and have a main effect on quality for everyone in all conditions.

Step 3: Conduct Prototype Evaluation (10-12 Min)

We will conduct a team satisfaction survey to understand team members' *satisfaction level* and System Usability Scale survey to understand the *ease of use* with the prototype. First, we will ask each provider to complete a Web-based user satisfaction survey to measure individual team members' satisfaction for using the prototype [77]. This teamwork process-specific survey focuses on organizational context, team task design, information sharing, and team processes [78]. Research has shown that it is difficult to capture team-specific activities through commonly used surveys such as National Aeronautics and Space Administration Task Load Index [29]. This survey (6-point Likert scale) has been used for understanding team dynamics in *other successful fields* when evaluating group decision support tools [79-85]. Data analysis will include factor analysis, scale reliability analysis, aggregation analysis, and path analysis [77]. Finally, the ease of use of the prototype will be evaluated using the System Usability Scale, a rapidly administered, 10-question, 100-point scale designed to evaluate a user's subjective assessment of usability [86]. Data analysis will include total score calculations based on the participants' answers.

Dependent Variables

We will have 2 dependent variables, diagnostic accuracy and overall team diagnostic decision quality. For *diagnostic accuracy*, the presence of the correct diagnosis in the top 3 items of the diagnostic differential will be computed as a dichotomous (yes or no) variable. For example, if the clinical team correctly diagnoses the top 2 of the 3 diagnoses in the vignettes, it will be counted as *yes*. The *overall team diagnostic decision quality* will be an aggregate score created from the combination of the (1) correct diagnosis, (2) rating of the confidence of the final diagnosis (on a scale of 0-3, with 0 being the lowest confidence rating), and (3) correctly ordered diagnostic tests. The overall score will range from 0 to 10, with correct diagnoses receiving 4 points and confidence ratings and correctly ordered tests receiving 3 points each.

Independent Variables

Time pressure is an independent variable because we will be assigning *high time pressure* as less than 3 min and *low time pressure* as less than 6 min.

Procedures

We will explain the procedure and ask participants to finish 4 cases under high time pressure (<3 min) and 4 cases under low time pressure (<6 min). Initially, all team members, the nurse, the resident, and the physician, will be distant and reviewing the case independently. They will use the decision-making prototype (loaded in laptops) to communicate among themselves for sharing information to establish an explanation for the diagnosis. They will have the final 1 min to discuss, as a group, the high time pressure cases and the final 2 min for low time pressure cases to reach consensus about the correct diagnosis. We will ask each team to rate their confidence in the diagnosis. We will also note the responsible team members who voice their concerns regarding each of the complex patient cases.

Data Analysis

We will use Chi-square test to evaluate association between the independent variables with the decision quality. We will use analysis of variance (ANOVA) to calculate the mean difference within and between ED expert teams' and non-ED expert teams' decision quality. The within- and between-group design will provide us with a sample size adequate for an ANOVA test. The proportion of decisions made with the correct diagnosis and overall decision quality will be shown as a percentage value using ANOVA. If the distribution is not normal, we will use the General Linear Model for the data analysis [87].

Overall Study Measures

The overall study measures are as follows: (1) providers' comments about the initial design, (2) number of times assistance was required before and after demonstration, (3) scores for team decision quality, and (4) survey responses.

Study Subjects and Recruitment Methods

We will recruit 12 teams with each team (6 ED experts and 6 non-ED experts) comprising a physician, a resident, and a nurse (36 providers: US \$50 gift card will be provided) by emails and phone calls. The inclusion criterion for the ED team is that members should have at least 6 months' experience working in the ED, and non-ED teams should include providers with expertise in other clinical domains.

Sample Size Justifications and Power Calculation

Previous studies successfully enrolled 7 to 36 providers for similar usability studies [74,88-93]. The 12 teams and 8 case vignettes in this within- and between-group design with a 2-tailed alpha of .05 and a moderate effect size give a power of 0.83.

Limitations

Reasonable efforts will be made to ensure the prototype realistically simulates a shared workspace for team collaboration. However, the assessment provides initial steps in understanding team diagnostic decision quality, serving as a foundation for future study in real-world situations.

Acknowledgments

The authors would like to thank the Baylor College of Medicine team for helping and supporting ideas in this protocol. In addition, the authors acknowledge an internal funding supporting this research from the Western University of Health Sciences, College of Pharmacy and Chapman University, School of Pharmacy.

Conflicts of Interest

None declared.

References

1. Upadhyay DK, Sittig DF, Singh H. Ebola US Patient Zero: lessons on misdiagnosis and effective use of electronic health records. *Diagnosis (Berl)* 2014;1(4):283-287 [[FREE Full text](#)] [doi: [10.1515/dx-2014-0064](https://doi.org/10.1515/dx-2014-0064)] [Medline: [26705511](https://pubmed.ncbi.nlm.nih.gov/26705511/)]

Results

We are collecting preliminary data for this study between the period of 2019 and 2020. The results are expected to be published between 2020 and 2021.

Discussion

Collaborative Decision Support Design

Studies have shown that uneven information can result from the exclusion of team members from messages or the failure of team members to share uniquely held information [94-96]. Studies also show that task conflict can arise when some team members operate with incomplete information, suggesting that when information is provided, agreement can quickly be reached [97-99]. Collaborative decision support tools have proven to be effective in *other successful fields* in resolving conflict by providing a platform to coordinate team tasks.

This protocol addresses the problem of diagnostic error through innovative approaches for reducing the loss of vital patient information and effectively sharing key information to form correct diagnosis as a team. The robustness of the methodology used in this protocol has been applied to other successful fields. Observation, HTA (aim 1), and team CTA (aim 2) methods have been applied in military, naval warfare, aviation, air traffic control, emergency services, and railway maintenance [100-105]. This Web-based prototype, in the long term, can be integrated with EHR as well as installed in mobile (app-based) devices for providers to capture the transitional information and share this information with team members to reach the correct diagnosis. For this protocol, we are exploring the prototype only as front end; it will not be integrated or installed into any systems or any EHR. The protocol is planned over a period of 5 years. The research team is experienced and plans to execute the project before the timeline.

Conclusions

The results from this study can shed light on improving diagnostic decision making by incorporating diagnostics rationale from team members. We believe a positive direction to move forward in solving diagnostic errors is by incorporating all team members, and using informatics.

2. Okafor N, Payne VL, Chathampally Y, Miller S, Doshi P, Singh H. Using voluntary reports from physicians to learn from diagnostic errors in emergency medicine. *Emerg Med J* 2016 Apr;33(4):245-252. [doi: [10.1136/emermed-2014-204604](https://doi.org/10.1136/emermed-2014-204604)] [Medline: [26531860](https://pubmed.ncbi.nlm.nih.gov/26531860/)]
3. Werner NE, Holden RJ. Interruptions in the wild: development of a sociotechnical systems model of interruptions in the emergency department through a systematic review. *Appl Ergon* 2015 Nov;51:244-254. [doi: [10.1016/j.apergo.2015.05.010](https://doi.org/10.1016/j.apergo.2015.05.010)] [Medline: [26154223](https://pubmed.ncbi.nlm.nih.gov/26154223/)]
4. Popovici I, Morita PP, Doran D, Lapinsky S, Morra D, Shier A, et al. Technological aspects of hospital communication challenges: an observational study. *Int J Qual Health Care* 2015 Jun;27(3):183-188. [doi: [10.1093/intqhc/mzv016](https://doi.org/10.1093/intqhc/mzv016)] [Medline: [25855753](https://pubmed.ncbi.nlm.nih.gov/25855753/)]
5. Monteiro SD, Sherbino JD, Ilgen JS, Dore KL, Wood TJ, Young ME, et al. Disrupting diagnostic reasoning: do interruptions, instructions, and experience affect the diagnostic accuracy and response time of residents and emergency physicians? *Acad Med* 2015 Apr;90(4):511-517. [doi: [10.1097/ACM.0000000000000614](https://doi.org/10.1097/ACM.0000000000000614)] [Medline: [25565260](https://pubmed.ncbi.nlm.nih.gov/25565260/)]
6. Berg LM, Källberg AS, Göransson KE, Östergren J, Florin J, Ehrenberg A. Interruptions in emergency department work: an observational and interview study. *BMJ Qual Saf* 2013 Aug;22(8):656-663. [doi: [10.1136/bmjqs-2013-001967](https://doi.org/10.1136/bmjqs-2013-001967)] [Medline: [23584208](https://pubmed.ncbi.nlm.nih.gov/23584208/)]
7. Weaver SJ, Dy SM, Rosen MA. Team-training in healthcare: a narrative synthesis of the literature. *BMJ Qual Saf* 2014 May;23(5):359-372 [FREE Full text] [doi: [10.1136/bmjqs-2013-001848](https://doi.org/10.1136/bmjqs-2013-001848)] [Medline: [24501181](https://pubmed.ncbi.nlm.nih.gov/24501181/)]
8. Moreira A, Vieira V, del Arco JC. Sanar: A Collaborative Environment to Support Knowledge Sharing with Medical Artifacts. In: Proceedings of the 2012 Brazilian Symposium on Collaborative Systems. 2012 Presented at: SBSC'12; October 15-18, 2012; Sao Paulo, Brazil.
9. Zwaan L, Schiff GD, Singh H. Advancing the research agenda for diagnostic error reduction. *BMJ Qual Saf* 2013 Oct;22(Suppl 2):ii52-ii57 [FREE Full text] [doi: [10.1136/bmjqs-2012-001624](https://doi.org/10.1136/bmjqs-2012-001624)] [Medline: [23942182](https://pubmed.ncbi.nlm.nih.gov/23942182/)]
10. Kachalia A, Gandhi TK, Puopolo AL, Yoon C, Thomas EJ, Griffey R, et al. Missed and delayed diagnoses in the emergency department: a study of closed malpractice claims from 4 liability insurers. *Ann Emerg Med* 2007 Feb;49(2):196-205. [doi: [10.1016/j.annemergmed.2006.06.035](https://doi.org/10.1016/j.annemergmed.2006.06.035)] [Medline: [16997424](https://pubmed.ncbi.nlm.nih.gov/16997424/)]
11. Singh H. Editorial: helping health care organizations to define diagnostic errors as missed opportunities in diagnosis. *Jt Comm J Qual Patient Saf* 2014 Mar;40(3):99-101. [doi: [10.1016/S1553-7250\(14\)40012-6](https://doi.org/10.1016/S1553-7250(14)40012-6)] [Medline: [24730204](https://pubmed.ncbi.nlm.nih.gov/24730204/)]
12. Bond WF, Schwartz LM, Weaver KR, Levick D, Giuliano M, Graber ML. Differential diagnosis generators: an evaluation of currently available computer programs. *J Gen Intern Med* 2012 Feb;27(2):213-219 [FREE Full text] [doi: [10.1007/s11606-011-1804-8](https://doi.org/10.1007/s11606-011-1804-8)] [Medline: [21789717](https://pubmed.ncbi.nlm.nih.gov/21789717/)]
13. El-Kareh R, Hasan O, Schiff GD. Use of health information technology to reduce diagnostic errors. *BMJ Qual Saf* 2013 Oct;22(Suppl 2):ii40-ii51 [FREE Full text] [doi: [10.1136/bmjqs-2013-001884](https://doi.org/10.1136/bmjqs-2013-001884)] [Medline: [23852973](https://pubmed.ncbi.nlm.nih.gov/23852973/)]
14. Ramnarayan P, Kapoor RR, Coren M, Nanduri V, Tomlinson AL, Taylor PM, et al. Measuring the impact of diagnostic decision support on the quality of clinical decision making: development of a reliable and valid composite score. *J Am Med Inform Assoc* 2003;10(6):563-572 [FREE Full text] [doi: [10.1197/jamia.M1338](https://doi.org/10.1197/jamia.M1338)] [Medline: [12925549](https://pubmed.ncbi.nlm.nih.gov/12925549/)]
15. Dupuis EA, White HF, Newman D, Sobieraj JE, Gokhale M, Freund KM. Tracking abnormal cervical cancer screening: evaluation of an EMR-based intervention. *J Gen Intern Med* 2010 Jun;25(6):575-580 [FREE Full text] [doi: [10.1007/s11606-010-1287-z](https://doi.org/10.1007/s11606-010-1287-z)] [Medline: [20204536](https://pubmed.ncbi.nlm.nih.gov/20204536/)]
16. Carter AJ, Davis KA, Evans LV, Cone DC. Information loss in emergency medical services handover of trauma patients. *Prehosp Emerg Care* 2009;13(3):280-285. [doi: [10.1080/10903120802706260](https://doi.org/10.1080/10903120802706260)] [Medline: [19499462](https://pubmed.ncbi.nlm.nih.gov/19499462/)]
17. Laxmisan A, Hakimzada F, Sayan OR, Green RA, Zhang J, Patel VL. The multitasking clinician: decision-making and cognitive demand during and after team handoffs in emergency care. *Int J Med Inform* 2007;76(11-12):801-811. [doi: [10.1016/j.ijmedinf.2006.09.019](https://doi.org/10.1016/j.ijmedinf.2006.09.019)] [Medline: [17059892](https://pubmed.ncbi.nlm.nih.gov/17059892/)]
18. Balogh E, Miller BT, Ball JR. Improving Diagnosis in Health Care. Washington DC: The National Academies Press; 2015.
19. Nembhard IM, Singer SJ, Shortell SM, Rittenhouse D, Casalino LP. The cultural complexity of medical groups. *Health Care Manage Rev* 2012;37(3):200-213. [doi: [10.1097/HMR.0b013e31822f54cd](https://doi.org/10.1097/HMR.0b013e31822f54cd)] [Medline: [21934512](https://pubmed.ncbi.nlm.nih.gov/21934512/)]
20. Fitzpatrick G. Integrated care and the working record. *Health Informatics J* 2016 Jul 25;10(4):291-302 [FREE Full text] [doi: [10.1177/1460458204048507](https://doi.org/10.1177/1460458204048507)]
21. Hardey M, Payne S, Coleman P. 'Scraps': hidden nursing information and its influence on the delivery of care. *J Adv Nurs* 2000 Jul;32(1):208-214. [doi: [10.1046/j.1365-2648.2000.01443.x](https://doi.org/10.1046/j.1365-2648.2000.01443.x)] [Medline: [10886453](https://pubmed.ncbi.nlm.nih.gov/10886453/)]
22. Hardstone G, Hartswood M, Procter R, Slack R, Voss A, Rees G. Supporting Informality: Team Working and Integrated Care Records. In: Proceedings of the 2004 ACM conference on Computer supported cooperative work. 2004 Presented at: CSCW'04; November 6-10, 2004; Chicago, Illinois, USA p. 142-151 URL: <http://doi.org/10.1145/1031607.1031632> [doi: [10.1145/1031607.1031632](https://doi.org/10.1145/1031607.1031632)]
23. Chen Y. Documenting Transitional Information in EMR. In: Proceedings of the SIGCHI Conference on Human Factors in Computing Systems. 2010 Presented at: CHI'10; April 10-15, 2010; Atlanta, Georgia, USA p. 1787-1796 URL: <https://dl.acm.org/citation.cfm?id=1753326.1753594>

24. Kelly KM, Andrews JE, Case DO, Allard SL, Johnson JD. Information seeking and intentions to have genetic testing for hereditary cancers in rural and Appalachian Kentuckians. *J Rural Health* 2007;23(2):166-172. [doi: [10.1111/j.1748-0361.2007.00085.x](https://doi.org/10.1111/j.1748-0361.2007.00085.x)] [Medline: [17397374](https://pubmed.ncbi.nlm.nih.gov/17397374/)]
25. Tang JC. Findings from observational studies of collaborative work. *Int J Man Mach Stud* 1991;34(2):143-160 [FREE Full text] [doi: [10.1016/0020-7373\(91\)90039-a](https://doi.org/10.1016/0020-7373(91)90039-a)]
26. Ha V, Inkpen K, Mandryk RL, Whalen T. Direct Intentions: The Effects of Input Devices on Collaboration Around a Tabletop Display. In: *Proceedings of the First IEEE International Workshop on Horizontal Interactive Human-Computer Systems*. 2006 Presented at: TABLETOP'06; January 5-7, 2006; Adelaide, SA, Australia, Australia p. 177-184 URL: <https://ieeexplore.ieee.org/abstract/document/1579210>
27. Gutwin C, Greenberg S, Roseman M. Workspace awareness in real-time distributed groupware: framework, widgets, and evaluation. In: Sasse A, Cunningham J, Winder R, editors. *People and Computers XI: Proceedings of the HCI'96 Conference*. Boston, Massachusetts, USA: Springer; 1996:281-298.
28. Poltrock S, Grudin J. Computer Supported Cooperative Work and Groupware. In: *Conference Companion on Human Factors in Computing Systems*. 1994 Presented at: CHI'94; April 24-28, 1994; Boston, Massachusetts, USA p. 355-356 URL: <https://dl.acm.org/citation.cfm?id=259963.260448> [doi: [10.1145/259963.260448](https://doi.org/10.1145/259963.260448)]
29. Gregory JF, Allen DW, James MH, Brent TM, Sheldon MR, Benjamin AK, et al. Techniques for Cyber Attack Attribution. 2012. Evaluation of Domain-Specific Collaboration Interfaces for Team Command and Control Tasks URL: <https://apps.dtic.mil/docs/citations/ADA562675> [accessed 2019-10-08]
30. Zheng X, Ke G, Zeng DD, Ram S, Lu H. Next-generation team-science platform for scientific collaboration. *IEEE Intell Syst* 2011;26(6):72-76 [FREE Full text] [doi: [10.1109/mis.2011.104](https://doi.org/10.1109/mis.2011.104)]
31. Annett J. Hierarchical task analysis. In: Hollnagel E, editor. *Handbook Of Cognitive Task Design (human Factors And Ergonomics)*. York - F0608 (York, United Kingdom): CRC Press; 2003:17-35.
32. DeRosier J, Stalhandske E, Bagian JP, Nudell T. Using health care Failure Mode and Effect Analysis: the VA National Center for Patient Safety's prospective risk analysis system. *Jt Comm J Qual Improv* 2002 May;28(5):248-67, 209. [doi: [10.1016/S1070-3241\(02\)28025-6](https://doi.org/10.1016/S1070-3241(02)28025-6)] [Medline: [12053459](https://pubmed.ncbi.nlm.nih.gov/12053459/)]
33. Patton MQ. Wiley Online Library. 2005. Qualitative Research URL: <https://onlinelibrary.wiley.com/doi/abs/10.1002/0470013192.bsa514> [accessed 2019-10-08]
34. Stahl K, Palileo A, Schulman CI, Wilson K, Augenstein J, Kiffin C, et al. Enhancing patient safety in the trauma/surgical intensive care unit. *J Trauma* 2009 Sep;67(3):430-3; discussion 433. [doi: [10.1097/TA.0b013e3181acbe75](https://doi.org/10.1097/TA.0b013e3181acbe75)] [Medline: [19741381](https://pubmed.ncbi.nlm.nih.gov/19741381/)]
35. Chisholm CD, Weaver CS, Whenthmouth L, Giles B. A task analysis of emergency physician activities in academic and community settings. *Ann Emerg Med* 2011 Aug;58(2):117-122. [doi: [10.1016/j.annemergmed.2010.11.026](https://doi.org/10.1016/j.annemergmed.2010.11.026)] [Medline: [21276642](https://pubmed.ncbi.nlm.nih.gov/21276642/)]
36. Kannampallil TG, Franklin A, Mishra R, Almoosa KF, Cohen T, Patel VL. Understanding the nature of information seeking behavior in critical care: implications for the design of health information technology. *Artif Intell Med* 2013 Jan;57(1):21-29. [doi: [10.1016/j.artmed.2012.10.002](https://doi.org/10.1016/j.artmed.2012.10.002)] [Medline: [23194923](https://pubmed.ncbi.nlm.nih.gov/23194923/)]
37. Gilardi S, Guglielmetti C, Pravettoni G. Interprofessional team dynamics and information flow management in emergency departments. *J Adv Nurs* 2014 Jun;70(6):1299-1309. [doi: [10.1111/jan.12284](https://doi.org/10.1111/jan.12284)] [Medline: [24138152](https://pubmed.ncbi.nlm.nih.gov/24138152/)]
38. Singh H, Meyer AND, Thomas EJ. The frequency of diagnostic errors in outpatient care: estimations from three large observational studies involving US adult populations. *BMJ Qual Saf* 2014 Sep;23(9):727-731 [FREE Full text] [doi: [10.1136/bmjqs-2013-002627](https://doi.org/10.1136/bmjqs-2013-002627)] [Medline: [24742777](https://pubmed.ncbi.nlm.nih.gov/24742777/)]
39. Wheelock A, Suliman A, Wharton R, Babu ED, Hull L, Vincent C, et al. The impact of operating room distractions on stress, workload, and teamwork. *Ann Surg* 2015 Jun;261(6):1079-1084. [doi: [10.1097/SLA.0000000000001051](https://doi.org/10.1097/SLA.0000000000001051)] [Medline: [26291954](https://pubmed.ncbi.nlm.nih.gov/26291954/)]
40. Islam R, Mayer J, Clutter J. Supporting novice clinicians cognitive strategies: system design perspective. *IEEE EMBS Int Conf Biomed Health Inform* 2016 Feb;2016:509-512 [FREE Full text] [doi: [10.1109/BHI.2016.7455946](https://doi.org/10.1109/BHI.2016.7455946)] [Medline: [27275020](https://pubmed.ncbi.nlm.nih.gov/27275020/)]
41. Fairbanks RJ, Guarrera TK, Bisantz AB, Venturino M, Westesson PL. Opportunities in IT support of workflow & information flow in the Emergency Department Digital Imaging process. *Proc Hum Factors Ergon Soc Annu Meet* 2010 Sep 1;54(4):359-363 [FREE Full text] [doi: [10.1177/154193121005400419](https://doi.org/10.1177/154193121005400419)] [Medline: [22398841](https://pubmed.ncbi.nlm.nih.gov/22398841/)]
42. Stanton NA. Hierarchical task analysis: developments, applications, and extensions. *Appl Ergon* 2006 Jan;37(1):55-79. [doi: [10.1016/j.apergo.2005.06.003](https://doi.org/10.1016/j.apergo.2005.06.003)] [Medline: [16139236](https://pubmed.ncbi.nlm.nih.gov/16139236/)]
43. Unertl KM, Weinger MB, Johnson KB, Lorenzi NM. Describing and modeling workflow and information flow in chronic disease care. *J Am Med Inform Assoc* 2009;16(6):826-836 [FREE Full text] [doi: [10.1197/jamia.M3000](https://doi.org/10.1197/jamia.M3000)] [Medline: [19717802](https://pubmed.ncbi.nlm.nih.gov/19717802/)]
44. Medicine IO, Balogh EP, Miller BT, Ball JR. Improving diagnosis in health care. *Committee on Diagnostic Error in Health Care; Board on Health Care Services; Institute of Medicine; The National Academies of Sciences, Engineering, and Medicine* 2015 [FREE Full text] [doi: [10.17226/21794](https://doi.org/10.17226/21794)] [Medline: [26803862](https://pubmed.ncbi.nlm.nih.gov/26803862/)]

45. Huang Y, Gramopadhye AK. Systematic engineering tools for describing and improving medication administration processes at rural healthcare facilities. *Appl Ergon* 2014 Nov;45(6):1712-1724. [doi: [10.1016/j.apergo.2014.06.003](https://doi.org/10.1016/j.apergo.2014.06.003)] [Medline: [25024094](https://pubmed.ncbi.nlm.nih.gov/25024094/)]
46. Raduma-Tomás MA, Flin R, Yule S, Close S. The importance of preparation for doctors' handovers in an acute medical assessment unit: a hierarchical task analysis. *BMJ Qual Saf* 2012 Mar;21(3):211-217. [doi: [10.1136/bmjqs-2011-000220](https://doi.org/10.1136/bmjqs-2011-000220)] [Medline: [22129935](https://pubmed.ncbi.nlm.nih.gov/22129935/)]
47. Yadav K, Chamberlain JM, Lewis VR, Abts N, Chawla S, Hernandez A, et al. Designing real-time decision support for trauma resuscitations. *Acad Emerg Med* 2015 Sep;22(9):1076-1084 [FREE Full text] [doi: [10.1111/acem.12747](https://doi.org/10.1111/acem.12747)] [Medline: [26300010](https://pubmed.ncbi.nlm.nih.gov/26300010/)]
48. Pirolli P, Card S. The Sensemaking Process and Leverage Points for Analyst Technology as Identified Through Cognitive Task Analysis. In: *Proceedings of International Conference on Intelligence Analysis*. 2005 Presented at: IA'05; 2005; McLean, VA, USA URL: <https://pdfs.semanticscholar.org/f6b5/4379043d0ee28bea45555f481af1a693c16c.pdf>
49. Ellington L, Kelly KM, Reblin M, Latimer S, Roter D. Communication in genetic counseling: cognitive and emotional processing. *Health Commun* 2011 Oct;26(7):667-675. [doi: [10.1080/10410236.2011.561921](https://doi.org/10.1080/10410236.2011.561921)] [Medline: [21660793](https://pubmed.ncbi.nlm.nih.gov/21660793/)]
50. Klein G. Cognitive task analysis of teams. In: Schraagen JM, Chipman SF, Shalin VL, editors. *Cognitive Task Analysis*. York - F0608 (York, United Kingdom): CRC Press; 2000.
51. Flanagan JC. The critical incident technique. *Psychol Bull* 1954 Jul;51(4):327-358. [doi: [10.1037/h0061470](https://doi.org/10.1037/h0061470)] [Medline: [13177800](https://pubmed.ncbi.nlm.nih.gov/13177800/)]
52. Islam R, Weir C, Fiol G. Heuristics in managing complex clinical decision tasks in experts' decision making. *IEEE Int Conf Healthc Inform* 2014 Sep;2014:186-193 [FREE Full text] [doi: [10.1109/ICHL.2014.32](https://doi.org/10.1109/ICHL.2014.32)] [Medline: [27275019](https://pubmed.ncbi.nlm.nih.gov/27275019/)]
53. Islam R, Weir CR, Jones M, Del Fiol G, Samore MH. Understanding complex clinical reasoning in infectious diseases for improving clinical decision support design. *BMC Med Inform Decis Mak* 2015 Nov 30;15:101 [FREE Full text] [doi: [10.1186/s12911-015-0221-z](https://doi.org/10.1186/s12911-015-0221-z)] [Medline: [26620881](https://pubmed.ncbi.nlm.nih.gov/26620881/)]
54. Schraagen JM, Chipman SF, Shalin VJ. *Cognitive Task Analysis*. London, England: Psychology Press; 2000.
55. Crandall B, Klein GA, Hoffman RR. *Working Minds: A Practitioner's Guide To Cognitive Task Analysis*. Cambridge, MA: The MIT Press; 2006.
56. Hoffman RR. Human factors contributions to knowledge elicitation. *Hum Factors* 2008 Jun;50(3):481-488. [doi: [10.1518/001872008X288475](https://doi.org/10.1518/001872008X288475)] [Medline: [18689057](https://pubmed.ncbi.nlm.nih.gov/18689057/)]
57. O'Hare D, Wiggins M, Williams A, Wong W. Cognitive task analyses for decision centred design and training. *Ergonomics* 1998 Nov;41(11):1698-1718. [doi: [10.1080/001401398186144](https://doi.org/10.1080/001401398186144)] [Medline: [9819582](https://pubmed.ncbi.nlm.nih.gov/9819582/)]
58. Klein C, DiazGranados D, Salas E, Le H, Burke CS, Lyons R, et al. Does team building work? *Small Group Res* 2009;40(2):181-222 [FREE Full text] [doi: [10.1177/1046496408328821](https://doi.org/10.1177/1046496408328821)]
59. Santana C, Curry LA, Nembhard IM, Berg DN, Bradley EH. Behaviors of successful interdisciplinary hospital quality improvement teams. *J Hosp Med* 2011 Nov;6(9):501-506 [FREE Full text] [doi: [10.1002/jhm.927](https://doi.org/10.1002/jhm.927)] [Medline: [22042750](https://pubmed.ncbi.nlm.nih.gov/22042750/)]
60. Morreim EH. Search eLibrary: SSRN. 2014. Conflict Resolution in Healthcare URL: https://papers.ssrn.com/sol3/papers.cfm?abstract_id=2458744 [accessed 2019-10-08]
61. Neuendorf KA. *The Content Analysis Guidebook*. Thousand Oaks, California: SAGE Publications Inc; 2002.
62. Stemler S. An overview of content analysis. *Pract Assess Res Eval* 2001;7(17):137-146 [FREE Full text]
63. Roosan D, Weir C, Samore M, Jones M, Rahman M, Stoddard GJ, et al. Identifying complexity in infectious diseases inpatient settings: an observation study. *J Biomed Inform* 2017 Jul;71S:S13-S21 [FREE Full text] [doi: [10.1016/j.jbi.2016.10.018](https://doi.org/10.1016/j.jbi.2016.10.018)] [Medline: [27818310](https://pubmed.ncbi.nlm.nih.gov/27818310/)]
64. Arthur W, Glaze RM, Bhupatkar A, Villado AJ, Bennett W, Rowe LJ. Team task analysis: differentiating between tasks using team relatedness and team workflow as metrics of team task interdependence. *Hum Factors* 2012 Apr;54(2):277-295. [doi: [10.1177/0018720811435234](https://doi.org/10.1177/0018720811435234)] [Medline: [22624293](https://pubmed.ncbi.nlm.nih.gov/22624293/)]
65. Dominguez C, Long WG, Miller TE, Wiggins SL. Design Directions for Support of Submarine Commanding Officer Decision Making. In: *Proceedings of 2006 Undersea HSI Symposium: Research, Acquisition and the Warrior*. 2006 Presented at: URL: <https://pdfs.semanticscholar.org/1e1b/088a7eab2634948056dee77ba535f3176df0.pdf.%20https://doi.org/10.1007/s10111-017-0413-7> [doi: [10.1007/s10111-017-0413-7](https://doi.org/10.1007/s10111-017-0413-7)]
66. Dominguez C, Uhlig P, Brown J, Gurevich O, Shumar W, Stahl G, et al. Studying and supporting collaborative care processes. *Proc Hum Factors Ergon Soc Annu Meet* 2005;49(11) [FREE Full text] [doi: [10.1177/154193120504901116](https://doi.org/10.1177/154193120504901116)]
67. Kvarnström S. Difficulties in collaboration: a critical incident study of interprofessional healthcare teamwork. *J Interprof Care* 2008 Mar;22(2):191-203. [doi: [10.1080/13561820701760600](https://doi.org/10.1080/13561820701760600)] [Medline: [18320453](https://pubmed.ncbi.nlm.nih.gov/18320453/)]
68. Markman KD, Klein WM, Suhr JA. *Handbook of Imagination and Mental Simulation*. London, England: Psychology Press; 2012.
69. Islam R, Weir C, Fiol G. Clinical complexity in medicine: a measurement model of task and patient complexity. *Methods Inf Med* 2016;55(1):14-22 [FREE Full text] [doi: [10.3414/ME15-01-0031](https://doi.org/10.3414/ME15-01-0031)] [Medline: [26404626](https://pubmed.ncbi.nlm.nih.gov/26404626/)]
70. Raven ME, Flanders A. Using contextual inquiry to learn about your audiences. *SIGDOC Asterisk J Comput Doc* 1996;20(1):1-13 [FREE Full text] [doi: [10.1145/227614.227615](https://doi.org/10.1145/227614.227615)]

71. Someren MW, Barnard YF, Sandberg JA. *The Think Aloud Method: A Practical Guide To Modelling Cognitive Processes*. London: Academic Press; 1994.
72. Roosan D, Fiol G, Butler J, Livnat Y, Mayer J, Samore M, et al. Feasibility of population health analytics and data visualization for decision support in the infectious diseases domain: a pilot study. *Appl Clin Inform* 2016;7(2):604-623 [FREE Full text] [doi: [10.4338/ACI-2015-12-RA-0182](https://doi.org/10.4338/ACI-2015-12-RA-0182)] [Medline: [27437065](https://pubmed.ncbi.nlm.nih.gov/27437065/)]
73. Roosan D, Samore M, Jones M, Livnat Y, Clutter J. Big-Data Based Decision-Support Systems to Improve Clinicians' Cognition. In: *Proceedings of the 2016 IEEE International Conference on Healthcare Informatics*. 2016 Presented at: ICHI'16; October 4-7, 2016; Chicago, IL, USA. [doi: [10.1109/ICHI.2016.39](https://doi.org/10.1109/ICHI.2016.39)]
74. Karahoca A, Bayraktar E, Tatoglu E, Karahoca D. Information system design for a hospital emergency department: a usability analysis of software prototypes. *J Biomed Inform* 2010 Apr;43(2):224-232 [FREE Full text] [doi: [10.1016/j.jbi.2009.09.002](https://doi.org/10.1016/j.jbi.2009.09.002)] [Medline: [19755173](https://pubmed.ncbi.nlm.nih.gov/19755173/)]
75. Lewis C. Testing a Walkthrough Methodology for Theory-based Design of Walk-Up-And-Use Interfaces. In: *Proceedings of the SIGCHI Conference on Human Factors in Computing Systems*. 1990 Presented at: CHI'90; April 1-5, 1990; Seattle, Washington, USA p. 235-242. [doi: [10.1145/97243.97279](https://doi.org/10.1145/97243.97279)]
76. Polson P, Lewis C, Rieman J, Wharton C. Cognitive walkthroughs: a method for theory-based evaluation of user interfaces. *Int J Man Mach Stud* 1992;36(5):741-773 [FREE Full text] [doi: [10.1016/0020-7373\(92\)90039-N](https://doi.org/10.1016/0020-7373(92)90039-N)]
77. Doolen T, Hacker M, van Aken E. The impact of organizational context on work team effectiveness: a study of production team. *IEEE Trans Eng Manage* 2003;50(3):285-296 [FREE Full text] [doi: [10.1109/TEM.2003.817296](https://doi.org/10.1109/TEM.2003.817296)]
78. Valentine MA, Nembhard IM, Edmondson AC. Measuring teamwork in health care settings: a review of survey instruments. *Med Care* 2015 Apr;53(4):e16-e30. [doi: [10.1097/MLR.0b013e31827feef6](https://doi.org/10.1097/MLR.0b013e31827feef6)] [Medline: [24189550](https://pubmed.ncbi.nlm.nih.gov/24189550/)]
79. Rama J, Bishop J. A Survey and Comparison of CSCW Groupware Applications. In: *Proceedings of the 2006 Annual Research Conference of the South African Institute of Computer Scientists and Information Technologists on IT Research in Developing Countries*. 2006 Presented at: SAICSIT'06; October 9-11, 2006; Somerset West, South Africa URL: <https://dl.acm.org/citation.cfm?id=1216284> [doi: [10.1145/1216262.1216284](https://doi.org/10.1145/1216262.1216284)]
80. Urnes T, Nejabi R. Semantic Scholar. 1994. Tools for Implementing Groupware: Survey and Evaluation URL: <https://pdfs.semanticscholar.org/daff/3a231ff8a9da690c250f6a179e27dee58379.pdf> [accessed 2019-10-08]
81. Herskovic V, Pino JA, Ochoa SF, Antunes P. Evaluation Methods for Groupware Systems. In: *Proceedings of the 13th International Conference on Groupware: Design Implementation, and Use*. 2007 Presented at: CRIWG'07; September 16-20, 2007; Bariloche, Argentina p. 328-336. [doi: [10.1007/978-3-540-74812-0_26](https://doi.org/10.1007/978-3-540-74812-0_26)]
82. Pinelle D, Gutwin C. A Review of Groupware Evaluations. In: *Proceedings of the 9th IEEE International Workshops on Enabling Technologies: Infrastructure for Collaborative Enterprises*. 2000 Presented at: WETICE'00; June 4-16, 2000; Gaithersburg, MD, USA p. 86-91. [doi: [10.1109/ENABL.2000.883709](https://doi.org/10.1109/ENABL.2000.883709)]
83. Glover W, Farris JA, van Aken EM, Doolen T. Critical success factors for the sustainability of Kaizen event human resource outcomes: an empirical study. *Int J Prod Econ* 2011;132(2):197-213 [FREE Full text] [doi: [10.1016/j.ijpe.2011.04.005](https://doi.org/10.1016/j.ijpe.2011.04.005)]
84. Demirbag M, Sahadev S, Kaynak E, Akgul A. Modeling quality commitment in service organizations: an empirical study. *Euro J Market* 2012;46(6):790-810 [FREE Full text] [doi: [10.1108/03090561211214609](https://doi.org/10.1108/03090561211214609)]
85. Frederick CV. Education Resources Information Center. 2009. Analyzing Learner Characteristics, Undergraduate Experience and Individual Teamwork Knowledge, Skills and Abilities: Toward Identifying Themes to Promote Higher Workforce Readiness URL: <https://eric.ed.gov/?id=ED532494> [accessed 2019-10-08]
86. Brooke J. SUS - A quick and dirty usability scale. In: Jordan PW, Thomas B, McClelland IL, Weerdmeester B, editors. *Usability Evaluation In Industry*. London: Taylor & Francis; 1996.
87. Altman DG. *Practical Statistics for Medical Research*. London: Chapman and Hall; 1990.
88. Kastner M, Lottridge D, Marquez C, Newton D, Straus SE. Usability evaluation of a clinical decision support tool for osteoporosis disease management. *Implement Sci* 2010 Dec 10;5:96 [FREE Full text] [doi: [10.1186/1748-5908-5-96](https://doi.org/10.1186/1748-5908-5-96)] [Medline: [21143978](https://pubmed.ncbi.nlm.nih.gov/21143978/)]
89. Abidi SR, Stewart S, Shepherd M, Abidi SS. Usability evaluation of family physicians' interaction with the Comorbidity Ontological Modeling and ExecuTion System (COMET). *Stud Health Technol Inform* 2013;192:447-451. [Medline: [23920594](https://pubmed.ncbi.nlm.nih.gov/23920594/)]
90. Neri PM, Pollard SE, Volk LA, Newmark LP, Varugheese M, Baxter S, et al. Usability of a novel clinician interface for genetic results. *J Biomed Inform* 2012 Oct;45(5):950-957 [FREE Full text] [doi: [10.1016/j.jbi.2012.03.007](https://doi.org/10.1016/j.jbi.2012.03.007)] [Medline: [22521718](https://pubmed.ncbi.nlm.nih.gov/22521718/)]
91. Salman YB, Cheng H, Patterson PE. Icon and user interface design for emergency medical information systems: a case study. *Int J Med Inform* 2012 Jan;81(1):29-35. [doi: [10.1016/j.ijmedinf.2011.08.005](https://doi.org/10.1016/j.ijmedinf.2011.08.005)] [Medline: [21920810](https://pubmed.ncbi.nlm.nih.gov/21920810/)]
92. Bury J, Hurt C, Roy A, Cheesman L, Bradburn M, Cross S, et al. LISA: a web-based decision-support system for trial management of childhood acute lymphoblastic leukaemia. *Br J Haematol* 2005 Jun;129(6):746-754. [doi: [10.1111/j.1365-2141.2005.05541.x](https://doi.org/10.1111/j.1365-2141.2005.05541.x)] [Medline: [15953000](https://pubmed.ncbi.nlm.nih.gov/15953000/)]
93. Li AC, Kannry JL, Kushniruk A, Chrimes D, McGinn TG, Edonyabo D, et al. Integrating usability testing and think-aloud protocol analysis with 'near-live' clinical simulations in evaluating clinical decision support. *Int J Med Inform* 2012 Nov;81(11):761-772. [doi: [10.1016/j.ijmedinf.2012.02.009](https://doi.org/10.1016/j.ijmedinf.2012.02.009)] [Medline: [22456088](https://pubmed.ncbi.nlm.nih.gov/22456088/)]

94. Cramton CD. Attribution in distributed work groups. In: Hinds PJ, Kiesler S, editors. Distributed Work. Cambridge, MA: The MIT Press; 2002:191-212.
95. Mortensen M, Hinds PJ. Conflict and shared identity in geographically distributed teams. *Int J Confl* 2001;12(3):212-238 [[FREE Full text](#)] [doi: [10.1108/eb022856](https://doi.org/10.1108/eb022856)]
96. Purdy J, Nye P, Balakrishnan P. The impact of communication media on negotiation outcomes. *Int J Confl* 2000;11(2):162-187 [[FREE Full text](#)] [doi: [10.1108/eb022839](https://doi.org/10.1108/eb022839)]
97. Weisband S. Maintaining awareness in distributed team collaboration: implications for leadership and performance. In: Hinds PJ, Kiesler S, editors. Distributed Work. Cambridge, MA: The MIT Press; 2002:311-333.
98. Mannix EA, Griffith TL, Neale MA. The phenomenology of conflict in distributed work teams. In: Hinds PJ, Kiesler S, editors. Distributed Work. Cambridge, MA: The MIT Press; 2002:213-233.
99. Simons TL, Peterson RS. Task conflict and relationship conflict in top management teams: the pivotal role of intragroup trust. *J Appl Psychol* 2000 Feb;85(1):102-111. [doi: [10.1037/0021-9010.85.1.102](https://doi.org/10.1037/0021-9010.85.1.102)] [Medline: [10740960](https://pubmed.ncbi.nlm.nih.gov/10740960/)]
100. Stanton NA, Stewart R, Harris D, Houghton RJ, Baber C, McMaster R, et al. Distributed situation awareness in dynamic systems: theoretical development and application of an ergonomics methodology. *Ergonomics* 2006;49(12-13):1288-1311. [doi: [10.1080/00140130600612762](https://doi.org/10.1080/00140130600612762)] [Medline: [17008257](https://pubmed.ncbi.nlm.nih.gov/17008257/)]
101. Stewart R, Stanton NA, Harris D, Baber C, Salmon P, Mock M, et al. Distributed situation awareness in an Airborne Warning and Control System: application of novel ergonomics methodology. *Cogn Tech Work* 2008;10(3):221-229. [doi: [10.1007/s10111-007-0094-8](https://doi.org/10.1007/s10111-007-0094-8)]
102. Walker G, Stanton NA, Baber C, Wells L, Gibson H, Salmon P, et al. From ethnography to the EAST method: a tractable approach for representing distributed cognition in Air Traffic Control. *Ergonomics* 2010 Feb;53(2):184-197. [doi: [10.1080/00140130903171672](https://doi.org/10.1080/00140130903171672)] [Medline: [20099173](https://pubmed.ncbi.nlm.nih.gov/20099173/)]
103. Houghton RJ, Baber C, McMaster R, Stanton NA, Salmon P, Stewart R, et al. Command and control in emergency services operations: a social network analysis. *Ergonomics* 2006;49(12-13):1204-1225. [doi: [10.1080/00140130600619528](https://doi.org/10.1080/00140130600619528)] [Medline: [17008253](https://pubmed.ncbi.nlm.nih.gov/17008253/)]
104. Salmon PM, Stanton NA, Walker GH, Jenkins D, Baber C, McMaster R. Representing situation awareness in collaborative systems: a case study in the energy distribution domain. *Ergonomics* 2008 Mar;51(3):367-384. [doi: [10.1080/00140130701636512](https://doi.org/10.1080/00140130701636512)] [Medline: [18311612](https://pubmed.ncbi.nlm.nih.gov/18311612/)]
105. Walker GH, Gibson H, Stanton NA, Baber C, Salmon P, Green D. Event Analysis of Systemic Teamwork (EAST): a novel integration of ergonomics methods to analyse C4i activity. *Ergonomics* 2006;49(12-13):1345-1369. [doi: [10.1080/00140130600612846](https://doi.org/10.1080/00140130600612846)] [Medline: [17008260](https://pubmed.ncbi.nlm.nih.gov/17008260/)]

Abbreviations

- ANOVA:** analysis of variance
- CIT:** Critical Incident Technique
- CTA:** cognitive task analysis
- ED:** emergency department
- EHR:** electronic health record
- HFMEA:** health care failure mode and effect analysis
- HTA:** hierarchical task analysis
- IOM:** Institute of Medicine
- IT:** information technology

Edited by G Eysenbach; submitted 28.08.19; peer-reviewed by J Chok, M Shahjalal; comments to author 11.09.19; revised version received 22.09.19; accepted 23.09.19; published 27.11.19.

Please cite as:

Roosan D, Law AV, Karim M, Roosan M

Improving Team-Based Decision Making Using Data Analytics and Informatics: Protocol for a Collaborative Decision Support Design
JMIR Res Protoc 2019;8(11):e16047

URL: <http://www.researchprotocols.org/2019/11/e16047/>

doi: [10.2196/16047](https://doi.org/10.2196/16047)

PMID: [31774412](https://pubmed.ncbi.nlm.nih.gov/31774412/)

©Don Roosan, Anandi V Law, Mazharul Karim, Moom Roosan. Originally published in JMIR Research Protocols (<http://www.researchprotocols.org/>), 27.11.2019. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction

in any medium, provided the original work, first published in JMIR Research Protocols, is properly cited. The complete bibliographic information, a link to the original publication on <http://www.researchprotocols.org>, as well as this copyright and license information must be included.

Protocol

Feasibility of Point-of-Care Testing for Influenza Within a National Primary Care Sentinel Surveillance Network in England: Protocol for a Mixed Methods Study

Simon de Lusignan^{1,2}, BSc, MBBS, MSc, MD; Uy Hoang², BSc, MBBS, MPH, MD; Harshana Liyanage², PhD; Ivelina Yonova², BA, MA; Filipa Ferreira², PhD; Javier Diez-Domingo³, MD, PhD; Tristan Clark⁴, BM, MD

¹Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, United Kingdom

²Department of Clinical and Experimental Medicine, University of Surrey, Guildford, United Kingdom

³Vaccine Research Department, Foundation for the Promotion of Health and Biomedical Research in the Valencian Region, Valencia, Spain

⁴Academic Unit of Clinical and Experimental Sciences, University of Southampton, Southampton, United Kingdom

Corresponding Author:

Simon de Lusignan, BSc, MBBS, MSc, MD
Department of Clinical and Experimental Medicine
University of Surrey
Leggett Building
Daphne Jackson Road
Guildford, GU2 7WG
United Kingdom
Phone: 44 1483 684802
Email: simon.delusignan@phc.ox.ac.uk

Abstract

Background: Point-of-care testing (POCT) for influenza promises to provide real-time information to influence clinical decision making and improve patient outcomes. Public Health England has published a toolkit to assist implementation of these tests in the UK National Health Service.

Objective: A feasibility study will be undertaken to assess the implementation of influenza POCT in primary care as part of a sentinel surveillance network.

Methods: We will conduct a mixed methods study to compare the sampling rates in practices using POCT and current virology swabbing practices not using POCT, and to understand the issues and barriers to implementation of influenza POCT in primary care workflows. The study will take place between March and May 2019. It will be nested in general practices that are part of the English national sentinel surveillance network run by the Royal College of General Practitioners Research and Surveillance Centre. The primary outcome is the number of valid influenza swabs taken and tested by the practices involved in the study using the new POCT.

Results: A total of 6 practices were recruited, and data collection commenced on March 11, 2019. Moreover, 312 swab samples had been collected at the time of submission of the protocol, which was 32.5% (312/960) of the expected sample size. In addition, 68 samples were positive for influenza, which was 20.1% (68/338) of the expected sample size.

Conclusions: To the best of our knowledge, this is the first time an evaluation study has been undertaken on POCT for influenza in general practice in the United Kingdom. This proposed study promises to shed light on the feasibility of implementation of POCT in primary care and on the views of practitioners about the use of influenza POCT in primary care, including its impact on primary care workflows.

International Registered Report Identifier (IRRID): DERR1-10.2196/14186

(*JMIR Res Protoc* 2019;8(11):e14186) doi:[10.2196/14186](https://doi.org/10.2196/14186)

KEYWORDS

diagnosis; influenza, human; point-of-care systems; general practice

Introduction

Background

Influenza is associated with high levels of morbidity and mortality [1]. Vaccination is suboptimally effective at preventing influenza in certain groups [2], and antivirals may improve clinical outcome, especially when administered early in the course of the disease [3].

The Royal College of General Practitioners' (RCGP) Research and Surveillance Centre (RSC) program of influenza and respiratory disease surveillance has been established since 1967, making it the longest established primary care sentinel network in Europe [4,5]. Its work contributes to several important public health outputs including the early identification of pandemics and the assessment of vaccine effectiveness.

Current antiviral treatment for influenza needs to be administered within 48 hours from the onset of symptoms for optimal efficacy [6,7], although new antiviral agents have recently been developed, which may prove more effective. These new antivirals such as Baloxavir promise to improve time to resolution of symptoms and reduce complications for patients with influenza [8], although their use will likely be restricted to patients with microbiologically confirmed diagnosis, given their cost.

However, currently only a small proportion of patients with influenza-like illness (ILI) in primary care undergo microbiological testing, with few patients receiving antiviral medications appropriately according to guidelines [9].

Point-of Care-Testing

Recently, highly accurate rapid molecular test platforms for influenza have become commercially available to hospitals and health care clinics. These near-patient or point-of-care tests (POCT) can produce results in under 30 minutes and so could be used to direct the use of antiviral medications for treatment and chemoprophylaxis of influenza [10,11]. Rapid molecular diagnostic testing for influenza has the potential to (1) improve clinical decision making regarding the use of antibiotics and antivirals, (2) improve patient outcomes due to the early appropriate use of antivirals, and (3) provide better information to inform sentinel surveillance and clinical research including studies of vaccine effectiveness and real-world trials.

In the United Kingdom, 2 commercially available, highly accurate molecular POCT platforms for influenza have recently been given the Conformité Européenne marking, the Cobas Liat test produced by Roche Diagnostics and the Abbott ID Now (formerly the Alere influenza A and B) test produced by Abbott Diagnostics [12].

Public Health England has advised that institutions interested in using POCT for influenza should consider a set of predefined questions ([Multimedia Appendix 1](#)) before implementation of these new tests [13]. However, these considerations do not specifically relate to implementation of POCT in primary care. In addition, guidelines have not been given regarding the specimen numbers needed for seasonal influenza situational

awareness, which would be necessary for influenza disease surveillance in primary care [14].

Objectives

We conducted this study to determine the feasibility of POCT for influenza in primary care, comparing its implementation with current practice for influenza specimen sampling within the RCGP RSC surveillance network, including the views of practitioners about the challenges of incorporating influenza POCT into primary care workflow.

Methods

Study Design

We will perform a mixed methods study to compare the sampling rates using POCT and current virology sampling practices within the RCGP RSC network and to understand the issues and barriers to the implementation of influenza POCT in primary care workflows.

Study Setting and Population

The study will take place from March to May 2019. It will be completed at the end of the influenza season (when no cases will be detected during 2 consecutive weeks or equivalent).

The study will be nested in the English national sentinel surveillance network run by the RCGP RSC. Previous work has shown that the age and gender distribution of patients in the sentinel network is broadly similar to the English National census distribution, although there is a significantly higher proportion of both males and females in the 25 to 44 years age band, when compared with the census, and a lower proportion of people in the 0 to 4 years age band [4].

Data Collection and Analysis

We will recruit 6 practices with a registered population of between 30,000 and 60,000 patients. Clinicians in the study practices will be encouraged to undertake nasal swabs from consented patients aged over 6 months presenting with an acute ILI (with symptoms of 5 days or less). The swabs will be tested for influenza in the practice using the POCT machine by the clinician or trained practitioner. The test will take approximately 15 min for a result to be displayed, and the clinician will be encouraged to record this result in the patients' medical record.

Currently, virology sampling practices within the sentinel networks take up to a maximum of 20 samples per week per practice before (to look for circulating flu) and during (to see which strains are circulating and any drift) the season and when the season is over. Moreover, 35% (881/2591) of the specimens collected through the sentinel network are laboratory-confirmed influenza. Thus, over a 10-week study period, we would expect 1200 samples to be taken with 427 influenza positive swabs.

The primary outcome is the number of valid influenza swabs taken and tested by the practices in the RCGP RSC network using the new POCT.

The baseline characteristics of the patients who receive influenza testing with POCT will be compared with other patients who

receive influenza specimen sampling within the sentinel surveillance network in terms of the following:

- Age group (6 months to 14 years, 15 to 64 years, and ≥ 65 years)
- Sex
- Chronic conditions that may make that individual more vulnerable to influenza infection (such as chronic pulmonary disease, cardiovascular disease, metabolic disorders, renal disease, treatment-induced immunosuppression and disease-induced immunosuppression, and medically attended obesity)
- Pregnancy status
- Socioeconomic status
- Ethnicity
- Influenza vaccination status or contraindication to influenza vaccination
- Pneumococcal vaccination
- Antibiotic and antiviral prescription
- Use of statins
- Smoking behavior or parental smoking behavior (for children)
- Perinatal and congenital risk factors (eg, birth weight and/or maturity at birth, perinatal factors, inborn errors of metabolism, and relevant malformations and congenital syndromes)
- Number of siblings (for children)
- Adherence to the local childhood vaccination program (for children)
- Number of health care visits 12 months before the study period, describing a study subjects' health care seeking behavior

Number of hospitalizations 12 months before the study period is to be used as proxy for the severity of the chronic conditions.

The primary quantitative data collection will be undertaken at each practice. Data processing will be coordinated by researchers at the Department of Clinical and Experimental Medicine of the University of Surrey. Any data provided to the research team will be stored in their secure servers, which are compliant with the relevant legal and National Health Service digital information governance requirements. Aggregated data will be presented from the final analysis and will not contain any patient identifiable information.

Secondary outcomes will include the utility of the influenza POCT in primary care and the issues and barriers to implementation of influenza POCT in primary care workflows. Data for secondary outcomes will be collected by a semistructured survey of clinicians/practice staff at the participating practices (see [Multimedia Appendix 2](#)). Information will be collected about the following domains previously found to be important to implementation of POCT sampling:

- Performance of the POCT platform
- Clinical pathways and training
- Result reporting
- Clinical governance
- Costs
- Monitoring of effectiveness.

The semistructured survey and results reported will be used to assess which practices were more successful at integrating POCTs into their practice processes by comparing business process models of the practices. Business process models are graphical representations of business-oriented processes within an organization. This is helpful to model collaborations and business transactions within health systems. Business processes are typically modeled using the Business Process Modeling Notation (BPMN). BPMN can be used to depict the end-to-end flow of a business process. The notation has been specifically designed to coordinate the sequence of processes and the messages that flow between different process participants in a related set of business activities [15].

Results

Ethical Approval

The study was funded in July 2018 by the Development of Robust and Innovative Vaccine Effectiveness (DRIVE) European Union, Innovative Medicines Initiative project. The study received ethical approval from the UK Health Research Authority on February 4, 2019, Integrated Research Application System reference: 252081, Research Ethics Committee reference: 19/WM/0015. Moreover, 6 practices were recruited to the study, and data collection commenced on March 11, 2019.

Initial Findings

In addition, 312 swab samples had been collected at the time of submission of the manuscript, which was 32.5% (312/960) of the expected sample size. Furthermore, 68 samples were positive for influenza, which was 20.1% (68/338) of the expected sample size. Qualitative interviews were being undertaken with practices, and the full results are expected to be published in summer 2019.

Discussion

Principal Findings

Our main finding from this study so far is that 312 influenza swabs have thus far been taken and tested using the new POCT machines in practices that are part of the RCGP RSC sentinel surveillance network.

To the best of our knowledge, this is the first time an evaluation study has been undertaken on POCT for influenza in general practice in the United Kingdom. Accurate, real-time monitoring of infectious diseases using rapid diagnostic POCT has been shown to improve outbreak preparedness and response compared with existing surveillance systems [16]. This proposed study will focus on the feasibility of implementation of POCT sampling in primary care versus current methods of influenza sampling in a sentinel network and on the views of practitioners about the use of influenza POCT in primary care, including its impact on primary care workflows.

The RCGP RSC sentinel network is appropriate for this research as the national sentinel surveillance network for England, and the implementation of POCT for influenza in general practices within this network have a potential to rapidly influence clinical care and public health surveillance.

Limitations of the Study

Generalizability

Although the study will be conducted in primary care, the general practices involved in the RCGP RSC sentinel surveillance network may not be representative of general

practices as a whole in the United Kingdom, as seen by the higher average practice scores in payment for results and higher average vaccination rates of practices within the network.

Sample Size

The small sample size used for this study makes it difficult to generalize our findings to a wider group of general practices.

Acknowledgments

The authors would like to thank the participating practices and patients for providing data for this study. The authors would also like to acknowledge the help of Dr Topi Turunen, Scientific Project Manager for the DRIVE project, and Manasa Tripathy and Mariya McGee, practice liaison officers for the RCGP RSC.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Point-of-care testing for influenza—implementation checklist.

[PDF File (Adobe PDF File), 277 KB - [resprot_v8i11e14186_app1.pdf](#)]

Multimedia Appendix 2

Semistructured questionnaire for primary care staff.

[PDF File (Adobe PDF File), 171 KB - [resprot_v8i11e14186_app2.pdf](#)]

References

1. Iuliano AD, Roguski KM, Chang HH, Muscatello DJ, Palekar R, Tempia S, Global Seasonal Influenza-Associated Mortality Collaborator Network. Estimates of global seasonal influenza-associated respiratory mortality: a modelling study. *Lancet* 2018 Mar 31;391(10127):1285-1300 [FREE Full text] [doi: [10.1016/S0140-6736\(17\)33293-2](#)] [Medline: [29248255](#)]
2. Domínguez A, Godoy P, Torner N. The effectiveness of influenza vaccination in different groups. *Expert Rev Vaccines* 2016 Jun;15(6):751-764. [doi: [10.1586/14760584.2016.1142878](#)] [Medline: [26775669](#)]
3. Public Health England. 2017. PHE Guidance on Use of Antiviral Agents for the Treatment and Prophylaxis of Seasonal Influenza URL: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/773369/PHE_guidance_antivirals_influenza.pdf [accessed 2019-09-19]
4. Correa A, Hinton W, McGovern A, van Vlymen J, Yonova I, Jones S, et al. Royal College of General Practitioners Research and Surveillance Centre (RCGP RSC) sentinel network: a cohort profile. *BMJ Open* 2016 Apr 20;6(4):e011092 [FREE Full text] [doi: [10.1136/bmjopen-2016-011092](#)] [Medline: [27098827](#)]
5. de Lusignan S, Correa A, Smith GE, Yonova I, Pebody R, Ferreira F, et al. RCGP research and surveillance centre: 50 years' surveillance of influenza, infections, and respiratory conditions. *Br J Gen Pract* 2017 Oct;67(663):440-441 [FREE Full text] [doi: [10.3399/bjgp17X692645](#)] [Medline: [28963401](#)]
6. Nie S, Roth RB, Stiles J, Mikhлина A, Lu X, Tang Y, et al. Evaluation of Alere i Influenza A&B for rapid detection of influenza viruses A and B. *J Clin Microbiol* 2014 Sep;52(9):3339-3344 [FREE Full text] [doi: [10.1128/JCM.01132-14](#)] [Medline: [24989611](#)]
7. Young S, Illescas P, Nicasio J, Sickler JJ. Diagnostic accuracy of the real-time PCR cobas Liat Influenza A/B assay and the Alere i Influenza A&B NEAR isothermal nucleic acid amplification assay for the detection of influenza using adult nasopharyngeal specimens. *J Clin Virol* 2017 Sep;94:86-90. [doi: [10.1016/j.jcv.2017.07.012](#)] [Medline: [28772170](#)]
8. Ison M, Portsmouth S, Yoshida Y, Shishido T, Hayden F, Uehara T. LB16. Phase 3 trial of Baloxavir Marboxil in high-risk influenza patients (CAPSTONE-2 study). *Open Forum Infect Dis* 2018;5(Suppl 1):S764-S765. [doi: [10.1093/ofid/ofy229.2190](#)]
9. Linder JA, Nieva HR, Blumentals WA. Antiviral and antibiotic prescribing for influenza in primary care. *J Gen Intern Med* 2009 Apr;24(4):504-510 [FREE Full text] [doi: [10.1007/s11606-009-0933-9](#)] [Medline: [19225847](#)]
10. Leland DS, Ginocchio CC. Role of cell culture for virus detection in the age of technology. *Clin Microbiol Rev* 2007 Jan;20(1):49-78 [FREE Full text] [doi: [10.1128/CMR.00002-06](#)] [Medline: [17223623](#)]
11. Zavattoni M, Percivalle E, Cattaneo E, Revello MG, Torsellini M, Gerna G. Optimized detection of respiratory viruses in nasopharyngeal secretions. *New Microbiol* 2003 Apr;26(2):133-140. [Medline: [12737194](#)]

12. Merckx J, Wali R, Schiller I, Caya C, Gore GC, Chartrand C, et al. Diagnostic accuracy of novel and traditional rapid tests for influenza infection compared with reverse transcriptase polymerase chain reaction: a systematic review and meta-analysis. *Ann Intern Med* 2017 Sep 19;167(6):394-409. [doi: [10.7326/M17-0848](https://doi.org/10.7326/M17-0848)] [Medline: [28869986](https://pubmed.ncbi.nlm.nih.gov/28869986/)]
13. Public Health England. 2018. Point of Care Tests for Influenza and Other Respiratory Viruses URL: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/762344/point_of_care_tests_for_influenza_and_other_respiratory_viruses.pdf [accessed 2019-09-19]
14. Rosenthal M, Anderson K, Tengelsen L, Carter K, Hahn C, Ball C. Evaluation of sampling recommendations from the influenza virologic surveillance right size roadmap for Idaho. *JMIR Public Health Surveill* 2017 Aug 24;3(3):e57 [FREE Full text] [doi: [10.2196/publichealth.6648](https://doi.org/10.2196/publichealth.6648)] [Medline: [28838883](https://pubmed.ncbi.nlm.nih.gov/28838883/)]
15. National Asthma Education and Prevention Program. Expert Panel Report 3 (EPR-3): guidelines for the diagnosis and management of asthma-summary report 2007. *J Allergy Clin Immunol* 2007 Nov;120(5 Suppl):S94-138. [doi: [10.1016/j.jaci.2007.09.043](https://doi.org/10.1016/j.jaci.2007.09.043)] [Medline: [17983880](https://pubmed.ncbi.nlm.nih.gov/17983880/)]
16. Meyers L, Ginocchio CC, Faucett AN, Nolte FS, Gesteland PH, Leber A, et al. Automated real-time collection of pathogen-specific diagnostic data: syndromic infectious disease epidemiology. *JMIR Public Health Surveill* 2018 Jul 6;4(3):e59 [FREE Full text] [doi: [10.2196/publichealth.9876](https://doi.org/10.2196/publichealth.9876)] [Medline: [29980501](https://pubmed.ncbi.nlm.nih.gov/29980501/)]

Abbreviations

BPMN: Business Process Modeling Notation

DRIVE: Development of Robust and Innovative Vaccine Effectiveness

ILI: influenza-like illness

POCT: point-of-care testing

RCGP: Royal College of General Practitioners

RSC: Research and Surveillance Centre

Edited by C Hoving; submitted 28.03.19; peer-reviewed by M Hartveit, A Alturkistani; comments to author 23.05.19; revised version received 16.07.19; accepted 14.08.19; published 11.11.19.

Please cite as:

de Lusignan S, Hoang U, Liyanage H, Yonova I, Ferreira F, Diez-Domingo J, Clark T

Feasibility of Point-of-Care Testing for Influenza Within a National Primary Care Sentinel Surveillance Network in England: Protocol for a Mixed Methods Study

JMIR Res Protoc 2019;8(11):e14186

URL: <http://www.researchprotocols.org/2019/11/e14186/>

doi: [10.2196/14186](https://doi.org/10.2196/14186)

PMID: [31710303](https://pubmed.ncbi.nlm.nih.gov/31710303/)

©Simon de Lusignan, Uy Hoang, Harshana Liyanage, Ivelina Yonova, Filipa Ferreira, Javier Diez-Domingo, Tristan Clark. Originally published in *JMIR Research Protocols* (<http://www.researchprotocols.org>), 11.11.2019. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in *JMIR Research Protocols*, is properly cited. The complete bibliographic information, a link to the original publication on <http://www.researchprotocols.org>, as well as this copyright and license information must be included.

Protocol

Implementing a Digital HIV Care Navigation Intervention (Health eNav): Protocol for a Feasibility Study

Sean Arayasirikul^{1,2,3}, PhD; Dillon Trujillo³, MPH; Caitlin M Turner³, MPH; Victory Le³, BA; Erin C Wilson³, DrPH

¹Department of Pediatrics, University of California San Francisco, San Francisco, CA, United States

²Department of Psychiatry, University of California San Francisco, San Francisco, CA, United States

³Center for Public Health Research, San Francisco Department of Public Health, San Francisco, CA, United States

Corresponding Author:

Sean Arayasirikul, PhD

Center for Public Health Research

San Francisco Department of Public Health

25 Van Ness Avenue, 5th Floor

San Francisco, CA, 94102

United States

Phone: 1 415 554 9036

Email: sean.arayasirikul@gmail.com

Abstract

Background: Young racial and ethnic minority men who have sex with men (MSM) and trans women are disproportionately affected by HIV and AIDS in the United States. Unrecognized infection, due to a low uptake of HIV testing, and poor linkage to care are driving forces of ongoing HIV transmission among young racial and ethnic minority MSM and trans women. Internet and mobile technologies, in combination with social network-based approaches, offer great potential to overcome and address barriers to care and effectively disseminate interventions.

Objective: We describe Health eNavigation (Health eNav), a digital HIV care navigation intervention that extends supportive care structures beyond clinic walls to serve youth and young adults living with HIV who are newly diagnosed, not linked to care, out of care, and not virally suppressed, at times when they need support the most.

Methods: This study leverages ecological momentary assessments for a period of 90 days and uses person-delivered short message service text messages to provide participants with digital HIV care navigation over a 6-month period. We aim to improve engagement, linkage, and retention in HIV care and improve viral suppression. Digital HIV care navigation includes the following components: (1) HIV care navigation, (2) health promotion, (3) motivational interviewing, and (4) digital social support.

Results: Recruitment began on November 18, 2016; enrollment closed on May 31, 2018. Intervention delivery ended on November 30, 2018, and follow-up evaluations concluded on October 31, 2019. In this paper, we present baseline sample characteristics.

Conclusions: We discuss real-world strategies and challenges in delivering the digital HIV care navigation intervention in a city-level, public health setting.

International Registered Report Identifier (IRRID): DERR1-10.2196/16406

(*JMIR Res Protoc* 2019;8(11):e16406) doi:[10.2196/16406](https://doi.org/10.2196/16406)

KEYWORDS

HIV/AIDS; digital navigation; young people living with HIV; mHealth

Introduction

Overview

Young racial and ethnic minority men who have sex with men (MSM) and trans women are disproportionately affected by HIV and AIDS in the United States [1-5]. Although MSM

represent just 2% of the US population, this group accounts for 57% of all new HIV infections and is the only risk group with new HIV infections rising each year [6]. The US Centers for Disease Control and Prevention estimates that among all MSM in the United States, black and Latino MSM account for the majority of HIV infections [7]. A recent study found an HIV incidence among black MSM to be 4.16% per year; in a

simulated cohort, authors found that almost 40% of black MSM would be infected with HIV by age 30 and approximately 60% by age 40 [8]. While there has been progress in reducing infections among racial minorities, new HIV infections among black MSM increased 22%, with the largest increase among young men who have sex with men (YMSM) [7]. Nationally, almost two-thirds of new infections in 2008 occurred among those 13-29 years of age, most of which were among African American and Latino MSM [6]. Similar to young racial and ethnic minority MSM, young racial and ethnic minority trans women also bear a huge burden of HIV infections in the United States [9,10]. Data in San Francisco, California, found a 39.5% HIV prevalence among adult trans women [11] and a 7% HIV prevalence among young trans women [12].

Unrecognized infection, due to a low uptake of HIV testing, and poor linkage to care are driving forces of ongoing HIV transmission among young racial and ethnic minority MSM and trans women. Compared to older MSM and white MSM, YMSM (aged 18-29 years) (63%) and racial and ethnic minority MSM (54%) were more likely to be unaware of their HIV infection [10]. In terms of linkage to care, 62% of African Americans and 67% of Latinos were linked to care within 3 months of diagnosis compared to 71% of whites; only 56% of those between 25 and 34 years of age were linked to care compared to about 70% in other age categories [10]. Ultimately, these subgroups were less likely to achieve viral suppression. Similarly, the burden of HIV in trans women is exacerbated by unrecognized infections and low access to HIV care [10]. In 2012, counseling and testing data from San Francisco public testing sites found that of the 17,898 HIV tests over the year, only 403 HIV tests were conducted with trans women [13]. Findings from a study of adult trans women living with HIV in the San Francisco Bay Area found that 77% of participants were linked to care but only 44% were virologically suppressed [14]. Research has found that trans women with HIV in San Francisco have a significantly higher average aggregate viral load (ie, *community viral load*) compared to other populations [15].

Internet and mobile technologies, in combination with social network-based approaches, offer great potential to overcome and address barriers to care and effectively disseminate interventions. Traditional delivery methods of linkage and engagement services for HIV care services may be less effective at reaching at-risk youth and young adult MSM and trans women living with HIV in today's social media-driven environment. As more individuals now have access to the Internet and other mobile technologies, social networking online and seeking health-related information on the Internet has become increasingly popular, especially among young sexual and gender minorities. Recent innovations in online methods for increasing HIV testing, initiating partner interventions and behavioral interventions, HIV care, self-management, and provider care have also demonstrated efficacy comparable to face-to-face interventions [16,17]. Interventions that leverage mobile technology and social media have also been found to have a greater impact in influencing behavior than radio and television campaigns [16]. There is evidence that social media can be effectively utilized to connect young adults with HIV and sexually transmitted disease information and increase condom

use [18]. This is particularly relevant to the sociocultural contexts of young racial and ethnic minority MSM and trans women who experience homophobia and transphobia, both within their own racial and ethnic communities and the larger society; this makes them often more hidden and inaccessible through traditional public health outreach efforts [9,19]. Through accessing and receiving Internet- and/or mobile technology-based HIV interventions, these young racial and sexual minority individuals can remain safe and maintain their privacy. Additionally, since youth and young adults have large social networks online [20], interventions delivered on the Internet or through mobile technology may have greater diffusion effects. Social network members can provide both tangible and intangible resources or support, which may facilitate or protect against health-related risks [21]. Furthermore, social network-specific norms can affect individuals' attitudes regarding sex, risk behaviors, and health-seeking behaviors [22].

Mobile-based interventions have high promise for engaging youth and young adults in their HIV care. Mobile phones represent a common thread for communication among almost all youth and young adults in the United States, where approximately 95% of those aged 18-29 years own their own mobile phone [23]. Importantly, according to the 2012 National Health Interview Survey, more than 70% of those living in wireless-only households (ie, with no landline) in 2011 were at or below 200% of the federal poverty threshold, contradicting the conventionally held idea that use of mobile technology is concentrated among better-resourced people [24]. In fact, mobile technology today is used by almost all Americans in all socioeconomic groups and by higher percentages of African Americans and Latinos than whites [24]. Short message service (SMS) text messaging via mobile phones has been used to provide sexual health information to young people [25]. A South African study used SMS text messaging for all participant interactions, from recruitment through to final follow-up, and found that 10 motivational-style SMS text messages increased HIV testing rates to a statistically significant degree when compared to the control group [26]. Furthermore, the WelTel Kenya1 trial demonstrated that SMS text messaging support via weekly messages to participants improved adherence to HIV treatment medications or antiretroviral therapy (ART) and increased viral load suppression; this occurred when participants were required to respond regarding whether they were doing well or if there was a problem [27]. SMS text messaging alerts are also relatively unobtrusive, offering the user confidentiality in environments where HIV is often taboo.

Issues that youth and young adults living with HIV experience are complex and may benefit from a combination of digital and mobile health technologies and clinical and community-based interventions to achieve positive health outcomes. Traditional HIV care services must move outside of clinical settings to incorporate digital and social media technologies. The San Francisco Department of Public Health's Center for Public Health Research developed a digital HIV care navigation intervention called Health eNavigation (Health eNav), which is designed for young and young adult (ages 18-34) MSM and trans women living with HIV. Among youth and young adults,

linkage to care is relatively high at more than 80%, but there is a steep drop-off in retention in care (ie, <50%) and low viral suppression (ie, <70%) 12 months from diagnosis [13]. Youth and young adults are a subpopulation in particular need of interventions to improve linkage, retention, and engagement in HIV care. Many youth and young adults may not have a medical home (ie, a consistent relationship with and access to a primary care provider) due to population-specific challenges and barriers, such as homelessness, needs related to identity development, and job insecurity.

Intervention Description

Overview

Health eNav is a 6-month, digital HIV care navigation intervention leveraging SMS text messaging to provide digital HIV care navigation services to young people living with HIV. During the intervention, participants are connected to their own digital HIV care navigator and receive the following components: (1) digital HIV care navigation and (2) ecological momentary assessments. Through the use of technology, Health eNav extends supportive care structures beyond clinic walls at times when youth and young adults living with HIV who are newly diagnosed, not linked to care, out of care, and not virally suppressed need support the most. Health eNav is an engagement and retention-in-HIV-care intervention, aimed at addressing critical gaps and barriers to successfully identifying, linking, engaging, and retaining youth and young adults living with HIV in medical care. The goal of Health eNav is to improve outcomes across the HIV care continuum, specifically retention in HIV care, ART initiation, and viral suppression.

Health eNav seeks to improve health outcomes by amplifying the reach and value of the patient-centered medical home (PCMH) model [28] with the use of digital technology. This PCMH model uses a care team approach to provide patients with focused and culturally relevant services, strong provider-patient relationships, the elimination of barriers to care, and increased efficiency and quality of care. In addition to the PCMH model, Health eNav delivers digital HIV care navigation that aligns with the chronic care model [29]. Health eNav seeks to provide increased linkages to community resources in a community-driven, cost-effective way; promote self-management that empowers participants to take an active role in their health; and offer clinical decision support, information sharing, and proactive care in real time [29,30].

Digital HIV Care Navigation

Digital HIV care navigation includes the following: (1) HIV care navigation, (2) health promotion, (3) motivational interviewing, and (4) digital social support.

HIV Care Navigation

HIV care navigation guides participants in knowing where, when, and how to access all health and related services and increases access to appropriate resources [31]. HIV care navigation services include the coordination of, and/or referrals to, the following services: (1) primary medical care, (2) specialty care, (3) mental health care and substance abuse services, (4) imaging and other diagnostic services, (5) laboratory services,

(6) health insurance, (7) housing, and (8) benefits, entitlements, and public assistance.

Health Promotion and Education

Health promotion and education ensures optimal health literacy for all participants by providing information on the biology of HIV, disease management, communication with providers, risk reduction and healthy behavior, and ART adherence. Health promotion content is tailored, personalized, and specific to the needs of each participant; it is also documented in their individual care plan and updated on an ongoing basis. Health promotion and education are delivered to meet participants' educational, developmental, language, gender, sexual, and cultural needs.

Motivational Interviewing

Motivational interviewing is a technique and a style of counseling that can help resolve the ambivalence that prevents patients from realizing their personal goals. Motivational interviewing builds on Carl Rogers' optimistic and humanistic theories about people's capabilities for exercising free choice and changing through a process of self-actualization. The therapeutic relationship for both Rogerian and motivational interviewers is a democratic partnership. Motivational interviewing is directive and aims at eliciting self-motivational statements and behavioral change from the client in addition to creating client discrepancy to enhance motivation for positive change [32,33]. Motivational interviewing activates the capability for beneficial change that everyone possesses [34]. Although some people can continue to change on their own, others require more formal treatment and support over the long journey of recovery. Even for participants with low readiness, motivational interviewing serves as a vital prelude to longer-term behavior change.

Social Support

The intervention provides patients with maximal access to social support from a digital navigator. The digital navigator maintains an open, nonjudgmental space with participants and provides social support through engaging in active listening, joint problem solving, and peer counseling on an as-needed and ongoing basis during the 6-month intervention period. They may also provide counseling to assist with disclosure where feasible and/or facilitate referrals to external social support providers (eg, community-based organizations) when appropriate.

Ecological Momentary Assessments and Harnessing the Power of Digital Sensing

Ubiquitous data collection in real time by using mobile technology can provide the critical contextual data needed to explain barriers to HIV care engagement. Ecological momentary assessment (EMA) is a behavioral medicine method used to collect data close in time to participants' experience and in their natural environment, shedding light on the dynamics of behavior in the context of real-world settings [35-38]. EMAs are delivered to participants in the form of a short, daily, SMS text message survey to assess or sense early indicators of barriers and facilitators to HIV care engagement and treatment adherence. In Health eNav, EMAs gauge participants' daily emotional affective state, mental health, substance use, and other risk

behaviors known to directly affect HIV care engagement and treatment adherence. Furthermore, EMA data are fed back into digital HIV care navigation through a dashboard. Digital sensing of daily changes in affect and/or mental health by using EMAs can prompt tailored digital discussions, facilitate timely personalized referrals, and inform our understanding of early predictors of engagement in HIV care and treatment adherence.

Methods

Reporting and Design

We have followed the Standard Protocol Items: Recommendations for Interventional Trials guidelines for reporting on protocols [39]. This is a single-arm, prospective, explanatory, mixed-methods, pre-post design feasibility study.

Setting

This intervention was housed physically in the Center for Public Health Research at the San Francisco Department of Public Health; however, most of the engagement in the intervention was virtual, through SMS text messaging.

Participants

Eligible participants were youth and young adults, aged 18-34 years, diagnosed with HIV infection, who identify as an MSM or a trans woman and report living in San Francisco, California. Eligible participants also met at least one of the following criteria: (1) newly diagnosed with HIV or have tested HIV positive for the first time within the last 12 months prior to enrollment, (2) not linked to HIV medical care or are aware of their HIV infection status but have never engaged in care or never had an HIV medical visit after being diagnosed with HIV, (3) out of care or diagnosed with HIV more than 12 months prior to enrollment and had a gap in their HIV care that was longer than 6 months, within the last 24 months, and (4) not virally suppressed or have a viral load of at least 200 copies/mL at their last lab test. If participants did not have access to a mobile phone, they were provided with a mobile phone, 2 years of cellular service, and unlimited SMS text messaging.

Ethics Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study protocol was approved by the Institutional Review Board (IRB) at the University of California, San Francisco (IRB number: 16-19675).

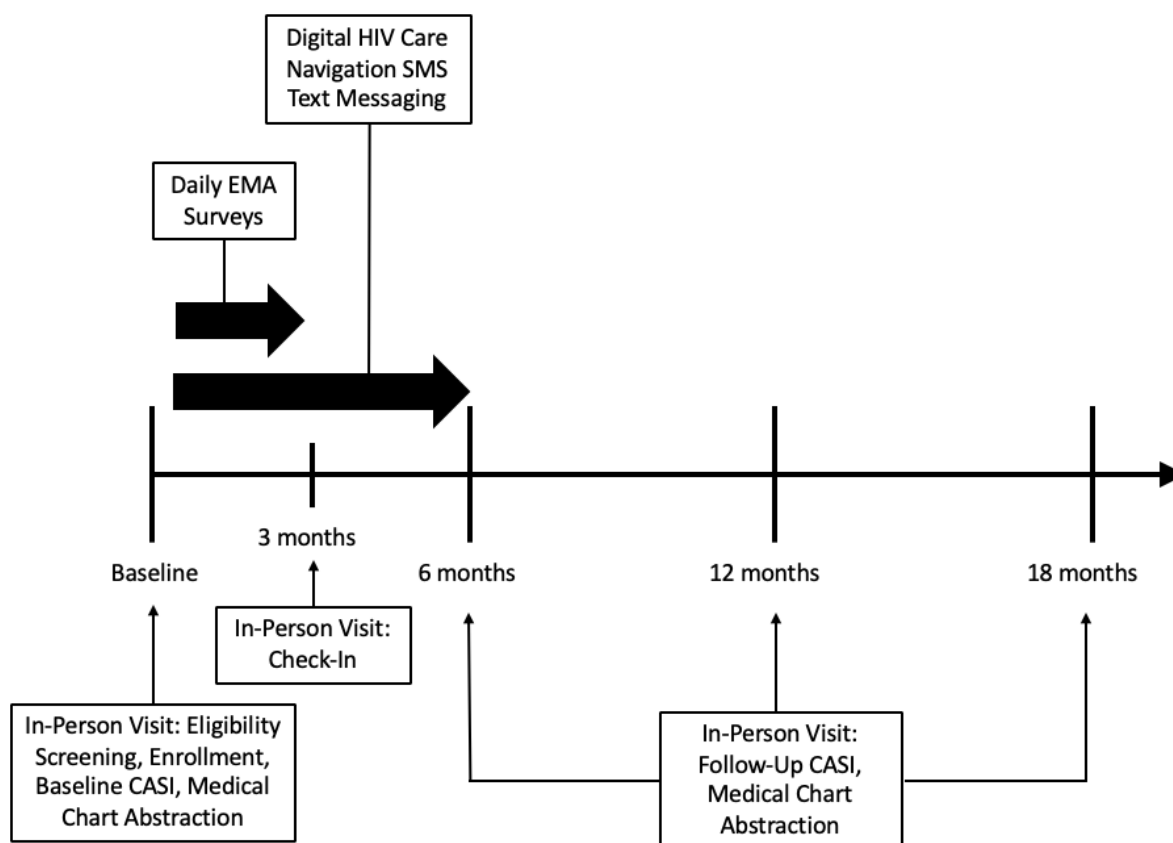
Recruitment

Recruitment took place at San Francisco Department of Public Health community clinics and community-based organizations (CBOs). Convenience sampling was used to recruit potential participants from five clinics and CBOs in San Francisco serving young people living with HIV. Recruiting materials (eg, flyers) and presentations to staff were used to advertise study recruitment. Staff referred potential participants to the study through phone and email communication and/or in-person meetings. Enrolled participants were also invited to refer peers from their social network. We screened 171 potential participants and 140 were eligible; 20 of these individuals were lost to follow-up following screening. A total of 120 participants were enrolled into the study.

Study Procedures and Data Collection Methods

At enrollment and baseline, participants were educated about the study, provided informed consent, and completed administrative paperwork. Participants met with their digital navigator and completed the following: a short qualitative interview, a comprehensive care plan, and computer-assisted self-interviewing (CASI) surveys. Participants received one-on-one training and instruction on SMS text messaging and completing EMA surveys. SMS text message and EMA data (ie, date and time, text, and responses) were collected using third-party vendors. Participants were sent automated EMA SMS text messages once per day at 8:00 am, 12:00 pm, or 8:00 pm for 90 consecutive days. They were required to respond to EMA surveys within 24 hours. Participants could receive between 17 and 31 daily EMA texts depending on their responses to programmed skip logic. EMAs tended to take less than 5 minutes to complete each day. Participants earned US \$1 for each completed EMA survey; if participants completed 90% or more, they earned a bonus of US \$100. At 3 months, participants met with their digital HIV care navigator in person for an informal check-in and were remunerated for the number of EMA surveys they completed during that period. Digital HIV care navigation continued for 6 months from enrollment. Participants were able to communicate with their digital HIV care navigator via SMS text message on an open schedule and conversations spanned any topic that participants would want discussed. The digital HIV care navigator would send weekly check-in messages to participants that included the following topics: general well-being, health education and health promotion, social support, and primary care appointment reminders, among others. CASIs were administered every 6 months for 18 months, and medical chart abstraction was conducted every 6 months for 18 months. [Figure 1](#) describes the study design.

Figure 1. Health eNavigation (Health eNav) study design. CASI: computer-assisted self-interviewing; EMA: ecological momentary assessment; SMS: short message service.



Results

Recruitment began on November 18, 2016, and the first participant was enrolled on December 16, 2016; enrollment closed on May 31, 2018. Intervention delivery ended on November 30, 2018, and all study-related follow-up and procedures concluded on October 31, 2019. We present baseline sample characteristics in [Table 1](#) below. Overall, the majority of participants were people of color, with the largest ethnic and racial minority subgroup being Latinx (38/120, 31.7%); 85.8% (103/120) identified as an MSM and 14.2% (17/120) identified

as a gender minority. At baseline, many participants reported experiencing unstable housing, with only 32.5% of participants (39/120) renting or owning an apartment or home. Over one-third of participants (43/120, 35.8%) reported temporary or transitional housing, and 14.2% (17/120) reported living at a shelter or being homeless. Over half of the participants (68/120, 56.7%) reported having some college education or more. Nearly a third were newly diagnosed, and 6.7% (8/120) had never received primary HIV care. While the majority of participants have accessed HIV care within the last 6 months (99/120, 82.5%) and are currently on ART (92/120, 76.7%), only about half (65/120, 54.2%) were virally suppressed.

Table 1. Overall baseline sample characteristics for Health eNav^a, 2017-2018 (N=120).

| Characteristics | Value |
|---|--------------|
| Demographics | |
| Age (years), mean (SD) | 27.75 (4.07) |
| Race or ethnicity, n (%) | |
| Black or African American | 22 (18.3) |
| Hispanic or Latinx | 38 (31.7) |
| Other ^b or multiple | 28 (23.3) |
| White | 32 (26.7) |
| Gender identity, n (%) | |
| Male | 103 (85.8) |
| Trans woman, genderqueer, gender nonconforming, or other | 17 (14.2) |
| Socioeconomic factors, n (%) | |
| Housing status | |
| Lives with a family member, friend, or partner who rents or owns a home | 21 (17.5) |
| Temporary or transitional housing ^c | 43 (35.8) |
| Homeless or lives in a shelter | 17 (14.2) |
| Rents or owns an apartment or house | 39 (32.5) |
| Income in the last month (US \$) | |
| 0-250 | 30 (25.0) |
| 251-600 | 30 (25.0) |
| 601-1300 | 30 (25.0) |
| 1301 or more | 29 (24.2) |
| Education | |
| High school or GED ^d | 39 (32.5) |
| Less than high school | 13 (10.8) |
| Some college or more | 68 (56.7) |
| HIV diagnosis status, n (%) | |
| Diagnosed in the last year | 38 (31.7) |
| Diagnosed more than 1 year ago | 82 (68.3) |
| Engagement in HIV care, n (%) | |
| Received primary HIV care | |
| No | 8 (6.7) |
| Yes | 112 (93.3) |
| Received primary HIV care in the last 6 months | |
| No | 21 (17.5) |
| Yes | 99 (82.5) |
| Currently undertaking ART^e | |
| No | 27 (22.5) |
| Yes | 92 (76.7) |
| Last viral load test result | |
| Undetectable | 65 (54.2) |
| Detectable | 32 (26.7) |

| Characteristics | Value |
|-----------------|-----------|
| Unknown | 15 (12.5) |

^aHealth eNav: Health eNavigation.

^bIncludes participants who identified as American Indian or Alaska Native (n=6) or Asian (n=7).

^cIncludes participants who lived in single-room occupancy hotels, motels, boarding houses, halfway houses, drug treatment centers, independent living units, domestic violence shelters, battered persons' shelters, or *safe houses*.

^dGED: General Educational Development.

^eART: antiretroviral therapy.

Discussion

We were able to serve and provide digital HIV care navigation to 120 youth and young adults living with HIV in San Francisco. Some of our successes, lessons learned, and challenges and barriers are described.

Successes

Delivering Personalized Social Support

The project was able to deliver personalized social support to youth and young adults living with HIV through innovative use of digital technology. For example, 1 participant was transitioning between HIV care providers and did not want his digital HIV care navigator to accompany him to the appointment. However, while he was in the waiting room, the participant was having a very difficult time fighting to not internalize the stigma from being in an HIV clinic. He went on to have a very difficult conversation with his new care provider. Meanwhile, he was able to speak with his personal digital HIV care navigator through this difficult clinical encounter. The digital HIV care navigator served as a caring source of support to listen to and support this participant; as a result, this participant was able to work through his feelings of stigma and other negative emotions to maintain linkage and engagement in care.

Collecting Real-Time Data

The project was able to collect timely individual-level data securely through mobile devices. After enrollment, participants received daily SMS text message surveys for 90 days on a variety of topics, including mental health and substance use. These data can impact individuals' linkage, engagement, and retention in HIV care. They are reviewed by the HIV care navigator who can deliver personalized social support depending on how participants responded to text surveys. For example, 1 participant went approximately 30 days with no feelings of depression or anxiety. Suddenly, the participant started to indicate that they were feeling anxious or depressed. The digital HIV care navigator checked in with the participant via SMS text message and found out that they had not been able to successfully get a job, even after multiple interviews. The digital HIV care navigator was able to provide timely emotional and informational support to a participant that may not have shared this kind of information with their usual care provider.

Challenges and Barriers

The Importance of Collaborative and Translational Communication

In our experience, technology vendors can be incredibly siloed. For example, few technology vendors have experience in health care or public health, let alone research. It is important to be acutely aware of these disciplinary boundaries as you may need to translate your research or public health needs for an audience who may not be aware of what exactly you do. Effective communication to foster understanding of purpose and organizational context will help aid negotiations and in scoping a project appropriately.

Keep Your Eye on the Front End and the Back End

It is important to emphasize both how the technology looks (ie, front end or user interface) and how it is structured in its programming code (ie, back end), as this can impact how data and metadata are collected and how databases are structured. For example, metadata are data that are collected on the back end. While the primary data might be SMS text messages, types of metadata might include date, time, and geolocation, among others. It may be important to consider how the data are collected, including metadata, and how the data are structured. For example, does the technology measure time using a 24-hour clock versus a 12-hour clock? Will the project need to calculate time? If so, the 24-hour clock might be a better measure to compute a new time variable using two time measurements. While seemingly minor, a detail like this might require a redesign with a hefty price tag, especially if there is a limited budget for adjustments.

Agree on a Contract That Lives On for the Length of a Project

When entering into a contract with a technology vendor, create a contract that spans the entire length of the project if possible. Important issues may include key software updates, ongoing technical support, and new features, among others. This will allow additional adjustments to be made along the way.

Tips for Implementation

1. Offer an alternative work schedule to incorporate flexibility in providing digital navigation and support conversations with participants at times that they prefer and are most accessible to them.
2. Prioritize initiating conversations with participants who have a higher acuity level versus those who have lower acuity.

3. Develop a quick reference guide of resources to provide to participants.
4. Utilize peers as digital HIV care navigators.
5. Implement creative ways to spark a conversation quickly.
6. Comprehensively assess participants' social media imprint and presence and provide digital HIV care navigation using all the platforms participants actively use.
7. Use direct, succinct, but conversational language, especially with SMS text messaging and participants with limited literacy.
8. If your technology platform allows, use alternative media, such as GIFs, emojis, and memes, among others.
9. Use non-HIV-related messages to develop rapport and build trust.
10. Be responsive in real time, if at all possible. While SMS text messaging is asynchronous, make an effort to be quick to respond when participants choose to engage.
11. Carve out time to engage in a lengthier SMS text message session in real time. Designate a day and time in the week to conduct a quick text message chat.
12. Develop and integrate a feedback loop for digital HIV care navigation to inform primary care and the care team.
13. SMS text messaging may be a viable, sensitive method for evaluating when participants have fallen out of care and/or when a particular mode of communication (eg, phone number) is no longer viable.
14. Incorporate an assessment process to understand individuals' attitudes toward digital technology; assess whether or not a digital intervention is suitable for a participant or not.
15. Do not use digital HIV care navigation to replace traditional navigation with high-acuity participants.

Acknowledgments

The authors would like to thank all participants in the study. This work was funded by the Health Resources and Services Administration (award number: H97HA28895). This study's funding sources had no role in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the article for publication.

Authors' Contributions

SA led the conception and design of the study protocol and oversaw implementation. DT served as the primary interventionist as the digital HIV care navigator. CMT provided expertise in statistical analyses. VL supported data collection and medical chart abstraction activities. ECW oversaw the plan for implementation and coordination of study activities.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Peer-reviewer report from the Health Resources and Services Administration.

[\[PDF File \(Adobe PDF File\), 70 KB - resprot_v8i11e16406_app1.pdf\]](#)

References

1. Clements-Nolle K, Marx R, Guzman R, Katz M. HIV prevalence, risk behaviors, health care use, and mental health status of transgender persons: Implications for public health intervention. *Am J Public Health* 2001 Jun;91(6):915-921. [doi: [10.2105/ajph.91.6.915](https://doi.org/10.2105/ajph.91.6.915)] [Medline: [11392934](https://pubmed.ncbi.nlm.nih.gov/11392934/)]
2. Garofalo R, Deleon J, Osmer E, Doll M, Harper GW. Overlooked, misunderstood and at-risk: Exploring the lives and HIV risk of ethnic minority male-to-female transgender youth. *J Adolesc Health* 2006 Mar;38(3):230-236. [doi: [10.1016/j.jadohealth.2005.03.023](https://doi.org/10.1016/j.jadohealth.2005.03.023)] [Medline: [16488820](https://pubmed.ncbi.nlm.nih.gov/16488820/)]
3. Herbst JH, Jacobs ED, Finlayson TJ, McKleroy VS, Neumann MS, Crepaz N, HIV/AIDS Prevention Research Synthesis Team. Estimating HIV prevalence and risk behaviors of transgender persons in the United States: A systematic review. *AIDS Behav* 2008 Jan;12(1):1-17. [doi: [10.1007/s10461-007-9299-3](https://doi.org/10.1007/s10461-007-9299-3)] [Medline: [17694429](https://pubmed.ncbi.nlm.nih.gov/17694429/)]
4. Brennan J, Kuhns LM, Johnson AK, Belzer M, Wilson EC, Garofalo R, Adolescent Medicine Trials Network for HIV/AIDS Interventions. Syndemic theory and HIV-related risk among young transgender women: The role of multiple, co-occurring health problems and social marginalization. *Am J Public Health* 2012 Sep;102(9):1751-1757 [FREE Full text] [doi: [10.2105/AJPH.2011.300433](https://doi.org/10.2105/AJPH.2011.300433)] [Medline: [22873480](https://pubmed.ncbi.nlm.nih.gov/22873480/)]
5. Denson DJ, Padgett PM, Pitts N, Paz-Bailey G, Bingham T, Carlos J, et al. Health care use and HIV-related behaviors of black and Latina transgender women in 3 US metropolitan areas: Results from the transgender HIV behavioral survey. *J Acquir Immune Defic Syndr* 2017 Jul 01;75 Suppl 3:S268-S275 [FREE Full text] [doi: [10.1097/QAI.0000000000001402](https://doi.org/10.1097/QAI.0000000000001402)] [Medline: [28604427](https://pubmed.ncbi.nlm.nih.gov/28604427/)]
6. Centers for Disease Control and Prevention (CDC). Prevalence and awareness of HIV infection among men who have sex with men: 21 cities, United States, 2008. *MMWR Morb Mortal Wkly Rep* 2010 Sep 24;59(37):1201-1207 [FREE Full text] [Medline: [20864920](https://pubmed.ncbi.nlm.nih.gov/20864920/)]

7. Centers for Disease Control and Prevention. Atlanta, GA: Centers for Disease Control and Prevention; 2019. HIV and African American gay and bisexual men URL: <https://www.cdc.gov/hiv/group/msm/bmsm.html> [accessed 2019-11-04]
8. Matthews DD, Herrick AL, Coulter RW, Friedman MR, Mills TC, Eaton LA, POWER Study Team. Running backwards: Consequences of current HIV incidence rates for the next generation of black MSM in the United States. *AIDS Behav* 2016 Jan;20(1):7-16 [FREE Full text] [doi: [10.1007/s10461-015-1158-z](https://doi.org/10.1007/s10461-015-1158-z)] [Medline: [26267251](https://pubmed.ncbi.nlm.nih.gov/26267251/)]
9. Herbst JH, Jacobs ED, Finlayson TJ, McKleroy VS, Neumann MS, Crepaz N, HIV/AIDS Prevention Research Synthesis Team. Estimating HIV prevalence and risk behaviors of transgender persons in the United States: A systematic review. *AIDS Behav* 2008 Jan;12(1):1-17. [doi: [10.1007/s10461-007-9299-3](https://doi.org/10.1007/s10461-007-9299-3)] [Medline: [17694429](https://pubmed.ncbi.nlm.nih.gov/17694429/)]
10. HIV Epidemiology Section staff. HIV/AIDS Epidemiology Annual Report 2008. San Francisco, CA: HIV Epidemiology Section, San Francisco Department of Public Health AIDS Office; 2009 Jul. URL: <https://www.sfdph.org/dph/files/reports/RptsHIVAIDS/HIVAIDAnnRpt2008.pdf> [accessed 2019-11-04]
11. Rapues J, Wilson EC, Packer T, Colfax GN, Raymond HF. Correlates of HIV infection among transfemales, San Francisco, 2010: Results from a respondent-driven sampling study. *Am J Public Health* 2013 Aug;103(8):1485-1492. [doi: [10.2105/AJPH.2012.301109](https://doi.org/10.2105/AJPH.2012.301109)] [Medline: [23763398](https://pubmed.ncbi.nlm.nih.gov/23763398/)]
12. Wilson E, Chen YH, Arayasirikul S, Fisher M, Pomart WA, Le V, et al. Differential HIV risk for racial/ethnic minority trans*female youths and socioeconomic disparities in housing, residential stability, and education. *Am J Public Health* 2015 Jul;105 Suppl 3:e41-e47 [FREE Full text] [doi: [10.2105/AJPH.2014.302443](https://doi.org/10.2105/AJPH.2014.302443)] [Medline: [25905826](https://pubmed.ncbi.nlm.nih.gov/25905826/)]
13. HIV Epidemiology Section staff. HIV Epidemiology Annual Report 2013. San Francisco, CA: HIV Epidemiology Section, San Francisco Department of Public Health; 2014 Aug. URL: <https://www.sfdph.org/dph/files/reports/RptsHIVAIDS/HIVAIDAnnRpt2013.pdf> [accessed 2019-11-04]
14. Santos G, Wilson EC, Rapues J, Macias O, Packer T, Raymond HF. HIV treatment cascade among transgender women in a San Francisco respondent driven sampling study. *Sex Transm Infect* 2014 Aug;90(5):430-433. [doi: [10.1136/sextrans-2013-051342](https://doi.org/10.1136/sextrans-2013-051342)] [Medline: [24714446](https://pubmed.ncbi.nlm.nih.gov/24714446/)]
15. Das M, Chu PL, Santos G, Scheer S, Vittinghoff E, McFarland W, et al. Decreases in community viral load are accompanied by reductions in new HIV infections in San Francisco. *PLoS One* 2010 Jun 10;5(6):e11068 [FREE Full text] [doi: [10.1371/journal.pone.0011068](https://doi.org/10.1371/journal.pone.0011068)] [Medline: [20548786](https://pubmed.ncbi.nlm.nih.gov/20548786/)]
16. Sullivan PS, Grey JA, Simon Rosser BR. Emerging technologies for HIV prevention for MSM: What we have learned, and ways forward. *J Acquir Immune Defic Syndr* 2013 Jun 01;63 Suppl 1:S102-S107 [FREE Full text] [doi: [10.1097/QAI.0b013e3182949e85](https://doi.org/10.1097/QAI.0b013e3182949e85)] [Medline: [23673879](https://pubmed.ncbi.nlm.nih.gov/23673879/)]
17. Kempf M, Huang C, Savage R, Safren SA. Technology-delivered mental health interventions for people living with HIV/AIDS (PLWHA): A review of recent advances. *Curr HIV/AIDS Rep* 2015 Dec;12(4):472-480 [FREE Full text] [doi: [10.1007/s11904-015-0292-6](https://doi.org/10.1007/s11904-015-0292-6)] [Medline: [26452644](https://pubmed.ncbi.nlm.nih.gov/26452644/)]
18. Bull S, Levine DK, Black SR, Schmiege SJ, Santelli J. Social media-delivered sexual health intervention: A cluster randomized controlled trial. *Am J Prev Med* 2012 Nov;43(5):467-474 [FREE Full text] [doi: [10.1016/j.amepre.2012.07.022](https://doi.org/10.1016/j.amepre.2012.07.022)] [Medline: [23079168](https://pubmed.ncbi.nlm.nih.gov/23079168/)]
19. Díaz RM, Ayala G, Bein E, Henne J, Marin BV. The impact of homophobia, poverty, and racism on the mental health of gay and bisexual Latino men: Findings from 3 US cities. *Am J Public Health* 2001 Jun;91(6):927-932. [doi: [10.2105/ajph.91.6.927](https://doi.org/10.2105/ajph.91.6.927)] [Medline: [11392936](https://pubmed.ncbi.nlm.nih.gov/11392936/)]
20. Lenhart A, Madden M, Hitlin P. *Teens and Technology: Youth Are Leading the Transition to a Fully Wired and Mobile Nation*. Washington, DC: Pew Internet & American Life Project; 2005 Jul 27. URL: <https://www.immagic.com/eLibrary/ARCHIVES/GENERAL/PEW/P050727L.pdf> [accessed 2019-11-04]
21. Berkman LF, Glass T. Social integration, social networks, social support, and health. In: Berkman LF, Kawachi I, editors. *Social Epidemiology*. New York, NY: Oxford University Press; 2000:137-173.
22. Hall A, Wellman B. Social networks and social support. In: Cohen S, Syme SL, editors. *Social Support and Health*. San Diego, CA: Academic Press; 1985:23-41.
23. Duggan M, Smith A. Pew Research Center. Washington, DC: Pew Internet & American Life Project; 2013 Sep 16. Cell Internet use 2013 URL: <https://www.pewresearch.org/internet/2013/09/16/cell-internet-use-2013/> [accessed 2019-11-04]
24. Blumberg SJ, Luke JV. National Center for Health Statistics. Atlanta, GA: Centers for Disease Control and Prevention; 2008 May 13. Wireless substitution: Early release of estimates from the National Health Interview Survey, July-December 2007 URL: <https://www.cdc.gov/nchs/data/nhis/earlyrelease/wireless200805.pdf> [accessed 2019-10-30]
25. Lim MS, Hocking JS, Aitken CK, Fairley CK, Jordan L, Lewis JA, et al. Impact of text and email messaging on the sexual health of young people: A randomised controlled trial. *J Epidemiol Community Health* 2012 Jan;66(1):69-74. [doi: [10.1136/jech.2009.100396](https://doi.org/10.1136/jech.2009.100396)] [Medline: [21415232](https://pubmed.ncbi.nlm.nih.gov/21415232/)]
26. de Tolly K, Skinner D, Nembaware V, Benjamin P. Investigation into the use of short message services to expand uptake of human immunodeficiency virus testing, and whether content and dosage have impact. *Telemed J E Health* 2012;18(1):18-23. [doi: [10.1089/tmj.2011.0058](https://doi.org/10.1089/tmj.2011.0058)] [Medline: [22150712](https://pubmed.ncbi.nlm.nih.gov/22150712/)]
27. van der Kop ML, Karanja S, Thabane L, Marra C, Chung MH, Gelmon L, et al. In-depth analysis of patient-clinician cell phone communication during the WeITel Kenya1 antiretroviral adherence trial. *PLoS One* 2012;7(9):e46033 [FREE Full text] [doi: [10.1371/journal.pone.0046033](https://doi.org/10.1371/journal.pone.0046033)] [Medline: [23049928](https://pubmed.ncbi.nlm.nih.gov/23049928/)]

28. Jackson GL, Powers BJ, Chatterjee R, Bettger JP, Kemper AR, Hasselblad V, et al. The patient centered medical home: A systematic review. *Ann Intern Med* 2013 Feb 05;158(3):169-178. [doi: [10.7326/0003-4819-158-3-201302050-00579](https://doi.org/10.7326/0003-4819-158-3-201302050-00579)] [Medline: [24779044](https://pubmed.ncbi.nlm.nih.gov/24779044/)]
29. Wagner EH, Austin BT, Von Korff M. Organizing care for patients with chronic illness. *Milbank Q* 1996;74(4):511-544. [Medline: [8941260](https://pubmed.ncbi.nlm.nih.gov/8941260/)]
30. Wagner EH, Austin BT, Von Korff M. Improving outcomes in chronic illness. *Manag Care Q* 1996;4(2):12-25. [Medline: [10157259](https://pubmed.ncbi.nlm.nih.gov/10157259/)]
31. Higa DH, Marks G, Crepez N, Liao A, Lyles CM. Interventions to improve retention in HIV primary care: A systematic review of US studies. *Curr HIV/AIDS Rep* 2012 Dec;9(4):313-325 [FREE Full text] [doi: [10.1007/s11904-012-0136-6](https://doi.org/10.1007/s11904-012-0136-6)] [Medline: [22996171](https://pubmed.ncbi.nlm.nih.gov/22996171/)]
32. Davidson R. Motivational issues in the treatment of addictive behaviour. In: Edwards G, Dare C, editors. *Psychotherapy, Psychological Treatments and the Addictions*. Cambridge, UK: Cambridge University Press; 1996:173-188.
33. Miller WR, Rollnick S, editors. *Motivational Interviewing: Helping People Change*. 3rd Edition. New York, NY: The Guilford Press; 2013.
34. Rollnick S, Miller WR. What is motivational interviewing? *Behav Cogn Psychother* 1995 Oct;23(4):325-334. [doi: [10.1017/s135246580001643x](https://doi.org/10.1017/s135246580001643x)]
35. Cook PF, McElwain CJ, Bradley-Springer LA. Brief report on ecological momentary assessment: Everyday states predict HIV prevention behaviors. *BMC Res Notes* 2016 Jan 04;9:9 [FREE Full text] [doi: [10.1186/s13104-015-1814-4](https://doi.org/10.1186/s13104-015-1814-4)] [Medline: [26728848](https://pubmed.ncbi.nlm.nih.gov/26728848/)]
36. Fazeli PL, Turan JM, Budhwani H, Smith W, Raper JL, Mugavero MJ, et al. Moment-to-moment within-person associations between acts of discrimination and internalized stigma in people living with HIV: An experience sampling study. *Stigma Health* 2017 Aug;2(3):216-228 [FREE Full text] [doi: [10.1037/sah0000051](https://doi.org/10.1037/sah0000051)] [Medline: [28966982](https://pubmed.ncbi.nlm.nih.gov/28966982/)]
37. Rowe C, Hern J, DeMartini A, Jennings D, Sommers M, Walker J, et al. Concordance of text message ecological momentary assessment and retrospective survey data among substance-using men who have sex with men: A secondary analysis of a randomized controlled trial. *JMIR Mhealth Uhealth* 2016 May 26;4(2):e44 [FREE Full text] [doi: [10.2196/mhealth.5368](https://doi.org/10.2196/mhealth.5368)] [Medline: [27230545](https://pubmed.ncbi.nlm.nih.gov/27230545/)]
38. Wray TB, Merrill JE, Monti PM. Using ecological momentary assessment (EMA) to assess situation-level predictors of alcohol use and alcohol-related consequences. *Alcohol Res* 2014;36(1):19-27 [FREE Full text] [Medline: [26258997](https://pubmed.ncbi.nlm.nih.gov/26258997/)]
39. Calvert M, Kyte D, Mercieca-Bebber R, Slade A, Chan A, King MT, The SPIRIT-PRO Group, et al. Guidelines for inclusion of patient-reported outcomes in clinical trial protocols: The SPIRIT-PRO extension. *JAMA* 2018 Feb 06;319(5):483-494. [doi: [10.1001/jama.2017.21903](https://doi.org/10.1001/jama.2017.21903)] [Medline: [29411037](https://pubmed.ncbi.nlm.nih.gov/29411037/)]

Abbreviations

ART: antiretroviral therapy
CASI: computer-assisted self-interviewing
EMA: ecological momentary assessment
GED: General Educational Development
Health eNav: Health eNavigation
IRB: Institutional Review Board
MSM: men who have sex with men
PCMH: patient-centered medical home
SMS: short message service
YMSM: young men who have sex with men

Edited by G Eysenbach; submitted 25.09.19; peer-reviewed by C El Morr, C Seebode; comments to author 20.10.19; revised version received 25.10.19; accepted 26.10.19; published 08.11.19.

Please cite as:

Arayasirikul S, Trujillo D, Turner CM, Le V, Wilson EC
Implementing a Digital HIV Care Navigation Intervention (Health eNav): Protocol for a Feasibility Study
JMIR Res Protoc 2019;8(11):e16406
URL: <http://www.researchprotocols.org/2019/11/e16406/>
doi: [10.2196/16406](https://doi.org/10.2196/16406)
PMID: [31702561](https://pubmed.ncbi.nlm.nih.gov/31702561/)

©Sean Arayasirikul, Dillon Trujillo, Caitlin M Turner, Victory Le, Erin C Wilson. Originally published in JMIR Research Protocols (<http://www.researchprotocols.org>), 08.11.2019. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in JMIR Research Protocols, is properly cited. The complete bibliographic information, a link to the original publication on <http://www.researchprotocols.org>, as well as this copyright and license information must be included.

Protocol

Real-Time Detection of Behavioral Anomalies of Older People Using Artificial Intelligence (The 3-PEGASE Study): Protocol for a Real-Life Prospective Trial

Antoine Piau^{1,2}, MD, PhD; Benoit Lepage³, MD, PhD; Carole Bernon⁴, PhD; Marie-Pierre Gleizes⁴, PhD; Fati Nourhashemi^{1,2}, MD, PhD

¹Gérontopôle, University Hospital of Toulouse, Toulouse, France

²UMR 1027, Inserm, Université Paul Sabatier, Toulouse, France

³Medical Information Department, University Hospital of Toulouse, Toulouse, France

⁴Toulouse Institute of Computer Science Research, Université Paul Sabatier, Toulouse, France

Corresponding Author:

Antoine Piau, MD, PhD

Gérontopôle

University Hospital of Toulouse

4 Rue du Pont St Pierre

Toulouse, F-31400

France

Phone: 33 659561628

Email: antoinepiau@hotmail.com

Abstract

Background: Most frail older persons are living at home, and we face difficulties in achieving seamless monitoring to detect adverse health changes. Even more important, this lack of follow-up could have a negative impact on the living choices made by older individuals and their care partners. People could give up their homes for the more reassuring environment of a medicalized living facility. We have developed a low-cost unobtrusive sensor-based solution to trigger automatic alerts in case of an acute event or subtle changes over time. It could facilitate older adults' follow-up in their own homes, and thus support independent living.

Objective: The primary objective of this prospective open-label study is to evaluate the relevance of the automatic alerts generated by our artificial intelligence-driven monitoring solution as judged by the recipients: older adults, caregivers, and professional support workers. The secondary objective is to evaluate its ability to detect subtle functional and cognitive decline and major medical events.

Methods: The primary outcome will be evaluated for each successive 2-month follow-up period to estimate the progression of our learning algorithm performance over time. In total, 25 frail or disabled participants, aged 75 years and above and living alone in their own homes, will be enrolled for a 6-month follow-up period.

Results: The first phase with 5 participants for a 4-month feasibility period has been completed and the expected completion date for the second phase of the study (20 participants for 6 months) is July 2020.

Conclusions: The originality of our real-life project lies in the choice of the primary outcome and in our user-centered evaluation. We will evaluate the relevance of the alerts and the algorithm performance over time according to the end users. The first-line recipients of the information are the older adults and their care partners rather than health care professionals. Despite the fast pace of electronic health devices development, few studies have addressed the specific everyday needs of older adults and their families.

Trial Registration: ClinicalTrials.gov NCT03484156; <https://clinicaltrials.gov/ct2/show/NCT03484156>

International Registered Report Identifier (IRRID): PRR1-10.2196/14245

(*JMIR Res Protoc* 2019;8(11):e14245) doi:[10.2196/14245](https://doi.org/10.2196/14245)

KEYWORDS

frailty; monitoring; sensors; artificial intelligence; older adults; participatory design

Introduction

Background

We are facing an increase in the number of older adults with a high prevalence of functional and cognitive decline [1,2]. Early preventive strategies could stabilize or even prevent this decline [1,3,4]. Most frail older individuals are living at home, and we recognize the difficulties in achieving seamless in-home monitoring for the early detection of subtle health changes over time [1,2]. Clinical assessments are usually performed too far apart and outside the person's own environment. These evaluations rely on self-reported information affected by recall bias and poor reliability [5]. A follow-up before functional or cognitive impairment could have a positive impact through personalized care plans when symptoms can still be treated.

Technology could potentially help to overcome this shortfall in terms of follow-up by providing continuous sensitive and ecologically valid measures. Several real-life studies confirm the relationship between sensor-based monitoring of physiological parameters and health outcomes [6,7]. The follow-up of health changes over time could also support the living choices made by older individuals and their care partners. Some people abandon their desire for independence in favor of the more reassuring environment of a dedicated living facility much earlier than necessary. Nevertheless, although information and communication technologies have been shown to be effective in many medical situations [8], few solutions are proposed to monitor the intrinsic capabilities of older adults in their own homes [9-11]. Beyond *organ-based* telemonitoring solutions (eg, heart failure or diabetes monitoring), a comprehensive function-based monitoring solution could be

beneficial to avoid the overlap and multiplication of technical tools in this complex population.

We hypothesized that a network of low-cost sensors could trigger alerts if an acute and unusual event is detected in activities of daily living—ADL (eg, use of the bathroom at night, followed by several hours of immobility) or subtle changes over time (eg, disorganization in stereotypical habits). Our solution based on nonintrusive sensors could provide relevant information to care partners and health professionals to support the monitoring of older people in their homes, thus promoting independent living.

Objectives

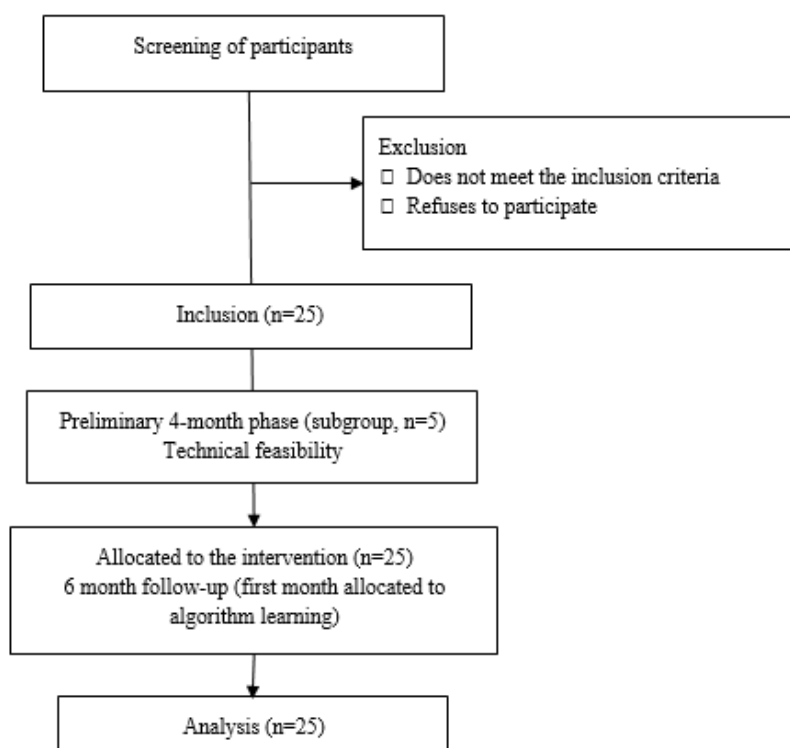
The primary objective is to evaluate the relevance of the alerts automatically generated by a sensor-based solution and the evolution of the algorithm's performance over time as judged by the recipients: older adults, care partners, and professional support workers. The secondary objective is to evaluate the ability of this solution to detect functional and cognitive decline and major medical events.

Methods

Study Design

This is a prospective open-label study. We will enroll 25 participants for a 6-month follow-up period. To allow for modifications to the solution in the event of technical issues before wider use, the first 5 participants are enrolled for a preliminary 4-month phase before the 6-month regular follow-up period. The enrollment process is spread out over time for the same reason. The flow chart is presented in [Figure 1](#).

Figure 1. The Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) flow chart.



Setting and Participants

All participants must give their written informed consent to take part in the study. Ethical approval was obtained from the Regional Independent Ethics Committee in June 2017 (ID-RCB: 2017-A01002-51).

This solution targets older adults, living with or at risk of functional or cognitive disability and living alone. The detailed inclusion criteria are as follows: aged 75 years or above, living alone at home; frail according to Fried criteria [12] or living with a disability but with an ADL score [13] 3 out of 6 or above; able to walk without help; and provision of written informed consent.

The exclusion criteria are as follows: patient presenting a Mini Mental State Examination (MMSE) <16 out of 30 and without daily care partner support; and under curatorship or guardianship.

Study participants are enrolled through a prescreening procedure on the basis of public administrative records held by several town halls in the region (person aged 75 years or above, living alone at home, and able to walk without help). A clinical research assistant (CRA) then conducts a preinclusion visit by

phone. The inclusion visit with the principal investigator (AP) takes place in the Geriatrics Unit at the Toulouse University Hospital.

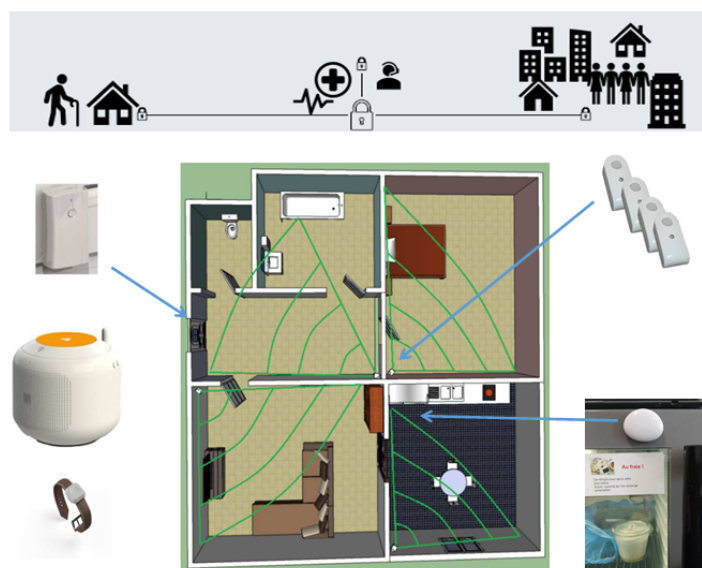
Procedure

The solution comprises a set of several minimally invasive sensors installed in the individual's home (see Table 1 and Figure 2). The solution transmits the data to a remote storage server via a *LIVE Intercom* gateway (a commercially available device). Data are then available for remote consultation by authorized users, that is, patients, care partners, or physicians. The *LIVE Intercom* also allows direct audio communication with the support center (call function) and preliminary data processing before 3G transmission to the remote secure health database. The *minimal sensor set* consists of 4 passive infrared (PIR) sensors to monitor activity (bedroom, kitchen, living room, and entrance hall) and 1 contact sensor on the main entrance door. A sensor on the refrigerator door, a pendant (or bracelet) with a push-button emergency alarm, and a detector under the bed will be available to several participants to assess the technical feasibility. The solution is unobtrusive, and no maintenance is required during the study. Technical support is provided in the event of dysfunction.

Table 1. Sensor network description.

| Device | Number per house | Technology |
|------------------------------------|------------------|---|
| Wireless motion detector | 4 | Passive infrared sensor |
| Wireless door sensor | 1 | Magnet proximity sensor |
| Emergency-alert pendant | 1 | Push button |
| Intercom with alert button | 1 | General packet radio services gateway |
| Wireless bed rest detector | Optional | 4 pressure sensors, 1 under each of the feet of the bed |
| Wireless physical activity tracker | Optional | Accelerometer |

Figure 2. Presentation of the overall solution. In this configuration, the solution comprises 4 passive infrared sensors to monitor activity (bedroom, kitchen, living room, and entrance hall); 1 contact sensor on the main entrance door; 1 cookie sensor on the fridge to monitor door opening; a pendant (or wristband) with a push-button emergency alarm; and a live intercom system (device in the left of the illustration) for direct audio communication with the support center (calling function).



The following data will be monitored: presence (yes/no) in specific rooms, for example, rooms associated with eating, bathing, and sleeping; time spent outdoors; total activity inside the home (estimated by the average number of sensor activations per day) [6]; fridge use; and sleeping patterns.

The solution can trigger 2 different types of alerts. The first consists of *conventional alerts*. They are generated by the participants using an alarm push button or through the intercom system. The second type of alert assessed in this project is automatically triggered by our artificial intelligence algorithm after an initial learning phase (eg, gradual change in sleeping pattern). The sensor-based alerts and the use of the Live intercom calling function are both directed to a telecare worker on a nationwide telecare platform (IMA/Serena) all 7 days a week and 24 hours a day. The telecare worker can suggest a range of actions, from direct contact with the older individual to a phone call to the care partner or to emergency services. The first month is dedicated to algorithm learning: all sensors are functional, but no automatic alert is generated from the platform. Activity data relating to sleeping, eating, and time spent

outdoors, and so on, are recorded and analyzed. After the first month, there will be sufficient data to detect unusual behaviors and eventually trigger an alert. The algorithm used to perform real-time detection of behavioral anomalies is described elsewhere [14].

Follow-Up Procedure

The first 5 participants are enrolled for a total of 10 months (an initial 4-month period followed by a 6-month follow-up period) and the other 20 participants for 6 months. An installation visit will take place in the days following enrollment. A remote follow-up evaluation will be carried out over the phone by a CRA every 2 months after the baseline assessment (see Table 2). The last visit will be conducted by the CRA in the participant's home after 6 months. For the first 5 participants enrolled in the study, the baseline for data analysis is defined as the beginning of the 6-month follow-up period at the end of the first preliminary 4-month period which is dedicated to technical feasibility. The proper regulatory and ethical conduct of the study is monitored by a clinical research technician, acting on behalf of the University Hospital.

Table 2. Data collection.

| Variables | Preinclusion (CRA ^a , in-person) | Baseline T0 (investigator) | T2 months (CRA, phone) | T4 months (CRA, phone) | T6 months (CRA, in-home visit) |
|--|---|----------------------------|------------------------|------------------------|--------------------------------|
| Informed consent | ✓ | ✓ | — ^b | — | — |
| Sociodemographic data | — | ✓ | — | — | — |
| ADL ^c , IADL ^d , MMSE ^e | — | ✓ | — | — | ✓ |
| Frailty criteria, SPPB ^f | — | ✓ | — | — | ✓ |
| Acceptability questionnaire, EQ5D ^g | — | ✓ | ✓ | ✓ | ✓ |
| Major medical events | — | ✓ | ✓ | ✓ | ✓ |
| Sensor data | — | Continuous measures | Continuous measures | Continuous measures | Continuous measures |

^aCRA: clinical research assistant.

^bData not collected.

^cADL: activities of daily living.

^dIADL: instrumental activities of daily living.

^eMMSE: mini mental state evaluation.

^fSPPB: short physical performance battery.

^gEQ5D-3L: EuroQol 5D score to describe and value health, quality of life questionnaire.

Study Measures

The primary aim is to assess the sensitivity and specificity of the solution, defined as the ability to trigger alerts deemed relevant by the recipients: older adults, care partners, and professional support workers. To this end, both conventional and automatic alerts will be recorded during the follow-up period. Following each alert, the CRA gathers subjective feedback from the participant (for automatic alerts only), the care partner, and the telecare worker: *Was it relevant to alert you?* The alerts are also described (number, time of the day, duration of the communication if a communication is established, subject of the call in case of a conventional alert, and solutions proposed).

The secondary aim is to evaluate the ability of the system to detect a functional or cognitive decline and any major event. All major medical events, defined as any event resulting in in-home physician or paramedic intervention, or a call to the emergency services, are collected retrospectively by the CRA every 2 months (by phone).

Sociodemographic and health data are collected at baseline. The participants' cognitive and functional parameters are assessed at baseline and at the end of follow-up: MMSE (ranging from 0 to 30; the greater the score, the greater the global cognition) [15]; ADL (ranging from 0 to 6, the greater the score; the greater the functional autonomy in daily life) [13]; Instrumental activities of daily living (ranging from 0 to 8; the greater the score, the greater the functional autonomy in daily life, eg,

ability to use the telephone) [16]; Cardiovascular Health Study frailty index criteria (unintentional weight loss, self-reported exhaustion, weakness, slow walking speed, and low physical activity) [12]; Short Physical Performance Battery (consisting of a balance test, a 3-m walking test, and a 5 chair-rises test; score ranging from 0 to 12 with 12 indicating the highest degree of functioning) [17].

The acceptability questionnaire is adapted from the Quebec User Evaluation of Satisfaction with Assistive Technology Scale (degree of satisfaction with technology ranging from 1=not satisfactory at all to 5=very satisfactory) [18]; EuroQol questionnaire to describe and assess health (EuroQol questionnaire 5 dimensions, each comprising 3 levels, are summarized into an index ranging from -0.59 to 1, with 1 indicating full health) [19]; and major medical events. Adverse events and their potential imputability to the monitoring procedure are collected by the CRA throughout the study.

Sample Size

To the best of our knowledge, no comparable study has evaluated a similar primary endpoint in this population. Therefore, a formal sample size calculation could not be carried out. However, we can expect more than 1 alert per individual during the 6-month period. The predictive value calculations (estimation of legitimate alerts) will be based on numbers over 25, a 95% CI accuracy of at least $\pm 20\%$. As an example, if a participant triggers 2 alerts on average during the study, with half of them rated as valid, a 95% CI close to 35.5% to 64.5% can be expected.

Statistical Analysis

The main analysis will be an intent-to-treat analysis. The quantitative outcomes will be estimated with 95% CI. Quantitative variables will be expressed by mean values and standard deviations. The 6-month follow-up period for the 25 participants will allow us to record the number and frequency of alerts generated by the solution. A total of 3 positive predictive value (PPV) calculations (estimation of legitimate alerts) will be done (95% CI, thanks to end users' feedback for the overall follow-up period and for each 2-month follow-up period: 0-2 months, 2-4 months, and 4-6 months) to estimate the progression of algorithm performance. For the secondary objective, we will also analyze these 3 periods to evaluate the performance of the automatic alerts in detecting changes in functional or cognitive autonomy or major events (sensitivity, specificity, predictive value, and receiver operating characteristic [ROC] curves). Alerts will be addressed with both a binary approach (no alert vs 1 alert to estimate sensibility, specificity, PPV, and negative predictive value) and a continuous approach (number of alerts over the period to plot an ROC graph and estimate the area-under-the-curve). The Department of Epidemiology at our University Hospital will conduct statistical analyses using SAS version 9.4 (SAS Institute, Inc).

Results

The trial was registered with ClinicalTrials.gov (NCT03484156) on March 30, 2018. The enrollment process is spread out to

allow for changes to the system in the event of technical problems.

The first phase with 5 participants (4-month feasibility period) has been completed and the expected completion date for the second phase of the study (20 participants for 6 months) is July 2020.

Discussion

Strengths and Limitations of Our Study

Older adults express the desire to live autonomously in their own homes. Clinicians, on the other hand, have difficulty monitoring the functional and cognitive autonomy of seniors over time because of the limitations associated with in-person measurements and self-reported data [5]. To date, despite the rapid pace at which research projects and commercial electronic health devices are developing, few solutions really meet these daily needs. We believe that, following a learning phase, our low-cost unobtrusive solution could trigger alerts if the sensors were to detect an acute, unusual event or a subtle change in everyday habits over time. This solution could provide relevant information to care partners and health professionals to support patient follow-up. The originality of our real-life project lies in the choice of the primary outcome and in our user-centered evaluation rather than in the technical specifications. We will evaluate the relevance of the alerts according to the end users and the progression of our algorithm performance over time. One of the main obstacles to the wide dissemination of alert systems is the low acceptability to end users (eg, false positive alarms) and the difficulty of integrating this approach into a complex and overburdened health care system. In our study, the primary endpoint is determined by the end users themselves. We strive to go beyond traditional medical event considerations such as severe falls, minor falls and minor events, and major events, which do not always make sense for older people. The strengths of our monitoring and support solution can be summarized in several points: it meets the needs of older people living alone; it includes an end user assessment; it is a nonintrusive solution; we use inexpensive sensors without heavy maintenance; and finally, the learning algorithm should increase the solution's performance over time based on the end user feedback.

Concerning the potential limitations, we plan to analyze the performance of automatic alerts in detecting major events and changes in participants' autonomy (to calculate the number of subjects to be included for a future study). Although our population is at high risk, it is likely that the duration of follow-up is insufficient, particularly for autonomy loss. However, our center implements other studies in comparable populations on which we can rely for such a sample size calculation.

Our Study in the Context of Previous Research

Several products on the market propose comparable monitoring solutions with very similar technologies [20-22]. However, we were unable to find objective evaluation reports supporting their advertised performance. A review of technologies for monitoring seniors' home activities identified 5 main types of promising

surveillance technologies: PIR motion detectors, worn body detectors, pressure sensors, video surveillance, and sound recognition. This area of research is not totally mature, and most studies did not take place in real-life settings [23]. In a previous study, Franco et al obtained interesting results by recording the electrical activity of 13 subjects monitored for a period of 6 months [24]. The results highlighted the possibility of differentiating between daily and nocturnal activities, and of calculating the probability of having eaten, bathed, or used the toilet with acceptable accuracy. Another study, conducted by Stucki et al, evaluated a nonintrusive, assistive technology system that recognizes and classifies ADL, thanks to passive sensors in each room (20 days, 10 healthy participants, mean age 49 years) with good sensitivity and specificity [25]. Urwyler et al also investigated the behavior of 20 participants using an

unobtrusive wireless sensor network for 20 consecutive days. Differences in ADL regimens were significant between healthy controls and patients with dementia [26]. Few academic studies addressed the specific everyday needs of older adults and their families using such a *bottom-up* approach. We think that our study complements previous works.

Conclusions and Perspectives

Our project brings together partners from the fields of health, technology, industry, and health insurance to develop a relevant but also economically sustainable solution. This is an opportunity for each partner to test the option of integrating such an innovative network into its current practices. Retrospective correlations will be used in this longitudinal study, which justifies further research to prospectively demonstrate the true predictive value of our algorithm.

Acknowledgments

The authors wish to extend their thanks to the following companies, namely, *Telemedecine Technologies*, *Orange*, *Telegrafik*, and *Serena* who developed the solution and provide assistance during the trial. This study is funded by a European Union (European Regional Development Fund) and a French South-West Regional Administrative grant through the EASYNOV-SILVER ECONOMY Program (Project Number EASYNOV-SILVER ECONOMY 201-15060378). The funder has not played any role in designing this study, implementing the trial, or analyzing and interpreting trial data and publishing research.

Conflicts of Interest

None declared.

References

1. Beard JR, Officer A, de Carvalho IA, Sadana R, Pot AM, Michel J, et al. The World report on ageing and health: a policy framework for healthy ageing. *Lancet* 2016 May 21;387(10033):2145-2154 [FREE Full text] [doi: [10.1016/S0140-6736\(15\)00516-4](https://doi.org/10.1016/S0140-6736(15)00516-4)] [Medline: [26520231](https://pubmed.ncbi.nlm.nih.gov/26520231/)]
2. Rodriguez-Mañas L, Fried LP. Frailty in the clinical scenario. *Lancet* 2015 Feb 14;385(9968):e7-e9. [doi: [10.1016/S0140-6736\(14\)61595-6](https://doi.org/10.1016/S0140-6736(14)61595-6)] [Medline: [25468154](https://pubmed.ncbi.nlm.nih.gov/25468154/)]
3. Pahor M, Guralnik JM, Ambrosius WT, Blair S, Bonds DE, Church TS, LIFE Study Investigators. Effect of structured physical activity on prevention of major mobility disability in older adults: the LIFE study randomized clinical trial. *J Am Med Assoc* 2014 Jun 18;311(23):2387-2396 [FREE Full text] [doi: [10.1001/jama.2014.5616](https://doi.org/10.1001/jama.2014.5616)] [Medline: [24866862](https://pubmed.ncbi.nlm.nih.gov/24866862/)]
4. Dedeyne L, Deschodt M, Verschueren S, Tournoy J, Gielen E. Effects of multi-domain interventions in (pre)frail elderly on frailty, functional, and cognitive status: a systematic review. *Clin Interv Aging* 2017;12:873-896 [FREE Full text] [doi: [10.2147/CIA.S130794](https://doi.org/10.2147/CIA.S130794)] [Medline: [28579766](https://pubmed.ncbi.nlm.nih.gov/28579766/)]
5. Wild KV, Mattek N, Austin D, Kaye JA. 'Are you sure?': lapses in self-reported activities among healthy older adults reporting online. *J Appl Gerontol* 2016 Jun;35(6):627-641 [FREE Full text] [doi: [10.1177/0733464815570667](https://doi.org/10.1177/0733464815570667)] [Medline: [25669877](https://pubmed.ncbi.nlm.nih.gov/25669877/)]
6. Kaye JA, Maxwell SA, Mattek N, Hayes TL, Dodge H, Pavel M, et al. Intelligent systems for assessing aging changes: home-based, unobtrusive, and continuous assessment of aging. *J Gerontol B Psychol Sci Soc Sci* 2011 Jul;66(Suppl 1):i180-i190 [FREE Full text] [doi: [10.1093/geronb/gbq095](https://doi.org/10.1093/geronb/gbq095)] [Medline: [21743050](https://pubmed.ncbi.nlm.nih.gov/21743050/)]
7. Kaye J, Mattek N, Dodge H, Buracchio T, Austin D, Hagler S, et al. One walk a year to 1000 within a year: continuous in-home unobtrusive gait assessment of older adults. *Gait Posture* 2012 Feb;35(2):197-202 [FREE Full text] [doi: [10.1016/j.gaitpost.2011.09.006](https://doi.org/10.1016/j.gaitpost.2011.09.006)] [Medline: [22047773](https://pubmed.ncbi.nlm.nih.gov/22047773/)]
8. van der Meij E, Anema JR, Leclercq WK, Bongers MY, Consten EC, Koops SE, et al. Personalised perioperative care by e-health after intermediate-grade abdominal surgery: a multicentre, single-blind, randomised, placebo-controlled trial. *Lancet* 2018 Jul 7;392(10141):51-59. [doi: [10.1016/S0140-6736\(18\)31113-9](https://doi.org/10.1016/S0140-6736(18)31113-9)] [Medline: [29937195](https://pubmed.ncbi.nlm.nih.gov/29937195/)]
9. 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;13(4):172-179. [doi: [10.1258/135763307780908058](https://doi.org/10.1258/135763307780908058)] [Medline: [17565772](https://pubmed.ncbi.nlm.nih.gov/17565772/)]
10. Savolainen L, Hanson E, Magnusson L, Gustavsson T. An internet-based videoconferencing system for supporting frail elderly people and their carers. *J Telemed Telecare* 2008;14(2):79-82. [doi: [10.1258/jtt.2007.070601](https://doi.org/10.1258/jtt.2007.070601)] [Medline: [18348753](https://pubmed.ncbi.nlm.nih.gov/18348753/)]

11. Schwenk M, Howe C, Saleh A, Mohler J, Grewal G, Armstrong D, et al. Frailty and technology: a systematic review of gait analysis in those with frailty. *Gerontology* 2014;60(1):79-89 [FREE Full text] [doi: [10.1159/000354211](https://doi.org/10.1159/000354211)] [Medline: [23949441](https://pubmed.ncbi.nlm.nih.gov/23949441/)]
12. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Cardiovascular Health Study Collaborative Research Group. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001 Mar;56(3):M146-M156. [doi: [10.1093/gerona/56.3.m146](https://doi.org/10.1093/gerona/56.3.m146)] [Medline: [11253156](https://pubmed.ncbi.nlm.nih.gov/11253156/)]
13. Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW, Studies of Illness in the Aged. The index of ADL: a standardized measure of biological and psychosocial function. *J Am Med Assoc* 1963 Sep 21;185:914-919. [doi: [10.1001/jama.1963.03060120024016](https://doi.org/10.1001/jama.1963.03060120024016)] [Medline: [14044222](https://pubmed.ncbi.nlm.nih.gov/14044222/)]
14. Verstaevael N, Bernon C, Georgé J, Gleyzes M. A Self-Organized Learning Model for Anomalies Detection: Application to Elderly People. In: Proceedings of the 12th IEEE International Conference on Self-Adaptive and Self-Organizing Systems. 2018 Presented at: SASO'18; September 3-7, 2018; Trento, Italy. [doi: [10.1109/saso.2018.00018](https://doi.org/10.1109/saso.2018.00018)]
15. Folstein MF, Folstein SE, McHugh PR. 'Mini-mental state'. A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975 Nov;12(3):189-198. [doi: [10.1016/0022-3956\(75\)90026-6](https://doi.org/10.1016/0022-3956(75)90026-6)] [Medline: [1202204](https://pubmed.ncbi.nlm.nih.gov/1202204/)]
16. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist* 1969;9(3):179-186. [doi: [10.1093/geront/9.3.Part_1.179](https://doi.org/10.1093/geront/9.3.Part_1.179)] [Medline: [5349366](https://pubmed.ncbi.nlm.nih.gov/5349366/)]
17. Guralnik JM, Ferrucci L, Simonsick EM, Salive ME, Wallace RB. Lower-extremity function in persons over the age of 70 years as a predictor of subsequent disability. *N Engl J Med* 1995 Mar 2;332(9):556-561. [doi: [10.1056/NEJM199503023320902](https://doi.org/10.1056/NEJM199503023320902)] [Medline: [7838189](https://pubmed.ncbi.nlm.nih.gov/7838189/)]
18. Demers L, Monette M, Lapierre Y, Arnold DL, Wolfson C. Reliability, validity, and applicability of the Quebec User Evaluation of Satisfaction with assistive Technology (QUEST 2.0) for adults with multiple sclerosis. *Disabil Rehabil* 2002;24(1-3):21-30. [doi: [10.1080/09638280110066352](https://doi.org/10.1080/09638280110066352)] [Medline: [11827151](https://pubmed.ncbi.nlm.nih.gov/11827151/)]
19. Dolan P. Modeling valuations for EuroQol health states. *Med Care* 1997 Nov;35(11):1095-1108. [doi: [10.1097/00005650-199711000-00002](https://doi.org/10.1097/00005650-199711000-00002)] [Medline: [9366889](https://pubmed.ncbi.nlm.nih.gov/9366889/)]
20. Care Innovations. Access and Leverage Smart Sensor Analytics URL: <https://www.careinnovations.com/solutions/smart-sensor-analytics/> [accessed 2019-07-12]
21. Telegrafik. URL: <https://www.telegrafik.fr/> [accessed 2019-07-12]
22. SmartThings. SmartThings Hub URL: <https://www.smarthings.com/products/smarthings-hub> [accessed 2019-07-12]
23. Peetoom KK, Lexis MA, Joore M, Dirksen CD, de Witte LP. Literature review on monitoring technologies and their outcomes in independently living elderly people. *Disabil Rehabil Assist Technol* 2015 Jul;10(4):271-294. [doi: [10.3109/17483107.2014.961179](https://doi.org/10.3109/17483107.2014.961179)] [Medline: [25252024](https://pubmed.ncbi.nlm.nih.gov/25252024/)]
24. Franco GC, Gallay F, Berenguer M, Mourrain C, Couturier P. Non-invasive monitoring of the activities of daily living of elderly people at home--a pilot study of the usage of domestic appliances. *J Telemed Telecare* 2008;14(5):231-235. [doi: [10.1258/jtt.2008.071207](https://doi.org/10.1258/jtt.2008.071207)] [Medline: [18632996](https://pubmed.ncbi.nlm.nih.gov/18632996/)]
25. Stucki RA, Urwyler P, Rampa L, Müri R, Mosimann UP, Nef T. A web-based non-intrusive ambient system to measure and classify activities of daily living. *J Med Internet Res* 2014 Jul 21;16(7):e175 [FREE Full text] [doi: [10.2196/jmir.3465](https://doi.org/10.2196/jmir.3465)] [Medline: [25048461](https://pubmed.ncbi.nlm.nih.gov/25048461/)]
26. Urwyler P, Stucki R, Rampa L, Müri R, Mosimann UP, Nef T. Cognitive impairment categorized in community-dwelling older adults with and without dementia using in-home sensors that recognise activities of daily living. *Sci Rep* 2017 Feb 8;7:42084 [FREE Full text] [doi: [10.1038/srep42084](https://doi.org/10.1038/srep42084)] [Medline: [28176828](https://pubmed.ncbi.nlm.nih.gov/28176828/)]

Abbreviations

- ADL:** activities of daily living
- CRA:** clinical research assistant
- MMSE:** mini mental state evaluation
- PIR:** passive infrared
- PPV:** positive predictive value
- ROC:** receiver operating characteristic

Edited by G Eysenbach; submitted 02.04.19; peer-reviewed by P Urwyler, L de Witte; comments to author 14.06.19; revised version received 16.07.19; accepted 16.07.19; published 18.11.19.

Please cite as:

Piau A, Lepage B, Bernon C, Gleizes MP, Nourhashemi F

Real-Time Detection of Behavioral Anomalies of Older People Using Artificial Intelligence (The 3-PEGASE Study): Protocol for a Real-Life Prospective Trial

JMIR Res Protoc 2019;8(11):e14245

URL: <http://www.researchprotocols.org/2019/11/e14245/>

doi: [10.2196/14245](https://doi.org/10.2196/14245)

PMID: [31738180](https://pubmed.ncbi.nlm.nih.gov/31738180/)

©Antoine Piau, Benoit Lepage, Carole Bernon, Marie-Pierre Gleizes, Fati Nourhashemi. Originally published in JMIR Research Protocols (<http://www.researchprotocols.org>), 18.11.2019. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in JMIR Research Protocols, is properly cited. The complete bibliographic information, a link to the original publication on <http://www.researchprotocols.org>, as well as this copyright and license information must be included.

Protocol

Evidence on User-Led Innovation in Diabetes Technology (The OPEN Project): Protocol for a Mixed Methods Study

Shane O'Donnell¹, PhD; Dana Lewis², BA; María Marchante Fernández¹, MSc; Mandy Wäldchen¹, MSc; Bryan Cleal³, PhD; Timothy Skinner^{3,4}, PhD; Klemens Raile⁵, MD; Adrian Tappe⁶, BSc; Tebbe Ubben^{6,7}; Ingrid Willaing³, MPH, RN; Bastian Hauck⁷, MA; Saskia Wolf⁷, Assessor Juris; Katarina Braune⁵, MD

¹School of Sociology, University College Dublin, Belfield, Ireland

²OpenAPS, Seattle, WA, United States

³Diabetes Management Research, Steno Diabetes Center Copenhagen, Gentofte, Denmark

⁴Institut for Psykologi, Københavns Universitet, Copenhagen, Denmark

⁵Department of Paediatric Endocrinology and Diabetes, Charité - Universitätsmedizin Berlin, Berlin, Germany

⁶AndroidAPS, Vienna, Austria

⁷#dedoc° Diabetes Online Community, Berlin, Germany

Corresponding Author:

Katarina Braune, MD

Department of Paediatric Endocrinology and Diabetes

Charité - Universitätsmedizin Berlin

Augustenburger Platz 1

Berlin, 13353

Germany

Phone: 49 30450616454

Email: katarina.braune@charite.de

Abstract

Background: Digital innovations in health care have traditionally followed a top-down pathway, with manufacturers leading the design and production of technology-enabled solutions and those living with chronic conditions involved only as passive recipients of the end product. However, user-driven open-source initiatives in health care are becoming increasingly popular. An example is the growing movement of people with diabetes, who create their own “Do-It-Yourself Artificial Pancreas Systems” (DIYAPS).

Objective: The overall aim of this study is to establish the empirical evidence base for the clinical effectiveness and quality-of-life benefits of DIYAPS and identify the challenges and possible solutions to enable their wider diffusion.

Methods: A research program comprising 5 work packages will examine the outcomes and potential for scaling up DIYAPS solutions. Quantitative and qualitative methodologies will be used to examine clinical and self-reported outcome measures of DIYAPS users. The majority of members of the research team live with type 1 diabetes and are active DIYAPS users, making *Outcomes of Patients' Evidence With Novel, Do-It-Yourself Artificial Pancreas Technology* (OPEN) a unique, user-driven research project.

Results: This project has received funding from the European Commission's Horizon 2020 Research and Innovation Program, under the Marie Skłodowska-Curie Action Research and Innovation Staff Exchange. Researchers with both academic and nonacademic backgrounds have been recruited to formulate research questions, drive the research process, and disseminate ongoing findings back to the DIYAPS community and other stakeholders.

Conclusions: The OPEN project is unique in that it is a truly patient- and user-led research project, which brings together an international, interdisciplinary, and intersectoral research group, comprising health care professionals, technical developers, biomedical and social scientists, the majority of whom are also living with diabetes. Thus, it directly addresses the core research and user needs of the DIYAPS movement. As a new model of cooperation, it will highlight how researchers in academia, industry, and the patient community can create patient-centric innovation and reduce disease burden together.

International Registered Report Identifier (IRRID): PRR1-10.2196/15368

(*JMIR Res Protoc* 2019;8(11):e15368) doi:[10.2196/15368](https://doi.org/10.2196/15368)

KEYWORDS

diabetes; digital health; open source; closed-loop insulin delivery systems; automated insulin delivery systems; #WeAreNotWaiting

Introduction

Type 1 diabetes (T1D) is a challenging chronic condition, which often leads to lowered life expectancy and diminished quality of life [1]. Despite significant advances in insulin therapy and technological developments, only 17% of youth and 21% of adults with diabetes achieve a glycated hemoglobin (HbA_{1c}) level of <7.0% (58 mmol/mol), as recommended in clinical guidelines [2,3].

Closing the Loop: Automated Insulin Delivery Systems

In general, closed-loop insulin delivery systems, also called “automated insulin delivery systems (AID)” or “artificial pancreas systems (APS),” combine sensors for continuous glucose monitoring (CGM) and insulin pumps with a control algorithm, and these are characterized by automated insulin delivery in response to the user’s glucose level. As subcutaneously administered insulin stays active for multiple hours, the algorithm used to calculate the amount of insulin needed has to predict future glucose values to operate safely. Closed-loop systems designed for commercial use have been shown to be safe and effective in reducing hyperglycemia and hypoglycemia in people with diabetes (PwD) of all age groups [4-8], and these systems are therefore seen as the gold standard of future diabetes therapy [9].

Qualitative research on commercially developed closed-loop systems has indicated that individuals using these systems for relatively short periods report reduced anxiety [10-14], improved quality of sleep [10,14-17], and reduced burden of managing diabetes [12,13,17-19] and this led to greater freedom and flexibility in their lifestyle as a result [12,16-18]. This is supported by a few quantitative studies that report less fear of hypoglycemia [10-13,20,21]—although possibly because of small sample sizes, the changes are not consistently significant—a reduction in diabetes-specific distress in 2 studies [13,20], and, in a single study, improved sleep quality [22]. These studies have used a range of closed-loop or technology-specific quality-of-life instruments, with the Diabetes Technology Questionnaire being the most widely used.

The Do-It-Yourself Artificial Pancreas:

#WeAreNotWaiting

However, although a variety of commercial APS are under development and some have recently become available in a limited number of countries, they are not universally available, accessible, or affordable. Behind the hashtag #WeAreNotWaiting, a community of PwD and their families have created new tools and systems to help PwD better utilize their devices and data. These systems are co-created in the Do-It-Yourself Artificial Pancreas System (DIYAPS) community, but each user has to build their own individual system themselves and use at their own risk. Instructions and code for these systems have been made universally available via open-source platforms [23]. The DIYAPS or “Open-Source Artificial Pancreas System” (OpenAPS) is one of the most

significant developments to emerge through this movement [24]. In these systems, insulin delivery is automated and remotely controlled by open-source algorithms and by reverse engineering and connecting commercially available and approved insulin pumps and CGM systems. The term “open source” describes software whose source code is publicly available. Open-source licenses usually deny liability and warranty and may require disclosing source code and referring to the project [25].

Initial observational studies on DIYAPS have described significant improvements in glycemic control, quality of life, and sleep quality in DIYAPS users of all age groups, including children and adolescents, where caregivers build and maintain these systems on their behalf [26-31]. A limited number of studies are also specifically reporting on the experience of using DIYAPS, and in addition to highlighting improved sleep [28,30,32] and reduced burden of diabetes management [32], they point to increased confidence, increased energy, and reduced mood swings [32].

Evidence of usage of DIYAPS is limited to date, as none of these systems have yet been evaluated by a randomized controlled trial, regarding safety and efficiency—although at least 1 is planned [33]. Observational studies largely describe outcomes self-reported by users and are mainly based on smaller cohort studies (up to n=80) [27]. There is an estimated 15+ million hours of real-world DIYAPS data, much of which have yet to be fully analyzed. A global investigation based on DIYAPS data is of interest to inform potential users of these systems regarding the benefits and challenges of using the system and to learn more about how clinical and quality-of-life outcomes are affected by different groups of DIYAPS users, as well as the mechanisms through which these results are being achieved.

Another fundamental question is who might get left behind in this user-driven technological innovation. DIYAPS aims to better target the complexity of diabetes self-management for the person with diabetes, reduce the cognitive and emotional burden on PwD, and improve clinical outcomes. Such an outcome would make an important contribution to reducing inequalities in outcomes that are linked to individual disparities in the capacity to cope with these burdens. However, there are numerous challenges to be overcome to achieve this objective, and the complexity of establishing and maintaining effective DIYAPS currently remains high for many PwD. Thus, a further challenge with respect to social inequality rests in how to ensure that the benefits of APS are widely diffused across the population so that no one is left behind in their diabetes care. Therefore, the challenges in this area are not exclusively medical or technical, but also ethical, sociological, and political in nature and require an interdisciplinary and intersectoral approach to be addressed effectively. Moreover, there is a rich vein of expertise and knowledge available from nontraditional experts within the DIYAPS community, which has traditionally been overlooked by both academia and industry. Successfully

bringing this nontraditional expertise into mainstream health care settings is key to addressing some of the core research opportunities and challenges that are likely to emerge as do-it-yourself (DIY) solutions become increasingly popular and shape digital innovations in diabetes care.

Objectives of the OPEN Project

Thus, the aim of the OPEN project (*Outcomes of Patients' Evidence With Novel, Do-It-Yourself Artificial Pancreas Technology*) is to examine what academia, industry, and PwD can learn from one another, with the goal of making artificial pancreas technology of all kinds available to everyone. The OPEN consortium achieves this by bringing together an intersectoral and interdisciplinary research team comprising patient innovators, academic researchers in biomedical and social sciences, health care professionals, and patient advocacy organizations to establish an empirical evidence base surrounding the impact of DIYAPS.

This collaboration is facilitated through a series of staff exchanges between high-profile nonacademic organizations dedicated to patient-driven approaches (Steno Diabetes Center Copenhagen, Denmark; Dedoc Labs, Germany) and leading research organizations in the field of diabetes research and connected health (Charité—Universitätsmedizin Berlin, Germany; University College Dublin, Ireland).

The central aims and objectives of the OPEN project have been developed on the basis of the priorities of the DIYAPS and wider diabetes communities. Furthermore, a key goal of the OPEN project is to tap into the expertise of the DIYAPS community to bring their knowledge and expertise to mainstream health care settings.

OPEN is already co-led by some of the key members of the DIYAPS movement and will actively continue to involve members of the DIYAPS and wider diabetes communities to facilitate their participation in OPEN, via staff secondments and further collaborations. Furthermore, members of the Diabetes Online Community are being recruited to assist with disseminating the findings of the project on an ongoing basis and maintain a consistent dialogue between OPEN and the wider diabetes community.

Methods

Overview

A total of 5 interdependent work packages (WPs) have been proposed: The first 2 WPs are focused on acquiring data to demonstrate what, if any, are the clinical, quality-of-life, and psychosocial benefits of DIYAPS. This will include engaging the community in sharing glucose and insulin dosing data, as well as self-reporting on their experience of living with DIYAPS. WP3 is focused on reducing the technical barriers to DIYAPS. This also feeds into the work of WP4, which is identifying the barriers to wider uptake of these user-led innovations and exploring ways to reduce them. The final WP relates to how the OPEN project will disseminate the results to the research, health care, and community of PwD.

Work Package 1: Clinical Outcomes and Guidelines

The purpose of this WP is to evaluate the clinical outcomes of DIYAPS users of all age groups globally and create a draft for future guidelines for closed-loop technology in clinical routine. Individuals using DIYAPS (any type) have the ability to anonymously donate their data to research projects, via the OpenAPS Data Commons, on the citizen science platform “Open Humans” [31]. Users specifically consent to share their data for research purposes, and they can choose to either manually upload data of their choice or upload data via an upload tool of their choice, with the data source of choice (for further details, please see the description of WP3). The OPEN team will request access to and utilize data from the OpenAPS Data Commons, which is considered pseudonymized for purposes of the OPEN project's use.

Glycemic outcomes will be analyzed in a pre-post evaluation of prospectively collected data from DIYAPS users. CGM sensor data will be analyzed to calculate certain parameters, such as the Time in Range (percentage of sensor glucose levels between 70 mg/dL and 180 mg/dL) before and after DIYAPS initiation as a primary key endpoint, as well as Time below Range (<70 mg/dL, <54 mg/dL) and Time above Range (>180 mg/dL, >250 mg/dL) as secondary endpoints. Other secondary key endpoints include self-reported parameters, such as HbA_{1c} levels, incidence of acute diabetes-related complications, such as severe hypoglycemic events and incidence and possible cause of diabetic ketoacidosis. Assessment of basic demographic and health data, such as specifications of diabetes treatment, socioeconomic status, gender, age, weight, height, comorbidities, and incidence of diabetes-related complications, will enable analysis of clinical outcomes for different user groups. To further validate accuracy of self-reported clinical data from patients and caregivers, data from a subcohort will be clinically compared with independent medical data repositories to add to the evidence base regarding the reliability of real-world data.

This WP is led by KB and KR, both PwDs and medical doctors at the Department of Pediatric Endocrinology and Diabetes at Charité University Medicine Berlin.

Work Package 2: Patient-Reported Outcomes

Alongside work to evaluate the clinical benefits of DIYAPS, we will seek to establish the quality of life and lived experiences of DIYAPS users. Given the lack of an internally consistent, reliable, sensitive, and validated T1D-specific quality-of-life questionnaire that also uses item wording that is widely acceptable to people with T1D [34], the project will take a facet approach to assessing the quality-of-life outcomes. For DIYAPS users and their primary caregivers and loved ones, we will assess the potential benefits of DIYAPS on emotional well-being, sleep quality, hypoglycemia-related anxiety and fears, the burden of diabetes, and flexibility of lifestyle. Furthermore, we will investigate motivations, barriers, and retention factors to building and maintaining DIYAPS in a questionnaire-based survey and whether there are additional benefits accrued by individuals assembling their own closed-loop systems [35,36]. We will also explore effects on individuals' sense of self-efficacy, social support, and the benefits accrued from joining a wider network of people with T1D.

In addition to the survey data on quality-of-life outcomes, the project will also undertake qualitative research with DIYAPS users to generate data about their lived experience with this technology. An objective here is to examine how the lived experiences of DIYAPS users vary across socioeconomic status, gender, ethnicity, and age. To achieve this, a purposively sampled select group of the project's participants will be asked to describe the day-to-day burden associated with T1D and DIYAPS. Such burdens might include but not be limited to out-of-pocket expenses, ability to carry out daily tasks in the work setting or at home, participation in social activities and other issues related to social connectedness, informal care provided by family members or relatives, and episodes of distress caused by living with diabetes.

This WP is led by IW, BC, and TS, diabetes management researchers at Steno Diabetes Center Copenhagen.

Work Package 3: Technical Development

This WP will focus on the evaluation and possible improvements of DIYAPS through statistical and machine learning techniques. The WP has 2 main objectives: (1) improving ease of use for DIYAPS users' data donation to support further research and evaluation and (2) evaluating existing DIYAPS platforms and implications for APS improvement.

We aim to improve DIYAPS users' ability to donate data for retrospective analysis for outcomes and future DIYAPS developments. This is designed for those who are interested in contributing to the DIYAPS community by donating their anonymized datasets, as described in WP1 [37].

The current workflow enables individuals using DIYAPS to upload data and contribute data anonymously to research, via the Open Humans platform. Users can either do a manual upload of their DIYAPS data, or they can utilize the "Nightscout Data Transfer" tool to pull data directly from Nightscout into Open Humans. Nightscout is an open-source remote monitoring platform commonly used for real-time visualization of disparate diabetes device data streams, also used for retrospective data analysis and to report generation, which is widely used by DIYAPS users [23]. Nightscout can capture behavioral data, such as exercise entries, temporary targets to adjust DIYAPS behavior, or meal entries, in addition to logging DIYAPS predictions and output at 5-min intervals, and it becomes a rich source for retrospective data analysis for research when donated to the OpenAPS Data Commons. However, not all individuals choose to use Nightscout, and other methods are therefore planned to increase the ease of data donation for research. The OPEN team also plans to add direct upload capabilities to one of the commonly used DIYAPS (AndroidAPS) that will authenticate directly with Open Humans and enable an additional data donation method to the OpenAPS Data Commons. The current uploading methods require the user to initiate any subsequent data uploads; both methods described above will permit users to opt in to enable automatic, regular data uploads. This both makes data donation easier and captures data that are often deleted, either accidentally or to free up storage space for the user. After enabling increased data donation with a wider and diverse population of DIYAPS users, we expect the OpenAPS Data Commons available dataset to be

increased from about 115 users to an estimated 300 or more users. As the dataset is based on real-world data, there may be concerns about data integrity. However, data are processed and connected in many ways with complex decision trees, which makes it hard to falsify data. Furthermore, studies have shown that real-world data are as robust as, if not more robust than, data gathered in clinical trials with predefined selected populations [38].

Although current studies have shown that DIYAPS users achieve positive outcomes (clinical and quality of life) [26-31], there are areas for improvement and further iteration in terms of usability, algorithm features, and optimizing individual settings and preferences, as well as areas of statistical learning, which are applicable to all APS (DIY or commercially developed). With several hundred (see above) pseudonymized datasets, we expect to be able to break down outcome data into subcohorts to better quantify the impact of different algorithm choices and settings. This may include comparing outcomes among individuals using varying versions of algorithms over time, comparing different feature choices between and across individuals, and evaluating settings (such as specifications of medical devices and insulin, target values, specific feature use, and mealtime dosing behaviors). This will enable identification of less optimal use patterns in the real world, which will yield recommendations for prioritization of future improvement areas in development of DIYAPS, insight into the biggest needs of varying subcohorts, and this also indicates the most popular or most effective features in DIYAPS, which could also be translated and adapted and inform the use of commercially developed APS.

This WP is led by DL, PwD and founder of OpenAPS, and AT, PwD and developer of AndroidAPS.

Work Package 4: Barriers to Scale-Up

This WP aims to explore the potential economic, social, cultural, legal, and political barriers to the scale-up of DIYAPS technology.

The first objective of this WP will be to examine the potential barriers to uptake experienced by PwD who are interested in DIYAPS but have so far opted not to build their own system, have opted out after an unsuccessful attempt, or otherwise chosen to discontinue DIYAPS. We observe that many people stay connected to the online DIYAPS community regardless of their initial choice to use DIYAPS or not, as indicated by the 10,000+ people participating in the main "Looped" group on Facebook, as compared with the estimated, approximately 3000 likely active users of DIYAPS. Members of the Facebook peer support group "Looped" and other related Facebook groups who have yet to build their own system will therefore be targeted through questionnaires that aim to capture the reasons for not doing so. The questionnaires will probe for indicators, such as lack of knowledge of the benefits of using DIYAPS, lack of confidence in one's own information technology (IT) skills, affordability of technologies, time and effort needed to build DIYAPS, and other reasons for stopping DIYAPS, such as the availability of a commercial solution or lack of support from health care providers. The content of these questionnaires will be generated on the basis of a list of potential barriers to uptake,

identified through the findings from WP2 [35,36] and qualitative in-depth interviews with a targeted sample of non-DIYAPS users. The overall outcome will be a greater understanding of the reasons why these individuals are not yet using DIYAPS or have chosen not to use DIYAPS, which will consequently help researchers to develop better ways of addressing barriers to access and adoption of APS.

The next defining point of this WP is committed to understanding the health equity implications associated with the progression of DIY technology-enabled solutions for chronic disease management. More specifically, we aim to capture the requirements of DIYAPS users with lower levels of IT literacy. This will be established through a series of one-to-one and focus group interviews. The interviews will inform the development of low-fidelity wireframes that can be demonstrated at user-experience design workshops for further feedback from less tech-savvy DIYAPS users. The result will be a series of use cases that will be made available for the benefit of DIYAPS developers and the medical device industry.

An additional aspect of WP4 is to examine the current extent to which there are observable social inequalities in terms of access to the technologies needed to build DIYAPS and how these inequalities might be addressed and minimized. From this perspective, we will utilize data from the T1International Out-of-Pocket Expenses survey to examine the out-of-pocket-expenses and other accessibility issues associated with DIYAPS-related technologies [39].

This WP is led by SO, PwD and sociologist at the School of Sociology, University College Dublin.

An overview of 4 scientific work packages is provided in [Multimedia Appendix 1](#).

Work Package 5: Communication and Dissemination

This WP will coordinate the training, communication, and dissemination activities of the OPEN project and its aims to ensure high visibility and direct impact in the community, involving relevant stakeholders. The objectives include (1) implementing dissemination actions and communication activities to targeted audiences, (2) promoting the project concept and vision by highlighting its unique structure connecting patient researchers and innovators with established research organizations through social media, workshops, our newsletter, and the project website, (3) ensuring technical and scientific dissemination of the project results through publications in journals and conferences, and (4) raising public awareness of the project's objectives.

Different target audiences will be engaged with information adjusted carefully to their needs, raising awareness among those who can benefit from the project results and encouraging multistakeholder dialogue. The consortium has identified potential target groups, including the scientific community, clinicians and health care professionals, PwD, the DIYAPS community, policy makers and regulators, the medical and IT industry, and the general public.

All academic outputs that result from this project will be published in open-access journals and on the project's public

dissemination channels. Conference presentations at academic, clinical, and industry events provide an important opportunity for researchers to disseminate findings to multiple audiences. DIYAPS is currently a hot topic within diabetes care, and face-to-face interaction with conference delegates presents an opportunity to generate dialogue among both the proponents and critics of DIYAPS. This consortium will not only contribute to a body of evidence that will help to move the terms of the discussion forward but it will also ensure that the patient voice remains center stage.

Social media will also be used to ensure that the project findings reach multiple stakeholders and that the findings will influence decisions in public policy and professional practice. Twitter, LinkedIn, Facebook, and YouTube will be used as dissemination vehicles, providing a headline or snapshot summaries of key takeaway messages from the project outcomes, which will attract the attention of key stakeholders. Scheduled dissemination and communication activities will be held throughout the duration of the project to ensure constant information flow. Targeted messages will be distributed to the public to ensure that impact is maximized.

Finally, it is important to note that any technical innovations that might emerge or evolve from this project will be shared with the public, including DIYAPS developers, and it will ultimately be their decision whether to use the findings of OPEN as the basis to implement any changes in DIYAPS, as our role is focused solely on research and establishing an evidence base. Thus, the organizations' efforts in this project are not directly involved in, and will remain separated from, any direct DIYAPS development.

This WP is led by BH, PwD and CEO of Dedoc Labs.

Results

This project has received funding from the European Commission's Horizon 2020 Research and Innovation Program, under the Marie Skłodowska-Curie Action Research and Innovation Staff Exchange grant agreement number 823902.

Initial results on clinical outcomes and patient-reported outcomes have been presented at the Advanced Diabetes Technologies and Treatments Conference in February 2019 in Berlin, Germany, and the American Diabetes Association 79th Scientific Sessions in San Francisco, the United States, in June 2019 [35,36,40,41]. A study on self-reported clinical outcomes of the pediatric population using DIYAPS has been recently published in *JMIR mHealth and uHealth* [26], showing improved glycemic outcomes across all pediatric age groups, which is in line with clinical trial results from commercially developed closed-loop systems.

Discussion

DIYAPS represents an important case study in how increasingly informed and connected patients are shaping the direction of technological innovation in diabetes care and, potentially, for other areas of health care. As outlined above, researching this global movement poses unique challenges and opportunities,

which necessitate a move away from traditional, top-down modes of scientific inquiry toward a more cooperative and interactive approach, which is largely driven by PwD themselves.

The OPEN project is uniquely placed to address these challenges, as it is a patient- and user-led research project that brings together an international, interdisciplinary, and intersectoral research group comprising health care professionals, technical developers, and biomedical and social scientists, many of whom live with diabetes and are active DIYAPS users. Thus, the OPEN consortium is poised to bring the benefits of expertise of all kinds combined with the prioritization and knowledge of on-the-ground patient needs in a way that, to the best of our knowledge, is not being addressed by other research projects and collaborative initiatives.

It is acknowledged that the nature of the OPEN project can pose potential limitations and challenges. For example, the clinical evaluation (WP1) may be potentially seen as lacking rigor because of its inclusion and use of user-provided data. However, it is precisely this aspect of our methodological approach which has the potential to make a significant contribution to the extant literature surrounding the effectiveness of APS technology. Most studies on APS technology, to date, have been carried out as randomized clinical trials in well-controlled clinical research settings. Therefore, little is known about efficacy of APS in real-world settings where outcomes are likely to be contingent on context [42]. Moreover, previous studies have, for the most part, focused on measuring biomedical disease specific-outcomes; therefore, many other consequences of using closed-loop systems, such as psychosocial outcomes, remain relatively poorly understood [43]. By being one of the first studies to generate evidence on the basis of reliable,

user-provided data from all 3 DIYAPS (OpenAPS, AndroidAPS, and Loop) in real-world settings, this study will be an important complement to the existing clinically led research studies in the field.

In this regard, it is important to point out that both positive and negative forms of evidence surrounding DIYAPS will be valued equally by the OPEN team. Negative results provide important learning opportunities for the further development and diffusion of APS technology and for understanding what works, for whom, and under what set of circumstances [44]. This is why WPs around barriers (WP4), outcomes across a broad population (WP1 and WP2), and improvements to technology (WP3) have been designed. For example, qualitative studies exploring the lived experience of DIYAPS users (WP2) will seek out instances where individuals have used a closed-loop system but subsequently discontinued use. Finally, although negative results tend to be underreported in much of the traditional evaluation research literature [45], the OPEN team will openly share and attempt to publish all results from each WP.

Overall, by providing empirical evidence on DIYAPS, this project addresses the core user needs of the DIYAPS community. In addition, it will offer insights around accelerating improvements and diffusion of APS technology across the wider population of PwD. Disseminating project results in academic and nonacademic settings will help lower barriers among key stakeholders and encourage other researchers, policy makers, regulators, and the medical device industry to work together and innovate in a truly patient- and user-centric manner. We believe this new model of cooperation has the potential to have a profound impact on those living with diabetes, their families, health care systems, and society as a whole.

Acknowledgments

This project has received funding from the European Commission's Horizon 2020 Research and Innovation Program, under the Marie Skłodowska-Curie Action Research and Innovation Staff Exchange grant agreement number 823902.

Conflicts of Interest

All authors have completed the Unified Competing Interest form and declare the following: KB reports grants from the Berlin Institute of Health, fees for medical consulting from Medtronic Diabetes as a member of the Advisory Board "Impact," medical consulting fees, and paid talks from Roche Diabetes Care, Dexcom, Medtronic Diabetes, Diabeloop, and Bertelsmann Stiftung, outside the submitted work. AT reports personal fees from Dexcom, Roche Diabetes Care, IME-DC, Ypsomed, nonfinancial support from Sooil, and personal fees from Gruber-Dehong GmbH, outside the submitted work. DL reports grants from the Robert Wood Johnson Foundation, JDRF, personal fees from Lilly, Diabeloop, Roche Diabetes Care, and Novo Nordisk and Tandem, outside the submitted work. BH reports personal fees from Roche Pharma, Roche Diabetes Care, Novo Nordisk, LifeScan, Bayer AG, and Medtronic Diabetes, outside the submitted work. KR is Advisory Board member of Lilly Diabetes Care and Abbott Diabetes Care outside the submitted work. SW reports paid talks from Dexcom, Roche Diabetes Care, and Mediq Direkt Diabetes, outside the submitted work. MW was employed at Medtronic Diabetes Germany until 2018. All other coauthors have no conflicts of interest to declare.

Multimedia Appendix 1

Overview of the four scientific work packages of the OPEN project.

[[PNG File, 521 KB - resprot_v8i11e15368_app1.png](#)]

References

1. Influence of intensive diabetes treatment on quality-of-life outcomes in the diabetes control and complications trial. *Diabetes Care* 1996 Mar;19(3):195-203. [doi: [10.2337/diacare.19.3.195](https://doi.org/10.2337/diacare.19.3.195)] [Medline: [8742561](https://pubmed.ncbi.nlm.nih.gov/8742561/)]
2. Foster NC, Beck RW, Miller KM, Clements MA, Rickels MR, DiMeglio LA, et al. State of type 1 diabetes management and outcomes from the T1D exchange in 2016-2018. *Diabetes Technol Ther* 2019 Feb;21(2):66-72. [doi: [10.1089/dia.2018.0384](https://doi.org/10.1089/dia.2018.0384)] [Medline: [30657336](https://pubmed.ncbi.nlm.nih.gov/30657336/)]
3. American Diabetes Association. 6. Glycemic targets: standards of medical care in diabetes-2018. *Diabetes Care* 2018 Jan;41(Suppl 1):S55-S64. [doi: [10.2337/dc18-S006](https://doi.org/10.2337/dc18-S006)] [Medline: [29222377](https://pubmed.ncbi.nlm.nih.gov/29222377/)]
4. Tauschmann M, Allen JM, Wilinska ME, Thabit H, Stewart Z, Cheng P, et al. Day-and-night hybrid closed-loop insulin delivery in adolescents with type 1 diabetes: a free-living, randomized clinical trial. *Diabetes Care* 2016 Jul;39(7):1168-1174 [FREE Full text] [doi: [10.2337/dc15-2078](https://doi.org/10.2337/dc15-2078)] [Medline: [26740634](https://pubmed.ncbi.nlm.nih.gov/26740634/)]
5. Garg SK, Weinzimer SA, Tamborlane WV, Buckingham BA, Bode BW, Bailey TS, et al. Glucose outcomes with the in-home use of a hybrid closed-loop insulin delivery system in adolescents and adults with type 1 diabetes. *Diabetes Technol Ther* 2017 Mar;19(3):155-163 [FREE Full text] [doi: [10.1089/dia.2016.0421](https://doi.org/10.1089/dia.2016.0421)] [Medline: [28134564](https://pubmed.ncbi.nlm.nih.gov/28134564/)]
6. Tauschmann M, Thabit H, Bally L, Allen JM, Hartnell S, Wilinska ME, APCam1 Consortium. Closed-loop insulin delivery in suboptimally controlled type 1 diabetes: a multicentre, 12-week randomised trial. *Lancet* 2018 Oct 13;392(10155):1321-1329 [FREE Full text] [doi: [10.1016/S0140-6736\(18\)31947-0](https://doi.org/10.1016/S0140-6736(18)31947-0)] [Medline: [30292578](https://pubmed.ncbi.nlm.nih.gov/30292578/)]
7. Tauschmann M, Allen JM, Nagl K, Fritsch M, Yong J, Metcalfe E, KidsAP Consortium. Home use of day-and-night hybrid closed-loop insulin delivery in very young children: a multicenter, 3-week, randomized trial. *Diabetes Care* 2019 Apr;42(4):594-600. [doi: [10.2337/dc18-1881](https://doi.org/10.2337/dc18-1881)] [Medline: [30692242](https://pubmed.ncbi.nlm.nih.gov/30692242/)]
8. Forlenza GP, Pinhas-Hamiel O, Liljenquist DR, Shulman DI, Bailey TS, Bode BW, et al. Safety evaluation of the MiniMed 670G system in children 7-13 years of age with type 1 diabetes. *Diabetes Technol Ther* 2019 Jan;21(1):11-19 [FREE Full text] [doi: [10.1089/dia.2018.0264](https://doi.org/10.1089/dia.2018.0264)] [Medline: [30585770](https://pubmed.ncbi.nlm.nih.gov/30585770/)]
9. German Diabetes Society. Framework Paper for a Code of Conduct Digital Health of the German Diabetes Society (DDG) on Digital Transformation URL: https://www.deutsche-diabetes-gesellschaft.de/fileadmin/Redakteur/Ueber_uns/Code_of_Conduct_der_DDG_Digital_Health_19092017.pdf [accessed 2019-10-03]
10. Barnard KD, Wysocki T, Allen JM, Elleri D, Thabit H, Leelarathna L, et al. Closing the loop overnight at home setting: psychosocial impact for adolescents with type 1 diabetes and their parents. *BMJ Open Diabetes Res Care* 2014;2(1):e000025 [FREE Full text] [doi: [10.1136/bmjdr-2014-000025](https://doi.org/10.1136/bmjdr-2014-000025)] [Medline: [25452866](https://pubmed.ncbi.nlm.nih.gov/25452866/)]
11. Weissberg-Benchell J, Hessler D, Polonsky WH, Fisher L. Psychosocial impact of the bionic pancreas during summer camp. *J Diabetes Sci Technol* 2016 Jul;10(4):840-844 [FREE Full text] [doi: [10.1177/1932296816640289](https://doi.org/10.1177/1932296816640289)] [Medline: [26993252](https://pubmed.ncbi.nlm.nih.gov/26993252/)]
12. Iturralde E, Tanenbaum ML, Hanes SJ, Suttiratana SC, Ambrosino JM, Ly TT, et al. Expectations and attitudes of individuals with type 1 diabetes after using a hybrid closed loop system. *Diabetes Educ* 2017 Apr;43(2):223-232. [doi: [10.1177/0145721717697244](https://doi.org/10.1177/0145721717697244)] [Medline: [28340542](https://pubmed.ncbi.nlm.nih.gov/28340542/)]
13. Farrington C, Stewart ZA, Barnard K, Hovorka R, Murphy HR. Experiences of closed-loop insulin delivery among pregnant women with Type 1 diabetes. *Diabet Med* 2017 Oct;34(10):1461-1469. [doi: [10.1111/dme.13406](https://doi.org/10.1111/dme.13406)] [Medline: [28631849](https://pubmed.ncbi.nlm.nih.gov/28631849/)]
14. Hendrieckx C, Poole LA, Sharifi A, Jayawardene D, Loh MM, Horsburgh JC, et al. 'It Is Definitely a Game Changer': A qualitative study of experiences with in-home overnight closed-loop technology among adults with type 1 diabetes. *Diabetes Technol Ther* 2017 Jul;19(7):410-416. [doi: [10.1089/dia.2017.0007](https://doi.org/10.1089/dia.2017.0007)] [Medline: [28537437](https://pubmed.ncbi.nlm.nih.gov/28537437/)]
15. Barnard KD, Wysocki T, Thabit H, Evans ML, Amiel S, Heller S, Angela Consortium. Psychosocial aspects of closed- and open-loop insulin delivery: closing the loop in adults with Type 1 diabetes in the home setting. *Diabet Med* 2015 May;32(5):601-608. [doi: [10.1111/dme.12706](https://doi.org/10.1111/dme.12706)] [Medline: [25615888](https://pubmed.ncbi.nlm.nih.gov/25615888/)]
16. Barnard KD, Wysocki T, Ullly V, Mader JK, Pieber TR, Thabit H, et al. Closing the loop in adults, children and adolescents with suboptimally controlled type 1 diabetes under free living conditions: a psychosocial substudy. *J Diabetes Sci Technol* 2017 Nov;11(6):1080-1088 [FREE Full text] [doi: [10.1177/1932296817702656](https://doi.org/10.1177/1932296817702656)] [Medline: [28367636](https://pubmed.ncbi.nlm.nih.gov/28367636/)]
17. Farrington C, Stewart Z, Hovorka R, Murphy H. Women's experiences of day-and-night closed-loop insulin delivery during type 1 diabetes pregnancy. *J Diabetes Sci Technol* 2018 Nov;12(6):1125-1131 [FREE Full text] [doi: [10.1177/1932296818800065](https://doi.org/10.1177/1932296818800065)] [Medline: [30288999](https://pubmed.ncbi.nlm.nih.gov/30288999/)]
18. Lawton J, Blackburn M, Rankin D, Allen JM, Campbell FM, Leelarathna L, et al. Participants' experiences of, and views about, daytime use of a day-and-night hybrid closed-loop system in real life settings: longitudinal qualitative study. *Diabetes Technol Ther* 2019 Mar;21(3):119-127 [FREE Full text] [doi: [10.1089/dia.2018.0306](https://doi.org/10.1089/dia.2018.0306)] [Medline: [30720338](https://pubmed.ncbi.nlm.nih.gov/30720338/)]
19. Young AJ, Thabit H, Heller SR, Evans ML, Amiel SA, Hovorka R, et al. Holistic impact of closed-loop technology on people with type 1 diabetes. *J Diabetes Sci Technol* 2015 Jul;9(4):932-933 [FREE Full text] [doi: [10.1177/1932296815580162](https://doi.org/10.1177/1932296815580162)] [Medline: [25852073](https://pubmed.ncbi.nlm.nih.gov/25852073/)]
20. Adams RN, Tanenbaum ML, Hanes SJ, Ambrosino JM, Ly TT, Maahs DM, et al. Psychosocial and human factors during a trial of a hybrid closed loop system for type 1 diabetes management. *Diabetes Technol Ther* 2018 Oct;20(10):648-653. [doi: [10.1089/dia.2018.0174](https://doi.org/10.1089/dia.2018.0174)] [Medline: [30239219](https://pubmed.ncbi.nlm.nih.gov/30239219/)]

21. Ziegler C, Liberman A, Nimri R, Muller I, Klemencic S, Bratina N, et al. Reduced worries of hypoglycaemia, high satisfaction, and increased perceived ease of use after experiencing four nights of MD-logic artificial pancreas at home (DREAM4). *J Diabetes Res* 2015;2015:590308 [FREE Full text] [doi: [10.1155/2015/590308](https://doi.org/10.1155/2015/590308)] [Medline: [26581230](https://pubmed.ncbi.nlm.nih.gov/26581230/)]
22. Sharifi A, de Bock MI, Jayawardene D, Loh MM, Horsburgh JC, Berthold CL, et al. Glycemia, treatment satisfaction, cognition, and sleep quality in adults and adolescents with type 1 diabetes when using a closed-loop system overnight versus sensor-augmented pump with low-glucose suspend function: a randomized crossover study. *Diabetes Technol Ther* 2016 Dec;18(12):772-783. [doi: [10.1089/dia.2016.0288](https://doi.org/10.1089/dia.2016.0288)] [Medline: [27835037](https://pubmed.ncbi.nlm.nih.gov/27835037/)]
23. The Nightscout Project. URL: <http://www.nightscout.info/> [accessed 2019-06-28]
24. OpenAPS. URL: <https://openaps.org/> [accessed 2019-10-22]
25. Choose a License. Licenses URL: <https://choosealicense.com/licenses/> [accessed 2019-10-18]
26. Braune K, O'Donnell S, Cleal B, Lewis D, Tappe A, Willaing I, et al. Real-world use of Do-It-Yourself artificial pancreas systems in children and adolescents with type 1 diabetes: online survey and analysis of self-reported clinical outcomes. *JMIR Mhealth Uhealth* 2019 Jul 30;7(7):e14087 [FREE Full text] [doi: [10.2196/14087](https://doi.org/10.2196/14087)] [Medline: [31364599](https://pubmed.ncbi.nlm.nih.gov/31364599/)]
27. Melmer A, Züger T, Lewis DM, Leibrand S, Stettler C, Laimer M. Glycaemic control in individuals with type 1 diabetes using an open source artificial pancreas system (OpenAPS). *Diabetes Obes Metab* 2019 Oct;21(10):2333-2337. [doi: [10.1111/dom.13810](https://doi.org/10.1111/dom.13810)] [Medline: [31183929](https://pubmed.ncbi.nlm.nih.gov/31183929/)]
28. Lewis D, Leibrand S, #OpenAPS Community. Real-world use of open source artificial pancreas systems. *J Diabetes Sci Technol* 2016 Nov;10(6):1411 [FREE Full text] [doi: [10.1177/1932296816665635](https://doi.org/10.1177/1932296816665635)] [Medline: [27510442](https://pubmed.ncbi.nlm.nih.gov/27510442/)]
29. Lewis DM, Swain RS, Donner TW. Improvements in A1C and Time-in-Range in DIY Closed-Loop (OpenAPS) Users. *Diabetes* 2018;67(Supplement 1):352-OR. [doi: [10.2337/db18-352-OR](https://doi.org/10.2337/db18-352-OR)]
30. Lewis D. History and perspective on DIY closed looping. *J Diabetes Sci Technol* 2019 Jul;13(4):790-793 [FREE Full text] [doi: [10.1177/1932296818808307](https://doi.org/10.1177/1932296818808307)] [Medline: [30348013](https://pubmed.ncbi.nlm.nih.gov/30348013/)]
31. Petruzelkova L, Soupal J, Plasova V, Jiranova P, Neuman V, Plachy L, et al. Excellent glycemic control maintained by open-source hybrid closed-loop AndroidAPS during and after sustained physical activity. *Diabetes Technol Ther* 2018 Nov;20(11):744-750. [doi: [10.1089/dia.2018.0214](https://doi.org/10.1089/dia.2018.0214)] [Medline: [30285476](https://pubmed.ncbi.nlm.nih.gov/30285476/)]
32. Hng T, Burren D. Appearance of Do-It-Yourself closed-loop systems to manage type 1 diabetes. *Intern Med J* 2018 Nov;48(11):1400-1404. [doi: [10.1111/imj.14105](https://doi.org/10.1111/imj.14105)] [Medline: [30387315](https://pubmed.ncbi.nlm.nih.gov/30387315/)]
33. The CREATE Trial. URL: <https://www.otago.ac.nz/christchurch/departments/paediatrics/research/otago717634.html> [accessed 2019-10-03]
34. Speight J, Conn J, Dunning T, Skinner TC, 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](https://doi.org/10.1016/j.diabres.2012.03.015)] [Medline: [22513346](https://pubmed.ncbi.nlm.nih.gov/22513346/)]
35. Braune K, O'donnell S, Cleal B, Lewis DM, Tappe A, Hauck B, et al. 117-LB: DIWHY: Factors influencing motivation, barriers, and duration of DIY artificial pancreas system use among real-world users. *Diabetes* 2019 Jun;68(Supplement 1):117-LB. [doi: [10.2337/db19-117-LB](https://doi.org/10.2337/db19-117-LB)]
36. Braune K, O'Donnell S, Cleal B, Willaing I, Tappe A, Lewis D, et al. DIWHY - Motivations, Barriers and Retention Factors of DIY Artificial Pancreas Users in Real World Use. ATTD19-0211. In: Proceedings of The Official Journal of ATTD Advanced Technologies & Treatments for Diabetes Conference. 2019 Feb Presented at: ATTD'19; February 20–23, 2019; Berlin, Germany. [doi: [10.1089/dia.2019.2525.abstracts](https://doi.org/10.1089/dia.2019.2525.abstracts)]
37. Ball MP, Lewis DM. figshare. 2017. OpenAPS Data Commons on Open Humans URL: https://figshare.com/articles/OpenAPS_Data_Commons_on_Open_Humans/5428498 [accessed 2019-11-13]
38. Garrison LP, Neumann PJ, Erickson P, Marshall D, Mullins CD. Using real-world data for coverage and payment decisions: the ISPOR Real-World Data Task Force report. *Value Health* 2007;10(5):326-335 [FREE Full text] [doi: [10.1111/j.1524-4733.2007.00186.x](https://doi.org/10.1111/j.1524-4733.2007.00186.x)] [Medline: [17888097](https://pubmed.ncbi.nlm.nih.gov/17888097/)]
39. T1International. Costs and Rationing of Insulin and Diabetes Supplies: Findings from the 2018 T1International Patient Survey URL: https://www.t1international.com/media/assets/file/T1International_Report_-_Costs_and_Rationing_of_Insulin_Diabetes_Supplies_2.pdf [accessed 2019-07-04]
40. Cleal B, Braune K, O'donnell S, Hauck B, Lewis DM, Skinner T, et al. 78-LB: Detailing the experiences of people with diabetes using Do-It-Yourself artificial pancreas systems—qualitative analysis of responses to open-ended items in an international survey. *Diabetes* 2019 Jun;68(Supplement 1):78-LB. [doi: [10.2337/db19-78-LB](https://doi.org/10.2337/db19-78-LB)]
41. Braune K, Raile K, Cleal B, Willaing I, Tappe A, Lewis D, et al. OPEN - Outcomes of Patients' Evidence with Novel, Artificial Pancreas Technology. ATTD19-0215. In: Proceedings of The Official Journal of ATTD Advanced Technologies & Treatments for Diabetes Conference. 2019 Presented at: ATTD'19; February 20–23, 2019; Berlin, Germany. [doi: [10.1089/dia.2019.2525.abstracts](https://doi.org/10.1089/dia.2019.2525.abstracts)]
42. Dalkin SM, Greenhalgh J, Jones D, Cunningham B, Lhussier M. What's in a mechanism? Development of a key concept in realist evaluation. *Implement Sci* 2015 Apr 16;10:49 [FREE Full text] [doi: [10.1186/s13012-015-0237-x](https://doi.org/10.1186/s13012-015-0237-x)] [Medline: [25885787](https://pubmed.ncbi.nlm.nih.gov/25885787/)]

43. Barnard KD, Hood KK, Weissberg-Benchell J, Aldred C, Oliver N, Laffel L. Psychosocial assessment of artificial pancreas (AP): commentary and review of existing measures and their applicability in AP research. *Diabetes Technol Ther* 2015 Apr;17(4):295-300 [FREE Full text] [doi: [10.1089/dia.2014.0305](https://doi.org/10.1089/dia.2014.0305)] [Medline: [25549042](https://pubmed.ncbi.nlm.nih.gov/25549042/)]
44. Pawson R, Tilley N. *Realistic Evaluation*. London: Sage Publications; 1997.
45. Mlinaric A, Horvat M, Smolcic VS. Dealing with the positive publication bias: why you should really publish your negative results. *Biochem Med (Zagreb)* 2017 Oct 15;27(3):030201 [FREE Full text] [doi: [10.11613/BM.2017.030201](https://doi.org/10.11613/BM.2017.030201)] [Medline: [29180912](https://pubmed.ncbi.nlm.nih.gov/29180912/)]

Abbreviations

APS: Artificial Pancreas System

CGM: continuous glucose monitoring

DIY: do-it-yourself

DIYAPS: Do-It-Yourself Artificial Pancreas Systems

HbA_{1c}: glycated hemoglobin

IT: information technology

OPEN: Outcomes of Patients' Evidence With Novel, Do-It-Yourself Artificial Pancreas Technology

OpenAPS: Open-Source Artificial Pancreas System

PwD: people with diabetes

T1D: type 1 diabetes

WP: work package

Edited by G Eysenbach; submitted 04.07.19; peer-reviewed by M Ford Holloway, L Heinemann, J Farzi; comments to author 01.09.19; revised version received 22.10.19; accepted 30.10.19; published 19.11.19.

Please cite as:

O'Donnell S, Lewis D, Marchante Fernández M, Wäldchen M, Cleal B, Skinner T, Raile K, Tappe A, Ubben T, Willaing I, Hauck B, Wolf S, Braune K

Evidence on User-Led Innovation in Diabetes Technology (The OPEN Project): Protocol for a Mixed Methods Study

JMIR Res Protoc 2019;8(11):e15368

URL: <http://www.researchprotocols.org/2019/11/e15368/>

doi: [10.2196/15368](https://doi.org/10.2196/15368)

PMID: [31742563](https://pubmed.ncbi.nlm.nih.gov/31742563/)

©Shane O'Donnell, Dana Lewis, María Marchante Fernández, Mandy Wäldchen, Bryan Cleal, Timothy Skinner, Klemens Raile, Adrian Tappe, Tebbe Ubben, Ingrid Willaing, Bastian Hauck, Saskia Wolf, Katarina Braune. Originally published in JMIR Research Protocols (<http://www.researchprotocols.org>), 19.11.2019. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in JMIR Research Protocols, is properly cited. The complete bibliographic information, a link to the original publication on <http://www.researchprotocols.org>, as well as this copyright and license information must be included.

Protocol

Development of an Early Warning System to Prevent Crises in the Palliative Home Care Setting of Patients and Their Informal Caregivers: Protocol for a Mixed Method Study

André Fringer^{1,2}, Prof Dr; Eleonore Arrer³, MSc; Edith Maier⁴, Prof Dr; Wilfried Schnepf², Prof Dr; Tom Ulmer⁴, Mag (FH)

¹Research Unit Nursing Science, Institute of Nursing, Department of Health, Zurich University of Applied Sciences, Winterthur, Switzerland

²Department of Nursing Science, Faculty of Health, Witten/Herdecke University, Witten, Germany

³Institute of Applied Nursing Science, FHS St Gallen, University of Applied Sciences, St Gallen, Switzerland

⁴Institute for Information and Process Management, FHS St Gallen, University of Applied Sciences, St Gallen, Switzerland

Corresponding Author:

André Fringer, Prof Dr

Research Unit Nursing Science, Institute of Nursing

Department of Health

Zurich University of Applied Sciences

Technikumstrasse 81

Winterthur, 8401

Switzerland

Phone: 41 58 934 64 79

Email: andre.fringer@zhaw.ch

Abstract

Background: Most people wish to die at home, but most people in Switzerland die in hospitals or nursing homes. Family caregivers often offer support so patients with palliative care needs can stay at home for as long as possible. However, crises and unplanned hospital admissions often occur in this setting because of family caregiver strain and symptom severity in patients. The so-called smart devices such as wearables or smartphones offer the opportunity to continuously monitor certain parameters and recording symptom deteriorations. By providing professionals with this information in a timely manner, crises in the home could be avoided.

Objective: The aim of this interdisciplinary study is to explore the symptom burden of people with palliative care needs who are cared for at home and to understand the development of crises in the home care setting. On the basis of the findings from this study, we will develop an early warning system to stabilize the home care situation and to prevent critical events from happening, thereby reducing avoidable hospitalizations.

Methods: A mixed method study is being conducted consisting of 4 main consecutive phases: (1) developing the monitoring system; (2) pretesting the system and adapting it to user needs; (3) conducting the study in the palliative home care setting with approximately 40 patients; and (4) distinguishing symptom patterns from the collected data specific to crisis emergence, followed by the development of an early warning system to prevent such crises. In study phase 3, each patient will receive an upper arm sensor and a symptom diary to assess symptom burden related to patients and family caregivers. A within-case analysis will be conducted for each patient's situation followed by a cross-case comparison to identify certain symptom patterns that may predict symptom deterioration (study phase 4).

Results: The collaboration with the local mobile palliative care team for participant recruitment and data collection has been established. Recruitment is forthcoming.

Conclusions: We expect the findings of this study to provide holistic insight into symptom burden and the well-being of patients with palliative care needs and of their family caregivers. This information will be used to develop an early warning system to avoid the occurrence of potential crises, thereby improving palliative care provision at home.

International Registered Report Identifier (IRRID): PRR1-10.2196/13933

(*JMIR Res Protoc* 2019;8(11):e13933) doi:[10.2196/13933](https://doi.org/10.2196/13933)

KEYWORDS

palliative care; eHealth; family caregivers; outpatient care

Introduction

Background

The demand for palliative care has been increasing as a result of our ageing population and the increase in the number of chronically ill people [1,2]. Most patients wish to die in their own homes [3,4], which—because of complex and instable symptom development—is often not possible. In this regard, family caregivers represent a significant resource in the care of people at the end of life. They help ensure that patients can remain at home for as long as possible, thereby also alleviating financial strains on our health care systems [5]. The social value of family care work in Switzerland alone amounts to more than Swiss Franc 3.5 billion per year according to federal statistics [6]. Yet, family caregivers are highly vulnerable and often feel exhausted and stressed, with multiple physical and psychosocial consequences. This can lead to crises for the family or to an unplanned hospital admission for the patient [7]. In fact, patients at the end of life are especially at risk for hospitalization, thus incurring high health care costs [8,9]. A study found that 80% of severely ill patients with cancer were admitted to hospital because of uncontrolled symptoms [8]. However, such admissions could be avoided by providing adequate specialist services within home care [8,10].

Research has also found that frequent visits by health care professionals in the home are correlated with higher quality of life for family caregivers [11]. However, such teams are not always readily available and in-person visits can be costly and time consuming [12].

This is where digital health or electronic health comes in. Digital health can be defined as any “mobile health, health information technology, wearable device, telehealth, telemedicine, and personalized medicine” according to the Food and Drug Administration. In recent years, digital health has successfully been implemented within palliative care in numerous projects [13-17]. It can improve patient–health care professional interaction and optimize human resources, especially in regions where access to palliative care services is limited. In addition, and more importantly, such tools can help deliver care interventions and improve the well-being and quality of life for both patients and their families [18]. Digital technologies, such as the use of sensors for remote monitoring, can offer new opportunities for supporting family caregivers through early recognition of critical situations and preventing them from escalating. This may be achieved, for instance, by linking them up to specialized health care providers and thus bridging the geographical gap [19].

Objectives

On the basis of these considerations, our study pursues the primary objective of exploring and understanding the home care setting of patients with palliative needs to stabilize critical situations and deflect crises. We aim to achieve this by continuously monitoring the relevant indicators and vital

parameters of patients with palliative care needs in home care and thus gain an in-depth insight into individual symptom burden. At the same time, we will collect data on family caregivers’ well-being as research has shown that they can also trigger or amplify crises in the household setting and can be greatly influenced by their loved one’s illness [20,21]. This information will be used to develop an early warning system for the home care environment.

To our knowledge, no such tool has been developed that focuses on providing holistic insight into the palliative home care environment of patients and that aims at preventing the onset of crises and subsequently burdensome and costly unplanned hospital admissions.

Methods

Overview

The researchers have chosen to conduct a mixed method case study to investigate the different dimensions of the research topic [22].

The explorative approach is of an interdisciplinary nature and involves digital health experts, designers, and developers as well as nursing scientists and palliative care experts. Thus, it complies with international and national recommendations regarding palliative care research [23,24]. In addition, the project team is accompanied and assisted by practitioners and representatives from relevant care organizations.

The study has 4 main consecutive phases: (1) developing the monitoring system that consists of an upper arm sensor and a symptom diary, (2) pretesting the system and adapting it to user needs, (3) conducting the study in the palliative home care setting together with mobile palliative care teams (MPCTs), and (4) detecting symptom patterns from the collected data characterizing emerging crises. Finally, an early warning system to prevent such crises will be developed.

Phase 1: Developing the Monitoring System

Before developing the monitoring system, we followed an iterative user-centered design process to ensure user acceptance. In the first phase, we conducted interviews with palliative care experts (physicians and nurses) to investigate the need and the feasibility of utilizing smart devices and symptom monitoring in the palliative home care setting. The focus of the study was primarily on the comprehensive expertise and experience of the participants. In addition, we conducted a scoping review on other monitoring systems that had been used in comparable environments.

On the basis of this preliminary work, we chose to opt for the noninvasive and nonobtrusive certified upper arm sensor from the firm Biovotion to objectively and continuously measure certain parameters automatically. These parameters include heart rate and heart rate variability, blood oxygenation, skin temperature, skin blood perfusion, respiratory rate, galvanic skin response, and micromovements. On the basis of the

literature, we especially expect heart rate and respiratory rate to provide information on possible crisis situations at the end of life [25,26]. In this study, we also hope to gain more insight regarding the other parameters and their possible association with crises. The sensor itself does not indicate any information to the patient directly on a user interface but continuously transmits the data to a server after having anonymized them. The server is run by the FHS St Gallen and is hosted by a provider in Switzerland.

In addition, we designed a symptom diary for patients and their family caregivers as well as health care professionals to report the patient's subjective symptoms 3 times per day on an intensity scale from 0 (no symptoms) to 10 (worst possible symptoms) based on the modified Edmonton Symptom Assessment System [27]. The date and time of self-symptom evaluation must be documented precisely for us to draw adequate conclusions by comparing the subjective diary data with the objective sensory data. In addition, the date will also provide us with information on the time of the year. This will be of interest for analysis purposes regarding the correlation of symptom burden or crises with, for instance, the winter months. The diary also contains the modified Caregiver Quality of Life Index—Cancer scale [28], which is filled in by the family caregiver once a week to determine the caregiver's well-being. Even though we did not restrict our sample to patients with cancer only, this questionnaire was applied considering that most of the MPCT's patients have cancer and that the instrument has also been used in research for family caregivers of palliative patients in general [29]. Both measuring instruments have been amended based on the feedback obtained from the expert interviews. For example, questions related to social interaction, visits by health care professionals, and overall daily burden have been added. In addition, patients and their family caregivers will be able to document their general experiences daily, including perceived crises as free text.

Phase 2: Pretest

Before the actual study commencement, we obtained ethical approval for the study from the responsible ethics committee of Eastern Switzerland. Once obtained, we tested the monitoring system within a so-called *living laboratory* supervised by the Interdisciplinary Centre of Competence for Ageing. This pretest was conducted in an older population without severe medical conditions with the objective to make sure both the device and diary are safe, practical, and easy to use without greatly impacting the daily living experience before using them in a vulnerable population. A living laboratory can be considered an experimental natural environment where persons in their private homes participate in testing digital devices and systems. Sensory devices were given to 7 participants who also received the symptom diary. Participants with an average age of 74 years were instructed in the handling of both the sensor and the diary and were encouraged to wear the sensor continuously on 7 consecutive days. After completion of the pretest, participants' feedback was incorporated into the development of the monitoring system and some minor adaptations were made. Overall, the participants found the sensor easy to use and said that they would be willing to wear it for a longer period than the pretest of 1 week if it was important for their health care

provision. This willingness also suggests that the sensor was not bothersome to wear and did not negatively impact everyday activities. All participants wore the sensor continuously and only took it off to charge it or when showering. They also found the information on how to use the symptom diary easy to understand.

Phase 3: Conducting the Study

Setting and Recruitment

Recruitment for the study is taking place in St Gallen, Switzerland. The city's MPCT unit has a gatekeeper function and is responsible for recruiting the participants with support from the research team. We chose this approach to not disrupt this vulnerable environment of severely ill patients being cared for at home. The MPCT in St Gallen cares for at least 80 patients annually with specialized palliative care needs. Most of their patients are diagnosed with advanced cancer and are being cared for by a family caregiver in their own home.

We are planning to recruit 40 patients within a period of 12 months. Patients are eligible to participate if they are being cared for by the MPCT in St Gallen, are at least 18 years of age, speak German, and are capable of filling in the diary and using the sensor accordingly—if necessary, by receiving support from their family caregiver. The primary family caregiver is identified routinely by the MPCT as the person with the most frequent informal contact with the patient (daily visits or cohabitation requirement) and who supports the patient at home. If a patient has a pacemaker, he or she is excluded from receiving the upper arm sensor but can still fill in the symptom diary that was requested by the MPCT to facilitate patient documentation and to also provide an in-depth insight into patient and caregiver burden. We chose this specific exclusion criterion as a precautionary measure only even though we had no indication that the sensor might interfere with such a device. The diary is also given to patients who are reluctant to use the sensor at recruitment based on the consideration that they might decide to use it at a later stage after having been introduced to the diary.

Procedures and Data Collection

The members of the MPCT select eligible patients and decide on whether they will receive the sensor, the diary, or both (target group). This decision is based on the Karnofsky Performance Status Scale, where we distinguish between these 3 groups based on their achieved percentage scores [30]. We identify patients with a score of 50% to 60% or larger to receive the diary (group 1), 20% to 40% to receive the sensor and the diary (group 2), and 10% to receive only the sensor (group 3). The choice of categorization was based on discussions with the MPCT regarding the high vulnerability of the patient group at the end of life. It was considered to diminish the burden on those most impaired (score of 10%) together with their family caregivers by not providing the diary. Staff members have been trained by the research team on how to use the symptom diary and on how to install the sensor in the patient's home.

Staff from the MPCT have been approaching the potential participants. Once they indicate their wish to participate, a staff member provides more information according to the allocated group and obtains informed consent. At the beginning of the

study, participants also fill in a survey with questions primarily regarding the demographic data of both the patient and family caregiver (eg, age, gender, diagnosis, social contacts, and relationship with the family caregiver) to conduct subgroup analyses. The selection of these data was based on considerations to what extent they might also contribute to crises, for example, older age of the family caregiver or few social contacts. If the participant is to receive a sensor, the staff will install the device that stores the data in the patient's home. The symptom diary will contain no information that can be tracked back to the patient, but the staff will document the diary number that also corresponds to the sensor in use. This number is essential so that we can compare the sensor data with the information documented in the diary.

The data collection period for each participant is 2 weeks, although for the entire study, data will be collected over 12 months. A time frame of 2 weeks was chosen based on considerations together with the MPCT regarding the high vulnerability of the patient group, the end-of-life situation, and the resource constraints. If a participant decides to discontinue the study before then, the data collected up to that time point will still be used for analysis, in line with the information given to the participants at recruitment. Patients (groups 1 and 2) are asked to fill in the diary 3 times daily and whenever a specific event takes place during the day that requires or indicates documentation, for instance, a crisis such as severe pain followed by specific measures. Participants of groups 2 and 3 are also asked to wear the sensor continuously during the 2 weeks and to charge it once a day (for approximately 2 hours).

After the 2 weeks of data collection, a staff member will ask the participants to fill in a survey to assess their experiences in connection with the monitoring system. Questions will, for instance, involve experiences of using the symptom diary and sensor, comfort and satisfaction, and expectations and wishes for future digital solutions. The staff member will then return the diary and the sensor to the research team, together with all other anonymous information collected.

Phase 4: Data Analysis and Development of an Early Warning System

The data analysis will incorporate aspects of a multiple cross-case study. A within-case analysis will be conducted for each participant followed by a cross-case comparison. Primarily, this will involve comparing the data from the sensor with the symptom diary from target group 2. To do so, we will apply quantitative and qualitative methods. The content analysis method by Schreier [31] will be applied to gain insight into the caregiver's crisis experience by analyzing the qualitative data from the diary. Two researchers will conduct the analysis using the software MAXQDA. The results will be discussed by the research team to avoid them from being influenced by the perspectives and assumptions of a single researcher. Qualitative data will later be transformed into quantitative data to compare sensor data with crisis experiences [32]. A statistician will conduct the quantitative data analysis (based on information from both the sensor and diary and the demographic data) with data comparisons, using SPSS Statistics 25 (IBM) software. Missing data, for instance, if someone forgot to fill in the diary

at one point or did not wear the sensor, will be addressed by applying missing-data imputations when feasible.

We expect to be able to draw conclusions that will allow the identification of personalized threshold values that can recognize a critical event before it sets in. These threshold values will relate to sensor information, such as heart rate and respiratory rate, which we anticipate to be essential for the design of the early warning system based on previous research [25,26]. The digital warning system will be integrated in the MPCT unit and linked to a patient's home. It will be calibrated individually for each patient including the conditions as to when the MPCT is to be alerted and the actions this will trigger.

Privacy and Security

To ensure participants' privacy and to protect this vulnerable study population, the research team will rely on the MPCT to be in direct contact with the patients and families. All digitally collected information will be stored in the cloud hosted by a Swiss provider and will be anonymized in a way that it cannot be tracked back to the user. Only the research team will later have access to this information. The written information collected by the MPCT will be made anonymous before data analysis conducted by the research team.

Results

Up to this stage, ethical clearance for the study has been obtained, the monitoring system, including the sensor and diary, has been set up, and it has been pretested in a living laboratory. The collaboration with the local MPCT for participant recruitment and data collection has been established. Recruitment is forthcoming.

Discussion

We anticipate that our results will greatly contribute to our knowledge about the emergence of crises in the palliative care environment at home. It will be especially interesting to find out how the sensor data are correlated with the data from the symptom diary and to what extent family caregivers are stressed by events that primarily involve the patient. It is precisely this tipping point that we aim to determine, so we can intervene proactively before a crisis sets in. This can only be achieved by means of an interdisciplinary approach and in close collaboration with practitioners and patients and their family caregivers.

Conclusions

We expect the findings of this study to provide holistic insight into the symptom burden and well-being of patients with palliative care needs and of their family caregivers. This information will be used to develop an early warning system to avoid the occurrence of crises within home care. Future provision of palliative care by professionals in a patient's home could thus be improved. Given the future challenges connected to demographic change, staff shortages, or economic pressures, the proposed early warning system has the potential to alleviate these pressures to some extent by complementing and enhancing patient–health care professional interaction and stabilizing the home care environment.

Acknowledgments

This project is funded by the Gebert Rüf Stiftung, Basel, Switzerland.

Conflicts of Interest

None declared.

References

1. Genet N, Boerma W, Kroneman M, Hutchinson A, Saltman RB. WHO/Europe. 2012. Home Care across Europe: Current structure and future challenges URL: http://www.euro.who.int/_data/assets/pdf_file/0008/181799/e96757.pdf [accessed 2018-03-08]
2. Tralongo P, Ferraù F, Borsellino N, Verderame F, Caruso M, Giuffrida D, et al. Cancer patient-centered home care: a new model for health care in oncology. *Ther Clin Risk Manag* 2011;7:387-392 [FREE Full text] [doi: [10.2147/TCRM.S22119](https://doi.org/10.2147/TCRM.S22119)] [Medline: [21941445](https://pubmed.ncbi.nlm.nih.gov/21941445/)]
3. Gomes B, Calanzani N, Gysels M, Hall S, Higginson IJ. Heterogeneity and changes in preferences for dying at home: a systematic review. *BMC Palliat Care* 2013 Feb 15;12:7 [FREE Full text] [doi: [10.1186/1472-684X-12-7](https://doi.org/10.1186/1472-684X-12-7)] [Medline: [23414145](https://pubmed.ncbi.nlm.nih.gov/23414145/)]
4. Higginson IJ, Sen-Gupta GJ. Place of care in advanced cancer: a qualitative systematic literature review of patient preferences. *J Palliat Med* 2000;3(3):287-300. [doi: [10.1089/jpm.2000.3.287](https://doi.org/10.1089/jpm.2000.3.287)] [Medline: [15859670](https://pubmed.ncbi.nlm.nih.gov/15859670/)]
5. Verbakel E, Tamlagsrønning S, Winstone L, Fjær EL, Eikemo T. Informal care in Europe: findings from the European Social Survey (2014) special module on the social determinants of health. *Eur J Public Health* 2017 Feb 1;27(suppl_1):90-95. [doi: [10.1093/eurpub/ckw229](https://doi.org/10.1093/eurpub/ckw229)] [Medline: [28355645](https://pubmed.ncbi.nlm.nih.gov/28355645/)]
6. Rudin M, Strub S. BASS. 2014. Zeitlicher Umfang und monetäre Bewertung der Pflege und Betreuung durch Angehörige URL: https://www.buerobass.ch/fileadmin/Files/2014/Spitex_Verband_2014_MonetaereBewertung_pflegerischeAngehoeerige_d.pdf [accessed 2019-10-09]
7. Perrig-Chiello P, Höpflinger F. Pflegende Angehörige älterer Menschen: Probleme, Bedürfnisse, Ressourcen und Zusammenarbeit mit der ambulanten Pflege. Bern: Huber; 2012.
8. Numico G, Cristofano A, Mozzicafreddo A, Cursio OE, Franco P, Courthod G, et al. Hospital admission of cancer patients: avoidable practice or necessary care? *PLoS One* 2015;10(3):e0120827 [FREE Full text] [doi: [10.1371/journal.pone.0120827](https://doi.org/10.1371/journal.pone.0120827)] [Medline: [25812117](https://pubmed.ncbi.nlm.nih.gov/25812117/)]
9. Scaccabarozzi G, Limonta F, Amodio E. Hospital, local palliative care network and public health: how do they involve terminally ill patients? *Eur J Public Health* 2017 Feb 1;27(1):25-30 [FREE Full text] [doi: [10.1093/eurpub/ckw152](https://doi.org/10.1093/eurpub/ckw152)] [Medline: [28177477](https://pubmed.ncbi.nlm.nih.gov/28177477/)]
10. Hjerstad MJ, Kolflaath J, Løkken AO, Hanssen SB, Normann AP, Aass N. Are emergency admissions in palliative cancer care always necessary? Results from a descriptive study. *BMJ Open* 2013 May 31;3(5):pii: e002515 [FREE Full text] [doi: [10.1136/bmjopen-2012-002515](https://doi.org/10.1136/bmjopen-2012-002515)] [Medline: [23793662](https://pubmed.ncbi.nlm.nih.gov/23793662/)]
11. Choi YS, Hwang SW, Hwang IC, Lee YJ, Kim YS, Kim HM, et al. Factors associated with quality of life among family caregivers of terminally ill cancer patients. *Psychooncology* 2016 Feb;25(2):217-224. [doi: [10.1002/pon.3904](https://doi.org/10.1002/pon.3904)] [Medline: [26152842](https://pubmed.ncbi.nlm.nih.gov/26152842/)]
12. Wächter M, Bommer A. palliative.ch. 2014. Mobile Palliative-Care-Dienste in der Schweiz – Eine Bestandsaufnahme aus der Perspektive dieser Anbieter URL: https://www.palliative.ch/fileadmin/user_upload/palliative/publikum/3_Ueber_uns/Mobile_Palliative_Care_Dienste_Schlussbericht.pdf [accessed 2017-11-22]
13. Blum D, Koeberle D, Omlin A, Walker J, von Moos R, Mingrone W, et al. Feasibility and acceptance of electronic monitoring of symptoms and syndromes using a handheld computer in patients with advanced cancer in daily oncology practice. *Support Care Cancer* 2014 Sep;22(9):2425-2434. [doi: [10.1007/s00520-014-2201-8](https://doi.org/10.1007/s00520-014-2201-8)] [Medline: [24705855](https://pubmed.ncbi.nlm.nih.gov/24705855/)]
14. Ferriolli E, Skipworth RJ, Hendry P, Scott A, Stensteth J, Dahele M, et al. Physical activity monitoring: a responsive and meaningful patient-centered outcome for surgery, chemotherapy, or radiotherapy? *J Pain Symptom Manage* 2012 Jun;43(6):1025-1035. [doi: [10.1016/j.jpainsymman.2011.06.013](https://doi.org/10.1016/j.jpainsymman.2011.06.013)] [Medline: [22269181](https://pubmed.ncbi.nlm.nih.gov/22269181/)]
15. Watanabe SM, Fairchild A, Pituskin E, Borgersen P, Hanson J, Fassbender K. Improving access to specialist multidisciplinary palliative care consultation for rural cancer patients by videoconferencing: report of a pilot project. *Support Care Cancer* 2013 Apr;21(4):1201-1207. [doi: [10.1007/s00520-012-1649-7](https://doi.org/10.1007/s00520-012-1649-7)] [Medline: [23161339](https://pubmed.ncbi.nlm.nih.gov/23161339/)]
16. Gustafson DH, DuBenske LL, Namkoong K, Hawkins R, Chih M, Atwood AK, et al. An eHealth system supporting palliative care for patients with non-small cell lung cancer: a randomized trial. *Cancer* 2013 May 1;119(9):1744-1751 [FREE Full text] [doi: [10.1002/cncr.27939](https://doi.org/10.1002/cncr.27939)] [Medline: [23355273](https://pubmed.ncbi.nlm.nih.gov/23355273/)]
17. Katalinic O, Young A, Doolan D. Case study: the interact home telehealth project. *J Telemed Telecare* 2013 Oct;19(7):418-424. [doi: [10.1177/1357633X13506513](https://doi.org/10.1177/1357633X13506513)] [Medline: [24218357](https://pubmed.ncbi.nlm.nih.gov/24218357/)]

18. Pinto S, Caldeira S, Martins JC. e-Health in palliative care: review of literature, Google Play and App Store. *Int J Palliat Nurs* 2017 Aug 2;23(8):394-401. [doi: [10.12968/ijpn.2017.23.8.394](https://doi.org/10.12968/ijpn.2017.23.8.394)] [Medline: [28854054](https://pubmed.ncbi.nlm.nih.gov/28854054/)]
19. Theile G, Klaas V, Tröster G, Guckenberger M. mHealth technologies for palliative care patients at the interface of in-patient to outpatient care: protocol of feasibility study aiming to early predict deterioration of patient's health status. *JMIR Res Protoc* 2017 Aug 16;6(8):e142 [FREE Full text] [doi: [10.2196/resprot.7676](https://doi.org/10.2196/resprot.7676)] [Medline: [28814378](https://pubmed.ncbi.nlm.nih.gov/28814378/)]
20. Gott M, Seymour J, Bellamy G, Clark D, Ahmedzai S. Older people's views about home as a place of care at the end of life. *Palliat Med* 2004 Jul;18(5):460-467. [doi: [10.1191/0269216304pm889oa](https://doi.org/10.1191/0269216304pm889oa)] [Medline: [15332424](https://pubmed.ncbi.nlm.nih.gov/15332424/)]
21. Proot IM, Abu-Saad HH, ter Meulen RH, Goldsteen M, Spreeuwenberg C, Widdershoven GA. The needs of terminally ill patients at home: directing one's life, health and things related to beloved others. *Palliat Med* 2004 Jan;18(1):53-61. [doi: [10.1191/0269216304pm818oa](https://doi.org/10.1191/0269216304pm818oa)] [Medline: [14982208](https://pubmed.ncbi.nlm.nih.gov/14982208/)]
22. Creswell J, Clark V. *Designing And Conducting Mixed Methods Research*. Third Edition. Thousand Oaks, CA: Sage Publications; 2017.
23. Riffin C, Pillemer K, Chen EK, Warmington M, Adelman RD, Reid MC. Identifying key priorities for future palliative care research using an innovative analytic approach. *Am J Public Health* 2015 Jan;105(1):e15-e21 [FREE Full text] [doi: [10.2105/AJPH.2014.302282](https://doi.org/10.2105/AJPH.2014.302282)] [Medline: [25393169](https://pubmed.ncbi.nlm.nih.gov/25393169/)]
24. Schulte V, Steinebach C. *Innovative Palliative Care: Für eine neue Kultur der Pflege, Medizin und Betreuung*. 1. Aufl. Bern: Huber; 2014.
25. Shi K, Will C, Steigleder T, Michler F, Weigel R, Ostgathe C, et al. A Contactless System for Continuous Vital Sign Monitoring in Palliative and Intensive Care. In: *Proceedings of the 2018 Annual IEEE International Systems Conference*. 2018 Presented at: SysCon'18; April 23-26, 2018; Vancouver, BC, Canada. [doi: [10.1109/SYSCON.2018.8369507](https://doi.org/10.1109/SYSCON.2018.8369507)]
26. Finlay GD, Rothman MJ, Smith RA. Measuring the modified early warning score and the Rothman index: advantages of utilizing the electronic medical record in an early warning system. *J Hosp Med* 2014 Feb;9(2):116-119 [FREE Full text] [doi: [10.1002/jhm.2132](https://doi.org/10.1002/jhm.2132)] [Medline: [24357519](https://pubmed.ncbi.nlm.nih.gov/24357519/)]
27. Bruera E, Kuehn N, Miller MJ, Selmsler P, Macmillan K. The Edmonton Symptom Assessment System (ESAS): a simple method for the assessment of palliative care patients. *J Palliat Care* 1991;7(2):6-9. [doi: [10.1177/082585979100700202](https://doi.org/10.1177/082585979100700202)] [Medline: [1714502](https://pubmed.ncbi.nlm.nih.gov/1714502/)]
28. Weitzner MA, Jacobsen PB, Wagner H, Friedland J, Cox C. The Caregiver Quality of Life Index-Cancer (CQOLC) scale: development and validation of an instrument to measure quality of life of the family caregiver of patients with cancer. *Qual Life Res* 1999;8(1-2):55-63. [doi: [10.1023/a:1026407010614](https://doi.org/10.1023/a:1026407010614)] [Medline: [10457738](https://pubmed.ncbi.nlm.nih.gov/10457738/)]
29. Connell T, Fernandez RS, Tran D, Griffiths R, Harlum J, Agar M. Quality of life of community-based palliative care clients and their caregivers. *Palliat Support Care* 2013 Aug;11(4):323-330. [doi: [10.1017/S1478951512000260](https://doi.org/10.1017/S1478951512000260)] [Medline: [23083944](https://pubmed.ncbi.nlm.nih.gov/23083944/)]
30. Schag CC, Heinrich RL, Ganz PA. Karnofsky performance status revisited: reliability, validity, and guidelines. *J Clin Oncol* 1984 Mar;2(3):187-193. [doi: [10.1200/JCO.1984.2.3.187](https://doi.org/10.1200/JCO.1984.2.3.187)] [Medline: [6699671](https://pubmed.ncbi.nlm.nih.gov/6699671/)]
31. Schreier M. *Qualitative Content Analysis In Practice*. London: Sage Publications; 2012.
32. Boyatzis RE. *Transforming Qualitative Information: Thematic Analysis And Code Development*. Thousand Oaks, CA: Sage Publications; 1998.

Abbreviations

MPCT: mobile palliative care team

Edited by C Hoving; submitted 26.03.19; peer-reviewed by K Appleton, E Jablonski; comments to author 18.04.19; revised version received 29.08.19; accepted 06.09.19; published 28.11.19.

Please cite as:

Fringer A, Arrer E, Maier E, Schnepf W, Ulmer T

Development of an Early Warning System to Prevent Crises in the Palliative Home Care Setting of Patients and Their Informal Caregivers: Protocol for a Mixed Method Study

JMIR Res Protoc 2019;8(11):e13933

URL: <http://www.researchprotocols.org/2019/11/e13933/>

doi: [10.2196/13933](https://doi.org/10.2196/13933)

PMID: [31778114](https://pubmed.ncbi.nlm.nih.gov/31778114/)

©André Fringer, Eleonore Arrer, Edith Maier, Wilfried Schnepf, Tom Ulmer. Originally published in *JMIR Research Protocols* (<http://www.researchprotocols.org>), 28.11.2019. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in *JMIR Research Protocols*, is properly cited. The complete bibliographic

information, a link to the original publication on <http://www.researchprotocols.org>, as well as this copyright and license information must be included.

Original Paper

Nutritional Assessment of Childhood Cancer Survivors (the Swiss Childhood Cancer Survivor Study-Nutrition): Protocol for a Multicenter Observational Study

Fabiën Naomi Belle^{1,2}, PhD; Maja Beck Popovic³, MD, PD; Marc Ansari^{4,5}, MD, PD; Maria Otth¹, MD; Claudia Elisabeth Kuehni^{1,6}, MSc, MD; Murielle Bochud², MD, PhD

¹Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland

²Center for Primary Care and Public Health (Unisanté), University of Lausanne, Lausanne, Switzerland

³Pediatric Hematology-Oncology Unit, Lausanne University Hospital, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland

⁴Pediatric Onco-Hematology Unit, Geneva University Hospital, Geneva, Switzerland

⁵CANSEARCH Research Laboratory, Geneva Medical School, Geneva, Switzerland

⁶Children's University Hospital of Bern, University of Bern, Bern, Switzerland

Corresponding Author:

Fabiën Naomi Belle, PhD

Institute of Social and Preventive Medicine

University of Bern

Mittelstrasse 43

Bern, 3012

Switzerland

Phone: 41 31 631 33 47

Email: fabien.belle@ispm.unibe.ch

Abstract

Background: Childhood cancer survivors are at high risk of developing adverse late health effects. Poor nutritional intake may contribute to this risk, but information about dietary intake is limited.

Objective: This study will assess childhood cancer survivors' dietary intake and compare two dietary assessment tools: a self-reported food frequency questionnaire, and dietary measurements from urine spot samples.

Methods: In a substudy of the Swiss Childhood Cancer Survivor Study (SCCSS), SCCSS-Nutrition, we assessed childhood cancer survivors' dietary intake via a validated food frequency questionnaire. We sent a urine spot collection kit to a subset of 212 childhood cancer survivors from the French-speaking region of Switzerland to analyze urinary sodium, potassium, urea, urate, creatinine, and phosphate content. We will compare the food frequency questionnaire results with the urine spot analyses to quantify childhood cancer survivors' intake of various nutrients. We collected data between March 2016 and March 2018.

Results: We contacted 1599 childhood cancer survivors, of whom 919 (57.47%) returned a food frequency questionnaire. We excluded 11 childhood cancer survivors who were pregnant or were breastfeeding, 35 with missing dietary data, and 71 who had unreliable food frequency questionnaire data, resulting in 802 childhood cancer survivors available for food frequency questionnaire analyses. To a subset of 212 childhood cancer survivors in French-speaking Switzerland we sent a urine spot collection kit, and 111 (52.4%) returned a urine sample. We expect to have the results from analyses of these samples in mid-2019.

Conclusions: The SCCSS-Nutrition study has collected in-depth dietary data that will allow us to assess dietary intake and quality and compare two dietary assessment tools. This study will contribute to the knowledge of nutrition among childhood cancer survivors and is a step toward surveillance guidelines and targeted nutritional recommendations for childhood cancer survivors in Switzerland.

Trial Registration: ClinicalTrials.gov NCT03297034; <https://clinicaltrials.gov/ct2/show/NCT03297034>

International Registered Report Identifier (IRRID): DERR1-10.2196/14427

(*JMIR Res Protoc* 2019;8(11):e14427) doi:[10.2196/14427](https://doi.org/10.2196/14427)

KEYWORDS

child; cancer survivors; urine specimen collection; diet surveys; food frequency questionnaire; Swiss Childhood Cancer Registry; Switzerland

Introduction

Background

Survival rates among childhood cancer patients have increased markedly and, due to new and improved treatments, now exceed 80% [1]. As patients live longer, strategies to promote long-term overall health of childhood cancer survivors (CCSs) become increasingly important. Complications and disabilities from treatment, such as chemotherapy and radiotherapy, cancer recurrence, or both, can affect morbidity and mortality many years after a cancer diagnosis [1,2]. The St. Jude Lifetime Cohort Study showed that a large proportion of CCSs experience late effects 25 years after diagnosis; 95% have had at least one chronic health condition and 80% have had a severe, life-threatening, or disabling condition [3]. Frequently reported late effects include cardiovascular diseases (CVDs), endocrine disorders, musculoskeletal problems, and secondary malignancies [2]. Such late effects may be increased by lifestyle habits and choices. Accumulating research in CCSs shows that late effects such as type 2 diabetes, metabolic syndrome, and CVD can be reduced through diet adaptations, weight management, and physical activity [4-7]. Nutrition is an important determinant of the health of CCSs.

However, little is known about the dietary habits of CCSs [8,9], and studies have shown that CCSs adhere poorly to dietary recommendations [10-13]. No evidence-based nutritional guidelines exist specifically for CCSs. Nutritional information can be obtained from, for example, self-reported food frequency questionnaires (FFQs) or 24-hour dietary recalls, whereas assays of biochemical indicators—nutrients or their metabolic products—in tissues or fluids, such as nails, feces, blood, and urine, can more directly quantify intake of nutrients [14]. Since self-reported dietary assessment tools are limited by misreporting and recall bias, which can lead to over- or underreporting, results need to be handled with caution [14]. This holds especially true for dietary assessment using FFQs; underestimation of dietary intake in 16 CCSs was greater when measured by the Block FFQ than by repeated 24-hour dietary recalls, validated by the doubly labelled water method [15]. A Canadian study among 80 CCSs showed that an FFQ could correctly rank CCSs according to their dietary intake when comparing it with 3-day food records [16].

The use of 24-hour urine samples to assess alkaline minerals, halide ions, and protein intake can complement self-reported dietary questionnaires, as well as producing nutritional indicators that potentially are more valid than data from questionnaires [14]. But collection of 24-hour urine samples can be a considerable burden for survivors, and it risks bias due to undetected incomplete sample collection and low response rates. Recent research has focused on the utility of estimating 24-hour urinary output from single spot urine samples [17]. These samples are less burdensome for participants and are more easily obtained by researchers, and potential under- or overcollection

is irrelevant [14,17]. By adjusting for parameters such as age, sex, height, and weight, and by taking urinary creatinine into account, samples can yield interpretable results [18]. This makes spot urine samples a practical and cost-saving alternative to collection of 24-hour urine samples. To the best of our knowledge, neither spot urine nor 24-hour urine samples have been studied in CCSs to assess dietary intake.

This study will, to our knowledge, for the first time obtain insight into the dietary intake of CCSs from self-reported FFQs and urinary measurements. It will compare the 2 dietary assessment tools and determine whether spot urine collection from CCSs is feasible.

Objectives

This study will generate detailed data on the diets of Swiss long-term CCSs. The study's main objective is to compare the self-reported FFQ dietary assessment tool with assays of urine spot samples. This will give us more information about the reliability of the FFQ, the actual dietary intake of CCSs, and potential associations between dietary intake and the occurrence of somatic late effects. A secondary objective is to evaluate this study itself—that is, to determine the response rate, cost, and CCS reactions of the self-reported FFQ and the dietary markers in spot urine of CCSs.

Methods

Study Design

This is a multicenter, observational study incorporated into the Swiss Childhood Cancer Survivor Study (SCCSS). The SCCSS is a population-based, long-term follow-up study of all childhood cancer patients registered in the Swiss Childhood Cancer Registry (SCCR [19]) with leukemia, lymphoma, central nervous system tumors, malignant solid tumors, or Langerhans cell histiocytosis diagnosed in Switzerland; who were under the age of 21 years at the time of diagnosis; who survived 5 years or more after the initial diagnosis of cancer; and who were alive at the time of the study [20-22]. This study is registered at clinicaltrials.gov (NCT03297034).

Eligibility

CCSs were eligible to participate in the SCCSS-Nutrition study if they had childhood cancer diagnosed between 1976 and 2005, completed a baseline SCCSS questionnaire between 2007 and 2013 [20], and were 18 years of age or older at the time of the follow-up survey in 2017. All CCSs who were enrolled in SCCSS-Nutrition received a follow-up questionnaire including an FFQ. CCSs living in the French-speaking part of Switzerland who returned the questionnaire were invited to provide a urine spot sample. Exclusion criteria were being pregnant or lactating at the time of the study, or having missing or implausible dietary intake information reported in the FFQ [23].

Recruitment

We traced the addresses of all adult CCSs who had completed the baseline questionnaire (n=2527 CCSs) between 2007 and 2013 [20]. Among these, 1749 were 18 years old or older at the time of the survey and thus were eligible for the follow-up questionnaire. In February 2017, we traced 1599 CCSs and sent them a follow-up questionnaire (Figure 1). Nonresponders received a reminder after 8 weeks (Figure 2). If they again did not respond, we sent a second reminder. Finally, 919 (57.47%) CCSs completed the FFQ. We excluded 11 survivors who were pregnant or lactating, 35 who did not report their dietary intake, 71 who had implausible dietary intake data (<850 kcal or >4500 kcal per day) [24], and 581 who lived outside the French-speaking region in Switzerland. We thus sent an

information letter signed by the project leader to 221 CCSs who lived in the French-speaking part of Switzerland and asked them for informed consent to provide a urine spot sample. Among these CCSs, 8 were no longer traceable, 1 was abroad, and 15 declined to participate. We sent urine collection kits to the CCSs who agreed to participate and asked them to collect a first morning sample within 2 weeks and post the sample by mail within 24 hours to the pediatric hematology-oncology unit of the University Hospital of Canton Vaud (Centre Hospitalier Universitaire Vaudois [CHUV]; Lausanne, Switzerland). Among these 212 CCS participants, 111 (52.4%) returned a sample. All 111 urine samples met the study protocol and will be available for dietary intake assessment comparison. Those enrolled received no compensation.

Figure 1. Response rates in the Swiss Childhood Cancer Survivor Study (SCCSS)-Nutrition study. The SCCSS-Nutrition study is subdivided into a food frequency questionnaire assessment (FFQ; gray) and a urine spot collection (black).

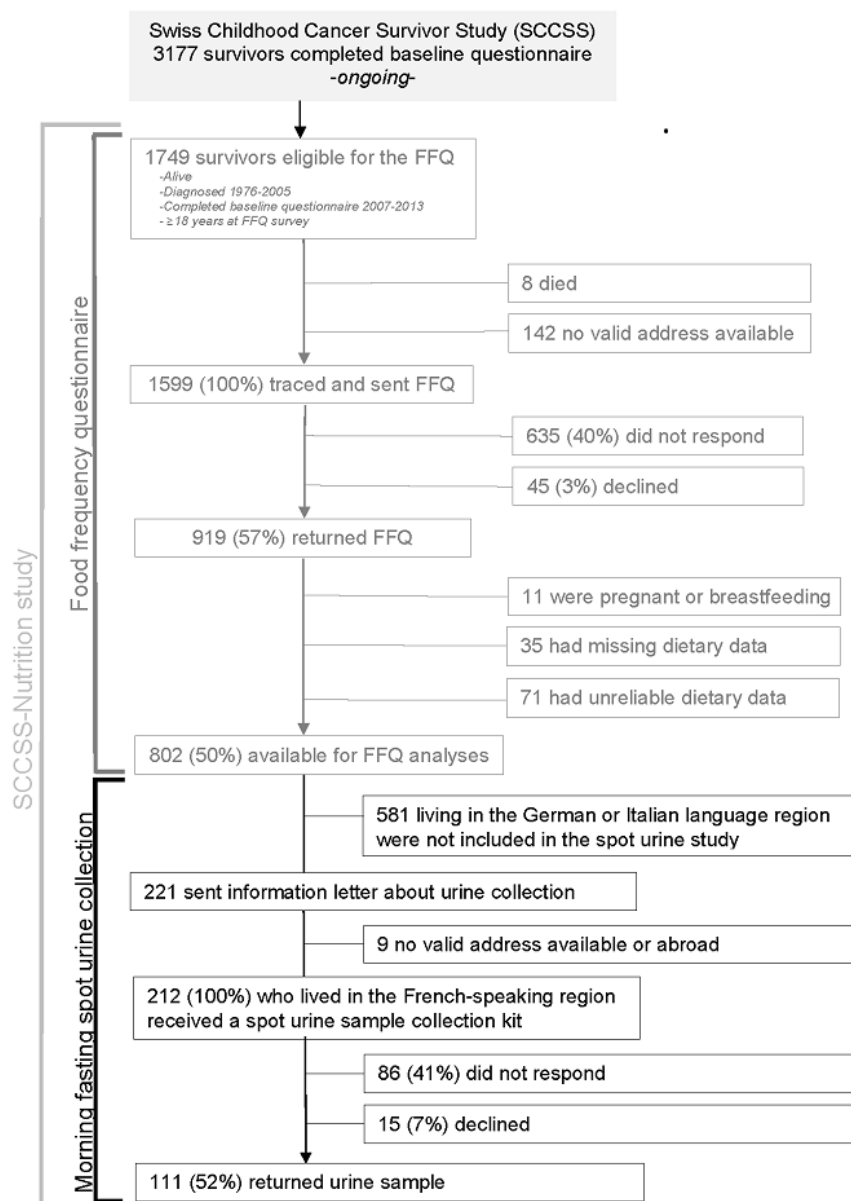
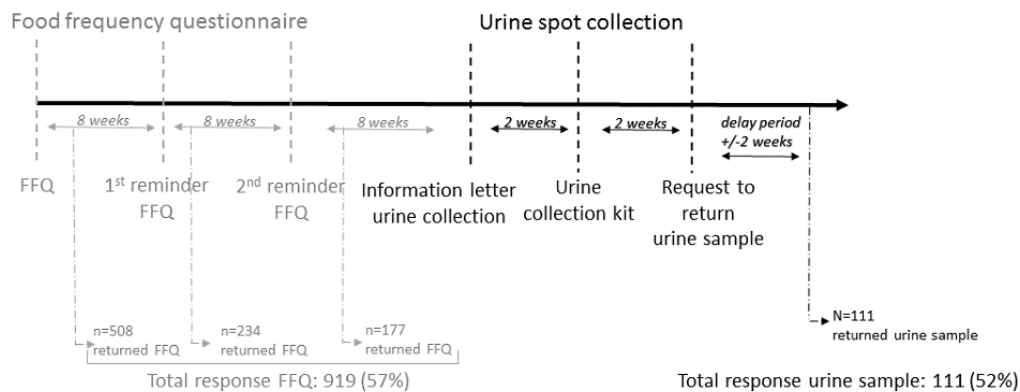


Figure 2. Timelines and response rates of food frequency questionnaire (FFQ) assessment and urine spot collection.

Data Collection

Baseline and Follow-Up Questionnaire

From baseline or follow-up questionnaires, we collected CCSs' data on sex, age at survey, language region in Switzerland in which they lived, country of birth, educational level, living situation, physical activity, smoking status, and height and weight to calculate body mass index. The baseline questionnaire included core questions from the US and UK CCS studies [25,26], with further questions from the Swiss Health Survey and the Swiss census of health-related behaviors and sociodemographic measures [27,28]. The main domains covered by the questionnaire were quality of life, somatic health, fertility, current medication and health services use, psychological distress, health behaviors, and socioeconomic status. The follow-up questionnaire repeated baseline questions on quality of life, somatic health, health behaviors, and socioeconomic status, with the addition of an FFQ to assess dietary intake in detail [29,30].

Food Frequency Questionnaire

We assessed CCSs' dietary intake, including information on portion sizes, with a self-administered, semiquantitative FFQ [31,32] (Multimedia Appendix 1). The FFQ was originally developed and validated against 24-hour dietary recalls for the adult Swiss population who are French speaking [29,31,33,34]. It solicits information on consumption frequency and portion sizes during the 4 previous weeks for 97 fresh and prepared food items organized into 12 food groups (dietary supplements not included). Consumption frequencies range from "never

during the last 4 weeks" to "2 or more times per day," and portion sizes are recorded as equal to, or smaller or larger than, a reference size. The reference portions were defined as common household measures representing the median portion size of a previous validation study performed with 24-hour dietary recalls [29]. The "smaller" and "larger" portions represented the first and fourth quartiles of this distribution. We used the French Information Center on Food Quality (Maisons-Alfort Cedex, France) food-composition table to convert the food portions into macro- and micronutrients [35].

Urine Collection

CCSs received a home specimen collection kit including an information sheet on how to perform first morning urine spot collection, a 50 mL plastic specimen tube with a screw-on lid, a sealed plastic bag, and a bubble-lined return envelope with postage-paid labels addressed to the pediatric hematology-oncology unit of CHUV. We asked CCSs to collect a first morning urine sample, filling the tube up to 40 mL, and to seal the tube and write the sample date and time on the lid. We asked CCSs not to mark personal information on the tube to preserve confidentiality, and to send their sample by post. The medical staff of the pediatric hematology-oncology unit cooled the urine spot samples as soon as they received them. They divided the samples into one 8-mL aliquot for direct urine chemistry and nine 3-mL aliquots for biobank storage; the 8-mL sample was sent within 1 hour to the CHUV laboratory for analyses. Levels of potassium, sodium, phosphate, urate, urea, and creatinine were measured using routine laboratory procedures (Table 1). The 3-mL urine samples were frozen at -80°C and stored in a biobank at CHUV for later analyses.

Table 1. Primary and secondary end points and outcomes of interest.

| End points and outcomes | Method | Quality promotion | (Expected) time point or window |
|--|--|--------------------------------|---|
| Primary | | | |
| Detailed dietary intake, macro- and micronutrients | Dietary intake assessed by a validated FFQ ^a providing information on consumption frequency and portion sizes during the 4 previous weeks for 97 fresh and prepared food items organized in 12 food groups. | Validated FFQ | CCSs ^b were expected to fill in and return the FFQ within 8 weeks. In case of nonresponse, a first and second reminder were sent. |
| Urinary measurements | Laboratory methods: <ul style="list-style-type: none"> • Sodium: indirect potentiometry • Potassium: indirect potentiometry • Urea: urease • Urate: uricase • Creatinine: Jaffe reaction • Phosphate: phosphomolybdate | Standard laboratory procedures | Analyses were performed together with routine analyses in the hospital laboratory of Centre Hospitalier Universitaire Vaudois with Cobas 8000 (Roche Diagnostics). Analyses were performed during the whole study period. |
| Secondary | | | |
| General response rate | The SCCSS ^c tracking system tracked the number of CCSs who did not respond or declined participation. | N/A ^d | Evaluation after finalizing the study. |
| Costs | Recording of costs, eg, laboratory, mailing, printing, urine collection sample kits. | N/A | Midterm evaluation and after finalizing the study. |
| Participants' reactions | Recording CCSs' reactions by telephone, emails, or letter. | N/A | Evaluation after finalizing the study. |

^aFFQ: food frequency questionnaire.

^bCCS: childhood cancer survivor.

^cSCCSS: Swiss Childhood Cancer Survivor Study.

^dN/A: not applicable.

Data Management

Coding

We gave each participant an 8-digit identification (ID) code number to maintain anonymity. We used these ID codes in lieu of patient names for all data and urine spot samples. Data labelled with participant ID codes are stored on encrypted devices or secured servers. All participant data and biological samples are strictly confidential, and disclosure to third parties is prohibited. The coding key is stored at the Institute of Social and Preventive Medicine (ISPM), University of Bern, Bern, Switzerland, and is only available to authorized personnel.

Storage

All biomedical material is archived for 10 years at CHUV. In case there is no intention for use or a participant withdraws consent, the respective biological material will be destroyed. FFQ answers and urine spot laboratory results will be archived on servers of the ISPM, Lausanne, Lausanne, Switzerland, and ISPM, Bern for at least 10 years. Timelines that record and archive outcomes are in line with Swiss regulation. All results will be archived at and analyzed by ISPM, Bern as a nested study of the SCCSS.

Statistical Analyses

We will include all CCSs who provided reliable dietary intake information and were neither pregnant nor lactating during the survey for FFQ analyses. Table 1 indicates the primary and secondary end points and outcomes of interest of the

SCCSS-Nutrition study. We will evaluate whether CCSs meet dietary recommendations for Germany, Austria, and Switzerland [36]. We will compare mean intake with the recommended intake or, when not available, the adequate intake. We will calculate mean intake based on age and sex recommendations weighted by the age and sex distribution of the study population. Nutritional goals will be set at 100, where the mean intake meets the recommended or adequate intake. Total energy intake will be calculated including calories from alcohol consumption. We will calculate correlation coefficients to examine the strength and direction of the associations between the FFQ and urinary spot measurements. To validate the agreement between the 2 dietary assessment tools, we will perform cross-classification analyses to investigate whether the 2 dietary assessment tools rank CCSs' dietary intake similarly. We will calculate the proportion of CCSs correctly classified in the same or contiguous category or in the opposite category (misclassified). We will use Bland-Altman plots to assess the level of agreement between the FFQ and the urine spot samples at the CCS group level. We will plot the difference between the 2 measurements against the mean of the 2 measurements for each CCS. We will use Stata (version 14; StataCorp LLC) for all analyses.

Ethics

The cantonal ethics committee Commission cantonal d'éthique de la Recherche sur l'être humain, Lausanne approved the SCCSS-Nutrition study in March 2016. In July 2017, the cantonal ethics committee Geneva Commission Cantonal d'éthique de la Recherche approved the study with an

amendment (protocol of both approvals: 2016-00031). Ethical approval of the SCCR and the SCCSS questionnaires was granted by the Ethics Committee of the Canton of Bern (KEK-BE: 166/2014).

Results

Characteristics of Participants and Nonparticipants

Table 2 presents the sociodemographic and lifestyle characteristics of both CCSs who completed the FFQ and those who did not, and those who participated in the collection of urine spot samples. The most common cancer diagnoses among

CCSs completing the FFQ were leukemia, lymphoma, and central nervous system tumors (Table 3). Median age at diagnosis was 10 years (interquartile range 4-14 years) and median time from diagnosis to survey was 26 years (interquartile range 20-32 years). Of the 902 FFQ participants, 99 (12.34%) experienced a relapse.

Costs

The costs of this study have remained within budget (Table 4). Costs include material, shipment of FFQs and urine spot sample collection kits, reminders, data entry, data management, and laboratory urine analyses.

Table 2. Sociodemographic and lifestyle characteristics of participants and nonparticipants in the food frequency questionnaire (FFQ) and the urine spot sample collection.

| Characteristics | FFQ | | Urine spot sample | |
|--|----------------------|--------------------------------------|----------------------|--------------------------------------|
| | Participants (n=802) | Nonparticipants ^a (n=797) | Participants (n=111) | Nonparticipants ^b (n=110) |
| Male sex, n (%) | 401 (50.0) | 443 (55.6) | 49 (44.1) | 53 (48.2) |
| Age at survey (years), n (%) | | | | |
| ≤30 | 248 (30.9) | 328 (41.2) ^c | 26 (23.4) | 44 (40.0) |
| 31-39 | 320 (39.9) | 305 (38.3) | 37 (33.3) | 37 (33.6) |
| ≥40 | 234 (29.2) | 164 (20.6) | 48 (43.2) | 29 (26.4) |
| Country of birth, n (%) | | | | |
| Switzerland | 763 (95.1) | 736 (92.3) | 101 (91.0) | 98 (89.1) |
| Other | 39 (4.9) | 60 (7.5) | 10 (9.0) | 12 (10.9) |
| Missing data | N/A ^d | 1 (0.1) | N/A | N/A |
| Education (highest degree), n (%) | | | | |
| Lower than university | 527 (65.7) | 681 (85.4) ^e | 69 (62.2) | 71 (64.6) |
| University | 270 (33.7) | 98 (12.3) | 42 (37.8) | 39 (35.5) |
| Missing data | 5 (0.6) | 18 (2.3) | N/A | N/A |
| Living situation, n (%) | | | | |
| Alone | 164 (20.4) | 129 (16.2) ^e | 19 (17.1) | 24 (21.8) |
| Other | 634 (79.1) | 655 (82.1) | 91 (82.0) | 86 (78.2) |
| Missing data | 4 (0.5) | 13 (1.6) | 1 (0.9) | N/A |
| Physical activity^f, n (%) | | | | |
| Inactive | 165 (20.6) | 204 (25.6) ^e | 32 (28.8) | 32 (29.1) |
| Active | 628 (78.3) | 572 (71.8) | 76 (68.5) | 77 (70.0) |
| Missing data | 9 (1.1) | 21 (2.6) | 3 (2.7) | 1 (0.9) |
| Smoking status, n (%) | | | | |
| Never | 532 (66.3) | 511 (64.1) ^e | 69 (62.2) | 65 (59.1) |
| Former | 132 (16.5) | 79 (9.9) | 15 (13.5) | 24 (21.8) |
| Current | 128 (16.0) | 207 (26.0) | 25 (22.5) | 21 (19.1) |
| Missing data | 10 (1.3) | N/A | 2 (1.8) | N/A |
| Body mass index at survey (kg/m²), n (%) | | | | |
| Underweight (<18.5) | 39 (4.9) | 57 (7.2) ^e | 7 (6.3) | 3 (2.7) |
| Normal (18.5-24.9) | 490 (61.1) | 500 (62.7) | 76 (68.5) | 67 (60.9) |
| Overweight (25-29.9) | 177 (22.1) | 141 (17.7) | 15 (13.5) | 25 (22.7) |
| Obese (≥30) | 75 (9.4) | 59 (7.4) | 10 (9.0) | 14 (12.7) |
| Missing data | 21 (2.6) | 40 (5.0) | 3 (2.7) | 1 (0.9) |

^aIncludes 635 childhood cancer survivors (CCSs) who did not respond, 45 who declined, 11 who were pregnant or breastfeeding, 35 with missing dietary data, and 71 with unreliable dietary data.

^bIncludes 9 CCSs with no valid address available anymore or who were abroad, 15 who declined, and 86 who did not respond.

^cAge at survey is calculated for FFQ nonparticipants by taking the average participants' date of filling in the questionnaire.

^dN/A: not applicable.

^eBased on information from the Swiss Childhood Cancer Survivor Study baseline questionnaire filled in between 2007 and 2013 by FFQ nonparticipants.

^fActive: ≥150 minutes of moderately intense or 75 minutes of vigorously intense or a combination of moderately and vigorously intense physical activity per week.

Table 3. Clinical characteristics of participants and nonparticipants in the food frequency questionnaire (FFQ) and the urine spot sample collection.

| Characteristics | FFQ | | Urine spot sample | |
|--|----------------------|--------------------------------------|----------------------|--------------------------------------|
| | Participants (n=802) | Nonparticipants ^a (n=797) | Participants (n=111) | Nonparticipants ^b (n=110) |
| ICCC-3^c diagnosis, n (%) | | | | |
| I: Leukemia | 246 (30.7) | 264 (33.1) | 30 (27.0) | 27 (24.6) |
| II: Lymphoma | 173 (21.6) | 139 (17.4) | 30 (27.0) | 30 (27.3) |
| III: CNS ^d tumor | 81 (10.1) | 140 (17.6) | 9 (8.1) | 17 (15.5) |
| IV: Neuroblastoma | 28 (3.5) | 31 (3.9) | 4 (3.6) | 3 (2.7) |
| V: Retinoblastoma | 12 (1.5) | 22 (2.8) | 2 (1.8) | 3 (2.7) |
| VI: Renal tumor | 52 (6.5) | 41 (5.1) | 4 (3.6) | 3 (2.7) |
| VII: Hepatic tumor | 6 (0.8) | 3 (0.4) | 1 (0.9) | 1 (0.9) |
| VIII: Bone tumor | 50 (6.2) | 29 (3.6) | 11 (9.9) | 5 (4.6) |
| IX: Soft tissue sarcoma | 66 (8.2) | 32 (4.0) | 7 (6.3) | 10 (9.1) |
| X: Germ cell tumor | 43 (5.4) | 42 (5.3) | 8 (7.2) | 4 (3.6) |
| XI and XII: Other tumor | 26 (3.2) | 17 (2.1) | 4 (3.6) | 3 (2.7) |
| Langerhans cell histiocytosis | 19 (2.4) | 37 (4.6) | 1 (0.9) | 4 (3.6) |
| Age at diagnosis (years), n (%) | | | | |
| <5 | 251 (31.3) | 262 (32.9) | 28 (25.2) | 29 (26.4) |
| 5-9 | 164 (20.4) | 211 (26.5) | 19 (17.1) | 23 (20.9) |
| 10-14 | 239 (29.8) | 222 (27.9) | 34 (30.6) | 27 (24.6) |
| 15-20 | 148 (18.5) | 102 (12.8) | 30 (27.0) | 31 (28.2) |
| Time since diagnosis (years), median (interquartile range) | 26.1 (20.2-31.7) | N/A ^e | 28.3 (21.0-32.7) | 22.8 (18.5-30.1) |
| History of relapse, n (%) | 99 (12.3) | 107 (13.4) | 18 (16.2) | 15 (13.6) |

^aIncludes 635 childhood cancer survivors (CCSs) who did not respond, 45 who declined, 11 who were pregnant or breastfeeding, 35 with missing dietary data, and 71 with unreliable dietary data.

^bIncludes 9 CCSs with no valid address available anymore or who were abroad, 15 who declined, and 86 who did not respond.

^cICCC3: International Childhood Cancer Classification, Third Edition.

^dCNS: central nervous system.

^eN/A: not applicable.

Table 4. Costs to perform the Swiss Childhood Cancer Survivor Study-Nutrition study.

| Expenses | Costs (US \$) |
|---|---------------|
| Material, eg. (return) envelopes, questionnaires, urine tubes | 6514 |
| Address update for childhood cancer survivors | 20,232 |
| Mailings | 7125 |
| Data entry for food frequency questionnaires | 13,360 |
| Laboratory analyses of urine spot samples | 2908 |
| Ethics committee approval | 602 |
| Total costs | 50,741 |

Childhood Cancer Survivor Reactions

CCSs had varied reactions to the FFQ. The majority of CCSs wanted to participate and welcomed a follow-up questionnaire.

Only a small number of the 1599 CCSs to whom FFQs were sent (n=45, 2.81%) declined to complete the FFQ. Of the 221 CCSs to whom information letters for urine collection were

sent, 15 declined to collect a urine spot sample (Figure 1). All CCSs who declined participation expressed a willingness to participate in future studies. A total of 26 CCSs contacted us by telephone (n=13), email (n=5), or letter (n=8) with questions about the purpose of the study, its setup, eligibility, or another question, or to notify the study team about a delay in FFQ response or urine collection. Overall, the CCSs were supportive and open to participation in the study. We received no angry or aggressive reactions.

We anticipate that the results of the SCCSS-Nutrition study will be available mid-2019.

Discussion

Principal Findings

SCCSS-Nutrition is, to our knowledge, the first study in Switzerland that has collected in-depth dietary data. It will allow researchers to assess dietary intake and quality in CCSs and to compare 2 dietary assessment tools: urine measurements and FFQs. Urine spot sample measurements can quantify nutrient intake objectively and can therefore complement self-reported dietary information from the FFQ.

Unhealthy dietary intake is an important element in the development of chronic morbidities such as type 2 diabetes, metabolic syndrome, and CVD in the general population. Populations with these morbidities are therefore widely recommended to consume a healthy and balanced diet. The extensively investigated Mediterranean diet, with high intakes of fish, fruit, vegetables, legumes, nuts, whole grains, and monounsaturated fats from olive oil, has been shown to reduce, or even prevent, CVD, diabetes, obesity, metabolic syndrome, and cancer in the general population [37-41] and in CCSs [5]. This makes nutrition one of the main determinants of health in the general population, and is particularly relevant for people with additional risk factors, including CCSs. Nevertheless, knowledge about CCSs' dietary intake and their nutritional status is lacking within Switzerland and is limited worldwide.

Strengths and Limitations

This study, nested within the SCCSS, assesses dietary intake information of CCSs and compares 2 dietary assessment tools: the FFQ and dietary measurements from urine spot samples. We found the SCCSS-Nutrition study to be well received and feasible. This is, to our knowledge, the first study to provide detailed dietary information on Swiss CCSs and to demonstrate the feasibility of such a study. With the addition of dietary indicators from urine spot samples, SCCSS-Nutrition makes

further comparison possible. Additionally, we had high response rates for completing the FFQ and collecting urine spot samples. Finally, we have access to detailed sociodemographic data from the SCCSS baseline and follow-up questionnaire, and high-quality clinical information extracted from medical records in the SCCR. This a very rich dataset available for analysis.

Limitations of this study were that some CCSs said the FFQ was too long. This might have influenced CCSs to either under- or overreport dietary intake. Also, we asked CCSs for a single spot urine sample rather than multiple spot samples or a 24-hour urine collection to minimize participation burden. Comparison of the self-reported FFQ data, representing habitual dietary intake over 4 weeks, with urine spot analysis data, indicative of the dietary intake during the day before, should therefore be regarded with caution. Seasonal influences could play a role in the FFQ assessment, as we assessed dietary intake for the past 4 weeks rather than the past year. Finally, the interval between the FFQ assessment and urine spot collection could produce differences in dietary intake due to seasonal influences.

Lessons Learned

Setting up this study provided valuable insight into several methodological and logistic issues. We asked CCSs to return urine samples within 2 weeks and to post their urine samples between Monday and Thursday. This prevented the samples from arriving during the weekend. The time frame of 2 weeks was too short; several CCSs contacted us to ask for an extension. The urine collection tubes had a diameter of 3 cm and did not fit the opening slit of an official Swiss mailbox when the CCSs placed a sample in a sealed plastic bag and a bubble-lined postal return envelope. Given this, the response rate was higher than we expected, and we reached the recruitment target because of the up-to-date address list and personal information of SCCR, and the high motivation of CCSs to participate. Furthermore, including a study center took longer than expected, due to arranging appropriate urine storage within the hospital, and an extra briefing about the potential hazards of CCSs' urine contaminated with chemotherapeutic agents in case of cancer recurrence to safeguard the safety of laboratory staff.

Conclusions

The SCCSS-Nutrition study collected in-depth dietary data that will enable an assessment of dietary intake and dietary quality in CCSs and a comparison of dietary assessment tools. The study will help fill nutrition knowledge gaps and is a first step toward surveillance guidelines and targeted nutritional recommendations in Switzerland.

Acknowledgments

The authors express their gratitude to all childhood cancer survivors for supporting this study. Additionally, we thank Sarah Blanc, Eléna Lemmel, Rosa-Emma Garcia, Rodolfo Lo Piccolo, Sandrine Estoppey-Younes, and the medical staff of CHUV for their support in study setup, recruitment, and urine collection. We thank the study team of the Swiss Childhood Cancer Survivor Study (Carole Dupont, Rahel Kasteler, Rahel Kuonen, Nadine Lötscher, Jana Remlinger, Christina Schindera, Grit Sommer, Nicolas Waespe, and Annette Weiss), the data managers of the Swiss Paediatric Oncology Group (Dr Claudia Althaus, Nadine Assbichler, Pamela Balestra, Heike Baumeler, Nadine Beusch, Dr Pierluigi Brazzola, Susann Drerup, Janine Garibay, Franziska Hochreutener, Monika Imbach, Friedgard Julmy, Heike Markiewicz, Dr Veneranda Mattiolo, Annette Reinberg, Dr Renate

Siegenthaler, Astrid Schiltknecht, Beate Schwenke, and Verena Stahel), and the team of the Swiss Childhood Cancer Registry (Meltem Altun, Erika Brantschen, Katharina Flandera, Elisabeth Kiraly, Verena Pfeiffer, Shelagh Redmond, Julia Ruppel, and Ursina Roder). Finally, we would like to thank Christopher Ritter for editorial assistance.

This study is supported by Swiss Cancer Research (KLS-3644-02-2015 and KFS-4722-02-2019) and FORCE Foundation. The work of the Swiss Childhood Cancer Registry is supported by the Swiss Paediatric Oncology Group, Schweizerische Konferenz der kantonalen Gesundheitsdirektorinnen und -direktoren, Swiss Cancer Research, Kinderkrebshilfe Schweiz, the Swiss Federal Office of Public Health, and the National Institute for Cancer Epidemiology and Registration.

Authors' Contributions

FB wrote the manuscript, which was modified and adapted by all other authors. MBP and MA were the principal investigators. CEK and MB supported study setup.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Food frequency questionnaire in French.

[\[PDF File \(Adobe PDF File\), 1882 KB - resprot_v8i11e14427_app1.pdf\]](#)

Multimedia Appendix 2

Peer-review report ethical committee.

[\[PDF File \(Adobe PDF File\), 301 KB - resprot_v8i11e14427_app2.pdf\]](#)

References

1. Bhatia S, Armenian SH, Armstrong GT, van Dulmen-den Broeder E, Hawkins MM, Kremer LCM, et al. Collaborative research in childhood cancer survivorship: the current landscape. *J Clin Oncol* 2015 Sep 20;33(27):3055-3064 [FREE Full text] [doi: [10.1200/JCO.2014.59.8052](https://doi.org/10.1200/JCO.2014.59.8052)] [Medline: [26304891](https://pubmed.ncbi.nlm.nih.gov/26304891/)]
2. Bhakta N, Liu Q, Ness KK, Baassiri M, Eissa H, Yeo F, et al. The cumulative burden of surviving childhood cancer: an initial report from the St Jude Lifetime Cohort Study (SJLIFE). *Lancet* 2017 Dec 09;390(10112):2569-2582 [FREE Full text] [doi: [10.1016/S0140-6736\(17\)31610-0](https://doi.org/10.1016/S0140-6736(17)31610-0)] [Medline: [28890157](https://pubmed.ncbi.nlm.nih.gov/28890157/)]
3. Hudson MM, Ness KK, Gurney JG, Mulrooney DA, Chemaitilly W, Krull KR, et al. Clinical ascertainment of health outcomes among adults treated for childhood cancer. *JAMA* 2013 Jun 12;309(22):2371-2381 [FREE Full text] [doi: [10.1001/jama.2013.6296](https://doi.org/10.1001/jama.2013.6296)] [Medline: [23757085](https://pubmed.ncbi.nlm.nih.gov/23757085/)]
4. Zhang FF, Parsons SK. Obesity in childhood cancer survivors: call for early weight management. *Adv Nutr* 2015 Sep;6(5):611-619 [FREE Full text] [doi: [10.3945/an.115.008946](https://doi.org/10.3945/an.115.008946)] [Medline: [26374183](https://pubmed.ncbi.nlm.nih.gov/26374183/)]
5. Tonorezos ES, Robien K, Eshelman-Kent D, Moskowitz CS, Church TS, Ross R, et al. Contribution of diet and physical activity to metabolic parameters among survivors of childhood leukemia. *Cancer Causes Control* 2013 Feb;24(2):313-321 [FREE Full text] [doi: [10.1007/s10552-012-0116-6](https://doi.org/10.1007/s10552-012-0116-6)] [Medline: [23187859](https://pubmed.ncbi.nlm.nih.gov/23187859/)]
6. Smith WA, Li C, Nottage KA, Mulrooney DA, Armstrong GT, Lanctot JQ, et al. Lifestyle and metabolic syndrome in adult survivors of childhood cancer: a report from the St. Jude Lifetime Cohort Study. *Cancer* 2014 Sep 01;120(17):2742-2750 [FREE Full text] [doi: [10.1002/cncr.28670](https://doi.org/10.1002/cncr.28670)] [Medline: [25070001](https://pubmed.ncbi.nlm.nih.gov/25070001/)]
7. Barnea D, Raghunathan N, Friedman DN, Tonorezos ES. Obesity and metabolic disease after childhood cancer. *Oncology (Williston Park)* 2015 Nov;29(11):849-855 [FREE Full text] [Medline: [26568532](https://pubmed.ncbi.nlm.nih.gov/26568532/)]
8. Ladas E. Nutritional counseling in survivors of childhood cancer: an essential component of survivorship care. *Children (Basel)* 2014 Aug 14;1(2):107-118 [FREE Full text] [doi: [10.3390/children1020107](https://doi.org/10.3390/children1020107)] [Medline: [27417470](https://pubmed.ncbi.nlm.nih.gov/27417470/)]
9. Zhang FF, Saltzman E, Must A, Parsons SK. Do childhood cancer survivors meet the diet and physical activity guidelines? A review of guidelines and literature. *Int J Child Health Nutr* 2012;1(1):44-58 [FREE Full text] [doi: [10.6000/1929-4247.2012.01.01.06](https://doi.org/10.6000/1929-4247.2012.01.01.06)] [Medline: [26973721](https://pubmed.ncbi.nlm.nih.gov/26973721/)]
10. Belle F, Wengenroth L, Weiss A, Sommer G, Beck Popovic M, Ansari M, Swiss Paediatric Oncology Group (SPOG). Low adherence to dietary recommendations in adult childhood cancer survivors. *Clin Nutr* 2017 Oct;36(5):1266-1274. [doi: [10.1016/j.clnu.2016.08.012](https://doi.org/10.1016/j.clnu.2016.08.012)] [Medline: [28277304](https://pubmed.ncbi.nlm.nih.gov/28277304/)]
11. Zhang FF, Ojha RP, Krull KR, Gibson TM, Lu L, Lanctot J, et al. Adult survivors of childhood cancer have poor adherence to dietary guidelines. *J Nutr* 2016 Dec;146(12):2497-2505 [FREE Full text] [doi: [10.3945/jn.116.238261](https://doi.org/10.3945/jn.116.238261)] [Medline: [27798341](https://pubmed.ncbi.nlm.nih.gov/27798341/)]
12. Zhang FF, Saltzman E, Kelly MJ, Liu S, Must A, Parsons SK, et al. Comparison of childhood cancer survivors' nutritional intake with US dietary guidelines. *Pediatr Blood Cancer* 2015 Aug;62(8):1461-1467 [FREE Full text] [doi: [10.1002/psc.25521](https://doi.org/10.1002/psc.25521)] [Medline: [25808589](https://pubmed.ncbi.nlm.nih.gov/25808589/)]

13. Berdan CA, Tangney CC, Scala C, Stolley M. Childhood cancer survivors and adherence to the American Cancer Society Guidelines on Nutrition and Physical Activity. *J Cancer Surviv* 2014 Dec;8(4):671-679. [doi: [10.1007/s11764-014-0376-0](https://doi.org/10.1007/s11764-014-0376-0)] [Medline: [24996982](https://pubmed.ncbi.nlm.nih.gov/24996982/)]
14. Willet W. Food Frequency Methods; Biochemical Indicators of Dietary Intake. In: *Nutritional Epidemiology. Monographs in Epidemiology and Biostatistics*. 2nd edition. New York, NY: Oxford University Press - Oxford New York; 1998.
15. Zhang FF, Roberts SB, Must A, Wong WW, Gilhooly CH, Kelly MJ, et al. Assessing dietary intake in childhood cancer survivors: food frequency questionnaire versus 24-hour diet recalls. *J Pediatr Gastroenterol Nutr* 2015 Oct;61(4):499-502 [FREE Full text] [doi: [10.1097/MPG.0000000000000826](https://doi.org/10.1097/MPG.0000000000000826)] [Medline: [25883059](https://pubmed.ncbi.nlm.nih.gov/25883059/)]
16. Morel S, Portolese O, Chertouk Y, Leahy J, Bertout L, Laverdière C, et al. Development and relative validation of a food frequency questionnaire for French-Canadian adolescent and young adult survivors of acute lymphoblastic leukemia. *Nutr J* 2018 Apr 21;17(1):45 [FREE Full text] [doi: [10.1186/s12937-018-0355-9](https://doi.org/10.1186/s12937-018-0355-9)] [Medline: [29679986](https://pubmed.ncbi.nlm.nih.gov/29679986/)]
17. Huang L, Crino M, Wu JHY, Woodward M, Barzi F, Land M, et al. Mean population salt intake estimated from 24-h urine samples and spot urine samples: a systematic review and meta-analysis. *Int J Epidemiol* 2016 Feb;45(1):239-250. [doi: [10.1093/ije/dyv313](https://doi.org/10.1093/ije/dyv313)] [Medline: [26796216](https://pubmed.ncbi.nlm.nih.gov/26796216/)]
18. Mente A, O'Donnell MJ, Dagenais G, Wielgosz A, Lear SA, McQueen MJ, et al. Validation and comparison of three formulae to estimate sodium and potassium excretion from a single morning fasting urine compared to 24-h measures in 11 countries. *J Hypertens* 2014 May;32(5):1005-14; discussion 1015. [doi: [10.1097/HJH.000000000000122](https://doi.org/10.1097/HJH.000000000000122)] [Medline: [24569420](https://pubmed.ncbi.nlm.nih.gov/24569420/)]
19. Swiss Childhood Cancer Registry. Bern, Switzerland: Institute of Social and Preventive Medicine, University of Bern; 2019. URL: <https://www.childhoodcancerregistry.ch> [accessed 2019-09-17]
20. Kuehni CE, Rueegg CS, Michel G, Rebholz CE, Strippoli MF, Niggli FK, Swiss Paediatric Oncology Group (SPOG). Cohort profile: the Swiss childhood cancer survivor study. *Int J Epidemiol* 2012 Dec;41(6):1553-1564. [doi: [10.1093/ije/dyr142](https://doi.org/10.1093/ije/dyr142)] [Medline: [22736394](https://pubmed.ncbi.nlm.nih.gov/22736394/)]
21. Michel G, von der Weid NX, Zwahlen M, Adam M, Rebholz CE, Kuehni CE, Swiss Childhood Cancer Registry, Swiss Paediatric Oncology Group (SPOG) Scientific Committee. The Swiss Childhood Cancer Registry: rationale, organisation and results for the years 2001-2005. *Swiss Med Wkly* 2007 Sep 08;137(35-36):502-509. [doi: [10.7892/boris.22081](https://doi.org/10.7892/boris.22081)] [Medline: [17990137](https://pubmed.ncbi.nlm.nih.gov/17990137/)]
22. Michel G, von der Weid NX, Zwahlen M, Redmond S, Strippoli MF, Kuehni CE, Swiss Paediatric Oncology Group (SPOG). Incidence of childhood cancer in Switzerland: the Swiss Childhood Cancer Registry. *Pediatr Blood Cancer* 2008 Jan;50(1):46-51. [doi: [10.1002/pbc.21129](https://doi.org/10.1002/pbc.21129)] [Medline: [17226849](https://pubmed.ncbi.nlm.nih.gov/17226849/)]
23. Willett WC, Howe GR, Kushi LH. Adjustment for total energy intake in epidemiologic studies. *Am J Clin Nutr* 1997 Apr;65(4 Suppl):1220S-1228S; discussion 1229S. [Medline: [9094926](https://pubmed.ncbi.nlm.nih.gov/9094926/)]
24. Marques-Vidal P, Vollenweider P, Grange M, Guessous I, Waeber G. Dietary intake of subjects with diabetes is inadequate in Switzerland: the CoLaus study. *Eur J Nutr* 2017 Apr;56(3):981-989. [doi: [10.1007/s00394-015-1146-0](https://doi.org/10.1007/s00394-015-1146-0)] [Medline: [26744301](https://pubmed.ncbi.nlm.nih.gov/26744301/)]
25. Robison LL, Mertens AC, Boice JD, Breslow NE, Donaldson SS, Green DM, et al. Study design and cohort characteristics of the Childhood Cancer Survivor Study: a multi-institutional collaborative project. *Med Pediatr Oncol* 2002 Apr;38(4):229-239. [doi: [10.1002/mpo.1316](https://doi.org/10.1002/mpo.1316)] [Medline: [11920786](https://pubmed.ncbi.nlm.nih.gov/11920786/)]
26. Hawkins MM, Lancashire ER, Winter DL, Frobisher C, Reulen RC, Taylor AJ, et al. The British Childhood Cancer Survivor Study: objectives, methods, population structure, response rates and initial descriptive information. *Pediatr Blood Cancer* 2008 May;50(5):1018-1025. [doi: [10.1002/pbc.21335](https://doi.org/10.1002/pbc.21335)] [Medline: [17849473](https://pubmed.ncbi.nlm.nih.gov/17849473/)]
27. Liebherr R, Marquis J, Storni M, Wiedenmayer G. *Gesundheit und Gesundheitsverhalten in der Schweiz 2007 Schweizerische Gesundheitsbefragung*. Neuchâtel, Switzerland: Neuchâtel Bundesamt für Statistik; 2010. URL: <https://www.bfs.admin.ch/bfs/de/home/statistiken/gesundheit/erhebungen/sgb.html> [accessed 2019-09-19]
28. Germann U. *Eidgenössische Volkszählung 2000: Abschlussbericht zur Volkszählung 2000*. Neuchâtel, Switzerland: Swiss Federal Statistical Office; Oct 2005:1-114.
29. Morabia A, Bernstein M, Kumanyika S, Sorenson A, Mabilia I, Prodolliet B, et al. [Development and validation of a semi-quantitative food questionnaire based on a population survey]. *Soz Praventivmed* 1994;39(6):345-369. [doi: [10.1007/bf01299666](https://doi.org/10.1007/bf01299666)] [Medline: [7817624](https://pubmed.ncbi.nlm.nih.gov/7817624/)]
30. Bochud M, Chatelan A, Blanco J, Beer-Borst S. Anthropometric characteristics and indicators of eating and physical activity behaviors in the Swiss adult population: results from menuCH 2014-2015. Report on behalf of the Federal Office of Public Health and the Food Safety and Veterinary Office. Contract Nr. OFSP 16.010537/204.0001/-1476 and contract Nr. FSVO 071400. Bern, Switzerland: Swiss Federal Food Safety and Veterinary Office; 2017. URL: <https://www.blv.admin.ch/dam/blv/de/dokumente/lebensmittel-und-ernaehrung/ernaehrung/menuch-bericht.pdf.download.pdf/menuch-bericht.pdf> [accessed 2019-09-30]
31. Bernstein L, Huot I, Morabia A. Amélioration des performances d'un questionnaire alimentaire semi-quantitatif comparé à un rappel des 24 heures [Improvement of the effectiveness of a food frequency questionnaire compared with a 24 hour recall survey]. *Santé Publique* 1995;7(4):403-413.

32. Bernstein M, Morabia A, Costanza MC, Landis JR, Ross A, Flandre P, et al. [Nutritional balance of the diet of the adult residents of Geneva]. *Soz Praventivmed* 1994;39(6):333-344. [doi: [10.1007/bf01299665](https://doi.org/10.1007/bf01299665)] [Medline: [7817623](https://pubmed.ncbi.nlm.nih.gov/7817623/)]
33. Beer-Borst S, Costanza MC, Pechère-Bertschi A, Morabia A. Twelve-year trends and correlates of dietary salt intakes for the general adult population of Geneva, Switzerland. *Eur J Clin Nutr* 2009 Feb;63(2):155-164. [doi: [10.1038/sj.ejcn.1602922](https://doi.org/10.1038/sj.ejcn.1602922)] [Medline: [17928805](https://pubmed.ncbi.nlm.nih.gov/17928805/)]
34. Morabia A, Bernstein M, Héritier S, Ylli A. Community-based surveillance of cardiovascular risk factors in Geneva: methods, resulting distributions, and comparisons with other populations. *Prev Med* 1997;26(3):311-319. [doi: [10.1006/pmed.1997.0146](https://doi.org/10.1006/pmed.1997.0146)] [Medline: [9144755](https://pubmed.ncbi.nlm.nih.gov/9144755/)]
35. French Agency for Food, Environmental and Occupational Health & Safety. CIQUAL French food composition table version 2017. Maisons-Alfort Cedex, France: Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail; 2017. URL: <https://ciqual.anses.fr/> [accessed 2019-07-08]
36. D-A-CH-Referenzwerte für die Nährstoffzufuhr, 2. Auflage. Bonn, Germany: Deutsche Gesellschaft für Ernährung, Österreichische Gesellschaft für Ernährung, Schweizerische Gesellschaft für Ernährung; 2015.
37. Widmer RJ, Flammer AJ, Lerman LO, Lerman A. The Mediterranean diet, its components, and cardiovascular disease. *Am J Med* 2015 Mar;128(3):229-238 [FREE Full text] [doi: [10.1016/j.amjmed.2014.10.014](https://doi.org/10.1016/j.amjmed.2014.10.014)] [Medline: [25447615](https://pubmed.ncbi.nlm.nih.gov/25447615/)]
38. Estruch R, Martínez-González MA, Corella D, Salas-Salvadó J, Ruiz-Gutiérrez V, Covas MI, PREDIMED Study Investigators. Effects of a Mediterranean-style diet on cardiovascular risk factors: a randomized trial. *Ann Intern Med* 2006 Jul 04;145(1):1-11. [doi: [10.7326/0003-4819-145-1-200607040-00004](https://doi.org/10.7326/0003-4819-145-1-200607040-00004)] [Medline: [16818923](https://pubmed.ncbi.nlm.nih.gov/16818923/)]
39. Kastorini C, Milionis HJ, Esposito K, Giugliano D, Goudevenos JA, Panagiotakos DB. The effect of Mediterranean diet on metabolic syndrome and its components: a meta-analysis of 50 studies and 534,906 individuals. *J Am Coll Cardiol* 2011 Mar 15;57(11):1299-1313 [FREE Full text] [doi: [10.1016/j.jacc.2010.09.073](https://doi.org/10.1016/j.jacc.2010.09.073)] [Medline: [21392646](https://pubmed.ncbi.nlm.nih.gov/21392646/)]
40. Sofi F, Cesari F, Abbate R, Gensini GF, Casini A. Adherence to Mediterranean diet and health status: meta-analysis. *BMJ* 2008 Sep 11;337:a1344 [FREE Full text] [doi: [10.1136/bmj.a1344](https://doi.org/10.1136/bmj.a1344)] [Medline: [18786971](https://pubmed.ncbi.nlm.nih.gov/18786971/)]
41. Rees K, Hartley L, Flowers N, Clarke A, Hooper L, Thorogood M, et al. 'Mediterranean' dietary pattern for the primary prevention of cardiovascular disease. *Cochrane Database Syst Rev* 2013 Aug 12(8):CD009825. [doi: [10.1002/14651858.CD009825.pub2](https://doi.org/10.1002/14651858.CD009825.pub2)] [Medline: [23939686](https://pubmed.ncbi.nlm.nih.gov/23939686/)]

Abbreviations

CCS: childhood cancer survivor

CHUV: Centre Hospitalier Universitaire Vaudois

CVD: cardiovascular disease

FFQ: food frequency questionnaire

ID: identification

ISPM: Institute of Social and Preventive Medicine

SCCR: Swiss Childhood Cancer Registry

SCCSS: Swiss Childhood Cancer Survivor Study

SCCSS-Nutrition: Swiss Childhood Cancer Survivor Study-Nutrition study

Edited by G Eysenbach; submitted 17.04.19; peer-reviewed by C de Mestral, S Khalatbari, G Michel; comments to author 24.05.19; revised version received 17.07.19; accepted 14.08.19; published 18.11.19.

Please cite as:

Belle FN, Beck Popovic M, Ansari M, Otth M, Kuehni CE, Bochud M

Nutritional Assessment of Childhood Cancer Survivors (the Swiss Childhood Cancer Survivor Study-Nutrition): Protocol for a Multicenter Observational Study

JMIR Res Protoc 2019;8(11):e14427

URL: <http://www.researchprotocols.org/2019/11/e14427/>

doi: [10.2196/14427](https://doi.org/10.2196/14427)

PMID: [31738177](https://pubmed.ncbi.nlm.nih.gov/31738177/)

©Fabiën Belle, Maja Beck Popovic, Marc Ansari, Maria Otth, Claudia Elisabeth Kuehni, Murielle Bochud. Originally published in JMIR Research Protocols (<http://www.researchprotocols.org>), 18.11.2019. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in JMIR Research Protocols, is properly cited. The complete bibliographic information, a link to the original publication on <http://www.researchprotocols.org>, as well as this copyright and license information must be included.

Protocol

Developing Strategies to Reduce Unnecessary Services in Primary Care: Protocol for User-Centered Design Charrettes

Mandi L Klamerus¹, MPH; Laura J Damschroder¹, MPH, MS; Jordan B Sparks¹, MPH; Sarah E Skurla¹, MPH; Eve A Kerr^{1,2,3}, MPH, MD; Timothy P Hofer^{1,2,3}, MSc, MD; Tanner J Caverly^{1,2,3}, MPH, MD

¹Center for Clinical Management Research, Department of Veterans Affairs, Ann Arbor, MI, United States

²Institute for Healthcare Policy and Innovation, University of Michigan, Ann Arbor, MI, United States

³Medical School, University of Michigan, Ann Arbor, MI, United States

Corresponding Author:

Mandi L Klamerus, MPH

Center for Clinical Management Research

Department of Veterans Affairs

University of Michigan North Campus Research Complex, Building 16

2800 Plymouth Road

Ann Arbor, MI, 48109

United States

Phone: 1 9062591009

Fax: 1 7342227503

Email: mandi.klamerus@va.gov

Abstract

Background: Overtreatment and overtesting expose patients to unnecessary, wasteful, and potentially harmful care. Reducing overtreatment or overtesting that has become ingrained in current clinical practices and is being delivered on a routine basis will require solutions that incorporate a deep understanding of multiple perspectives, particularly those on the front lines of clinical care: patients and their clinicians. Design approaches are a promising and innovative way to incorporate stakeholder needs, desires, and challenges to develop solutions to complex problems.

Objective: This study aimed (1) to engage patients in a design process to develop high-level deintensification strategies for primary care (ie, strategies for scaling back or stopping routine medical services that more recent evidence reveals are not beneficial) and (2) to engage both patients and primary care providers in further co-design to develop and refine the broad deintensification strategies identified in phase 1.

Methods: We engaged stakeholders in design charrettes—intensive workshops in which key stakeholders are brought together to develop creative solutions to a specific problem—focused on deintensification of routine overuse in primary care. We conducted the study in 2 phases: a 6.5-hour design charrette with 2 different groups of patients (phase 1) and a subsequent 4-hour charrette with clinicians and a subgroup of phase 1 patients (phase 2). Both phases included surveys and educational presentations related to deintensification. Phase 1 involved several design activities (mind mapping, business origami, and empathy mapping) to help patients gain a deeper understanding of the individuals involved in deintensification. Following that, we asked participants to review hypothetical scenarios where patients, clinicians, or the broader health system context posed a barrier to deintensification and then to brainstorm solutions. The deintensification themes identified in phase 1 were used to guide phase 2. This second phase primarily involved 1 design activity (*WhoDo*). In this activity, patients and clinicians worked together to develop concrete actions that specific stakeholders could take to support deintensification efforts. This activity included identifying barriers to the actions and approaches to overcoming those barriers.

Results: A total of 35 patients participated in phase 1, and 9 patients and 7 clinicians participated in phase 2. The analysis of the deintensification strategies and survey data is currently underway. The results are expected to be submitted for publication in early 2020.

Conclusions: Health care interventions are frequently developed without input from the people who are most affected. The exclusion of these stakeholders in the design process often influences and limits the impact of the intervention. This study employed design charrettes, guided by a flexible user-centered design model, to bring clinicians and patients with differing backgrounds and with different expectations together to cocreate real-world solutions to the complex issue of deintensifying medical services.

International Registered Report Identifier (IRRID): RR1-10.2196/15618

(JMIR Res Protoc 2019;8(11):e15618) doi:[10.2196/15618](https://doi.org/10.2196/15618)

KEYWORDS

quality of health care; user-centered design; design thinking; overtesting; medical overuse; overtreatment

Introduction

Background and Rationale

Many efforts to decrease low-value care (overuse) have focused on avoiding one-time diagnostic procedures or treatments, such as not treating acute sinusitis with antibiotics [1]. However, much of health care involves the *routine* use of medical services for chronic conditions or preventive services. Thus, developing effective strategies to motivate appropriate *deintensification*—the scaling back or stopping of routine medical services that more recent evidence reveals are not beneficial—is a key component of reducing overuse. Examples of deintensifying include decreasing the dose of oral sulfonyleurea medications for diabetes management, reducing the frequency of cancer screening, or stopping routine testing such as carotid artery screening that is no longer supported by the evidence. Deintensifying unneeded and potentially harmful services would improve quality of care by decreasing patient's exposure to harm [2]. Furthermore, deintensification has the potential to improve access to *necessary* services for those who need them the most [3]. Yet, research has shown that deintensification can be rare even when patients are at high risk for net harm [4-6].

Overuse is a *wicked problem* [7] with no easy solutions—and deintensification of routine care may prove even more challenging than attempts to reduce other types of low-value care. A long-standing challenge that applies equally to all types of overuse is that patients and the public may focus on small opportunities for improvement and ignore larger treatment risks [8-10]. In addition, patients and clinicians come to a health care encounter with their own knowledge and beliefs about the degree to which care is beneficial or appropriate, and each individual could be hesitant to deintensify for a variety of reasons [11]. These beliefs may be stronger in the context of long-term ongoing care and represent an even more challenging barrier for reducing this type of care compared with reducing a one-time test or treatment for a patient. Furthermore, without clear guidance on exactly when to deintensify ongoing care [2], lack of time and lack of communication tools may be even more important barriers to appropriate deintensification of services that have been a matter of routine practice for both the patient and clinician [12]. Finally, patients and clinicians are also embedded within larger health system contexts, with motivational structures and processes that influence care decisions. As many existing performance measures incentivize high-intensity care regardless of appropriateness [13], clinicians may feel compelled to continue with inappropriate treatment (eg, intensive glucose management) and be hesitant to adopt newer recommendations to deintensify.

Thus, even more than for reducing other types of low-value care, deintensifying care that is successfully delivered as a

matter of routine for both the patient and clinician will likely require innovative, multifaceted solutions and an in-depth understanding of multiple perspectives—particularly perspectives of those on the frontlines of clinical care: patients and clinicians. Moreover, as deintensifying care presents difficult challenges at multiple levels, simultaneously deploying multiple interventions may be required. We believe that to overcome these challenges, policy makers will need to do more than elicit knowledge and attitudes about deintensification from stakeholders [14]. A promising strategy is to directly engage patients and clinicians in the actual *design* of strategies to implement deintensification. In this paper, we detail the ways in which we employed user-centered design (UCD) activities to develop patient- and clinician-generated solutions, focusing both on digital health and nondigital (ie, traditional or *offline*) health, to the complex problem of deintensifying routine medical care within primary care clinics. Applying design approaches to interventions in health care is becoming more popular, and a recent review found that design processes may result in more practical, acceptable, and effective interventions as compared with other expert-driven methods [15].

Study Objectives

We employed design charrettes, guided by a flexible UCD model, to engage stakeholders in generating innovative strategies to support successful deintensification in primary care. (A charrette is defined as an intensive workshop or session in which key stakeholders are brought together to build off of each other's best ideas and develop creative solutions to a particular problem [16-18].)

The specific aims of the study were as follows:

1. To engage patients in developing high-level deintensification strategies for primary care (patient design charrettes [phase 1]).
2. To engage both patients and primary care providers in further developing and refining the broad deintensification strategies identified in phase 1 (patient-clinician design charrette [phase 2]).

Methods

User-Centered Design Overview

UCD is a discipline that seeks to ground the characteristics of an innovation within in-depth information about the individuals who will use the innovation [16]. Working closely with consultants from the University of Michigan Stamps School of Art & Design [19], we employed a set of design activities to help patients and providers generate strategies for deintensification.

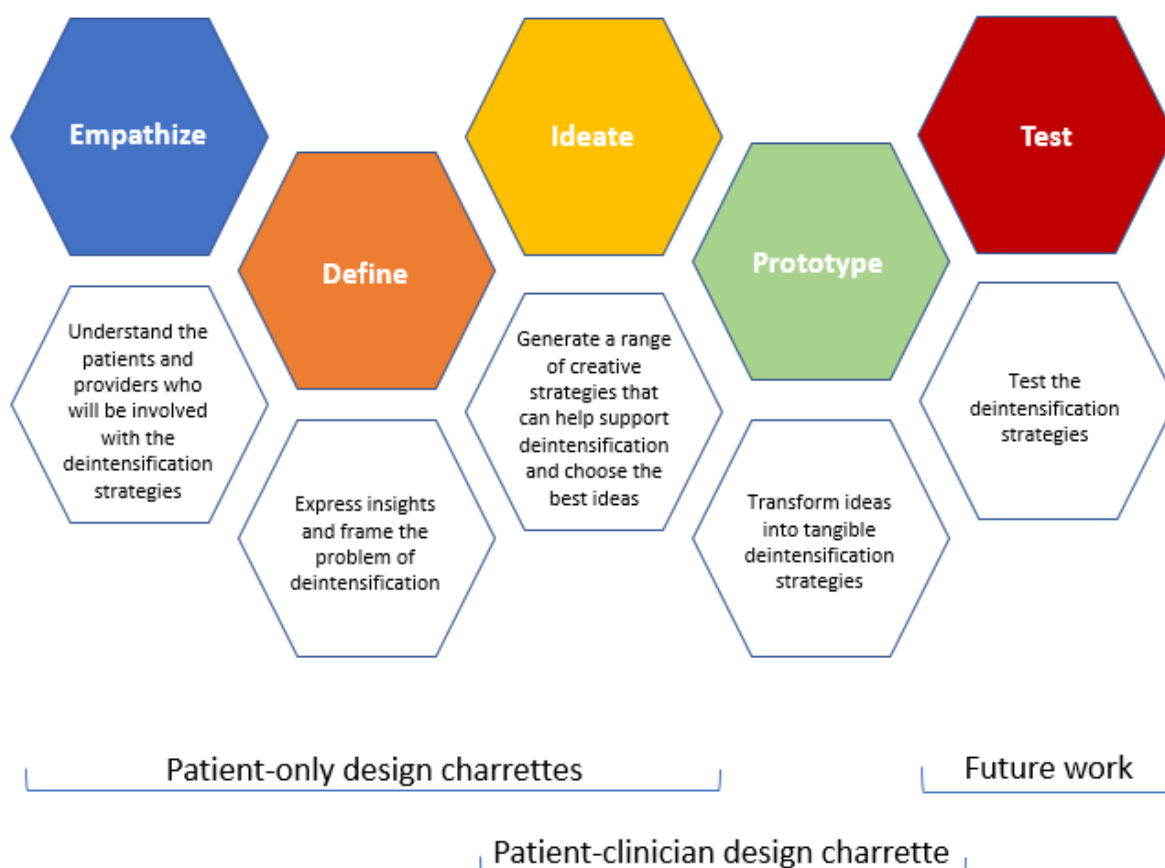
Design approaches prioritize deep empathy for end user desires, needs, and challenges to fully understand a complex problem

in hopes of developing more comprehensive and effective solutions [20]. Design incorporates stakeholder needs and feedback throughout the co-design process and is increasingly being used in a variety of health care settings and conditions [15]. Although many variations of design process models exist, we selected the frequently used model developed by the Hasso Plattner Institute of Design at Stanford (also known as the d.school) to guide our work (Figure 1) [21].

The design model includes the following 5 stages:

1. Empathize: Work to understand the people who you are trying to find a solution for.
2. Define: Clearly articulate the primary problem (ie, what needs to be fixed).
3. Ideate: Brainstorm as many creative solutions as possible.
4. Prototype: Create representations of the solutions identified in the prior stage.
5. Test: Elicit feedback about the prototypes.

Figure 1. Design process model. Figure adapted, with permission, from Stanford d.school.



Potential Benefits of Using a Design Approach to Develop Strategies for Deintensification

Design is a creative process to solve complex problems, such as the one addressed in this study: *stopping or reducing nonbeneficial medical services that have become part of a patient’s routine care*. We felt the following design approaches could support key goals for this project:

1. Participants would first be required to think through how other users involved in the deintensification process (eg, patients, providers, and caregivers) might feel about deintensification before beginning to develop solutions. This would guide participants toward a shared understanding of the users and ultimately more meaningful deintensification strategies.
2. Participants would consider the workflows in primary care, the competing demands and time constraints that providers

confront during a clinic appointment, the preferences and motivations of users (primary care patients, primary care clinicians, and others), and other relevant issues. This would help ensure that the strategies generated would be particularly relevant to the primary care setting.

3. Participants would be encouraged to brainstorm as many creative solutions as possible and to think outside the box. Thus, at the end of the project, we would have an extensive list of potentially innovative strategies for deintensification.

In addition, by allowing us to directly engage those on the front lines of care delivery to generate potential solutions (patients and primary care clinicians), we felt that the strategies generated would be perceived as more practical, feasible, and trustworthy to other patients and clinicians on the front lines, increasing their dissemination and implementation potential.

Study Design Overview

In an earlier part of the study, 37 recommendations for deintensification were validated by an expert panel using a modified RAND/UCLA Appropriateness Method [22]. These recommendations focused on common conditions and preventive care services encountered in adult ambulatory primary care. From these 37 recommendations, we reviewed deintensification recommendations that were rated highly by the expert panel. We selected 3 highly rated recommendations as topics for the charrettes, trying to identify a set of topics that are not only applicable to both genders but which might also elicit different concerns from participants (eg, cancer screening vs medications for cardiovascular prevention and diabetes treatment). The selected recommendations included the following:

1. Recommendation 1: Stop or decrease the dose of diabetes medications in patients aged 65 years and older who have low hemoglobin A1c ($HbA_{1c} < 6.5\%$).
2. Recommendation 2: Do not do screening colonoscopy in average-risk adults aged 80 years or older. In addition, do not conduct screening colonoscopies more often than every 10 years.
3. Recommendation 3: Do not screen for carotid artery stenosis in asymptomatic adult patients without a history of cerebrovascular disease.

We conducted a design charrette with patients (phase 1; July 9, 2018) and repeated the charrette with a new group of patients (phase 1; July 14, 2018). Following these charrettes, 1 patient-clinician design charrette was conducted (phase 2; November 29, 2018). Phase 1 focused on the empathize, define, and ideate stages of our guiding design process model. Phase 2 focused primarily on the ideate and prototype stages. A future phase of the project will focus on the final stage, that is, the test stage.

The local Department of Veterans Affairs (VA) Institutional Review Board approved the study.

Phase 1: Patient Design Charrette

Participant Recruitment

We stratified recruitment by gender and race to ensure a diversity of perspectives. Once a patient had been deemed conditionally eligible (see [Multimedia Appendix 1](#) for inclusion and exclusion criteria), a staff member mailed the patient a recruitment letter explaining the study and informing them that a study team member would be calling to invite them to participate. A copy of the study consent form was included with the mailing. Approximately 1 week after the mailing, staff phoned the patient to explain the study and ascertain their interest in participating. (Staff attempted to contact a patient up to 3 times.)

For each phase 1 charrette, patients were recruited until approximately 30 agreed to participate (10 who met the eligibility criteria for Recommendation 1 plus 20 who met the eligibility criteria for Recommendations 2 and 3).

Approximately 2 weeks before a charrette, relevant materials were mailed to the patients who agreed to participate. These materials included information on the goals of the full research

study, an explanation of what to expect during the charrette, a summary of the 3 recommendations that would be discussed at the session, and a map with driving directions to the session.

Design Charrette Overview

The phase 1 charrette lasted approximately 6.5 hours and was hosted at the VA Center for Clinical Management Research in Ann Arbor, Michigan. The registration process began by obtaining written informed consent. Once consent was obtained, participants were directed to their assigned group; each group focused on 1 of the 3 deintensification recommendations described above; 3 trained facilitators, 1 assigned to each group, guided the participants throughout the day (see [Multimedia Appendix 2](#) for the facilitator's guide). The participants completed a baseline survey ([Multimedia Appendix 3](#)).

Following a brief presentation by the project manager, to highlight the goals of the study and agenda for the day and introductions within groups, 8 design activities were conducted. The selected activities, which are commonly used in design charrettes, were assembled to help participants better understand the needs of clinicians, patients, and other clinical staff/leadership involved in the deintensification process, and to ground design of the deintensification strategies (the final product of the day) in information about the people who will ultimately be involved in carrying these strategies out in practice. Portions of the charrette were audiotaped.

Charrette Activities

The charrette activities supported broad, quick, and open idea generation. Imaginative, fresh, and creative ideas were encouraged (see [Multimedia Appendix 4](#)). Participants were asked to actively listen to others in their group and be open-minded and not critical (ie, "every idea is a good idea"). In addition, participants were instructed to go for volume (ie, "generate as many ideas as possible").

Presentation by a Veterans Affairs Primary Care Physician

A VA primary care provider gave a brief presentation to orient participants to how doctors think about deintensification, highlight some of the challenges in deintensifying, and assure participants that deintensifying is often the right thing to do (ie, "appropriately deintensifying does mean that you are getting the best care possible"). In addition, the presentation highlighted the importance of patient input to develop innovative and effective deintensification strategies.

Presentation by a Veterans Affairs Patient

Following the provider's presentation, a Veteran patient who receives his care at the Ann Arbor VA Medical Center gave a brief presentation to explain deintensification from a patient's perspective, to provide support to the doctor's presentation, and to help make the participants feel comfortable sharing their opinions. The Veteran patient met several times with the study team, before the charrette, to discuss and prepare content for the presentation.

Case Review

Each group was presented with a written case related to their deintensification topic (ie, related to the subgroup's specific recommendation; see [Multimedia Appendix 5](#)). The case included a patient persona, a provider persona, and a fictional story about scaling back, told from both the patient and provider perspectives. The case highlighted some of the reasons why deintensification can be so challenging and provided inspiration for the *gamestorming* UCD activities detailed in the following sections [17,23].

During the case review, the facilitator narrated the patient and clinician personas, and a session participant volunteered to narrate the corresponding story sections. After reading the case, the facilitator asked participants to reflect on what they heard in the case.

Mind Mapping

Mind mapping is a visual thinking tool to help organize the information [17]. Through nonlinear groupings and branches, it connects and organizes information around a central subject, thus allowing participants to better understand the relationships that exist. Mind mapping was used early in the charrette to help jump-start the creative process.

During this activity, session participants identified information that stood out, articulated their interpretation of issues and concepts mentioned in the case, and discussed ideas sparked by the case ([Multimedia Appendix 6](#)). During this discussion, facilitators wrote the group's comments on a flipchart, creating branches to represent words related to the central idea (ie, the story) and sub-branches to represent words that further expanded on the central idea. The mind mapping diagram remained on display throughout the entire session.

Business Origami

Business Origami is an activity that allows participants to collaboratively develop a physical representation of a system [17]. The aim of this activity is to help groups gain a deeper understanding of the people and things involved, the surrounding environment, and the interaction(s) between them.

In our design charrette, participants were instructed to imagine that the patient and provider in the case were meeting for a medical appointment. Participants were asked to think about what that medical appointment might look like and to map out the flow of the medical appointment between the patient and doctor in the case using 3-dimensional icons (ie, paper pop-up tokens); some icons were preprinted with potentially relevant actors (eg, doctor, nurse, and patient's spouse), artifacts (eg, doctor's computer, medicine, and educational materials), and places (eg, check-in station, waiting room, and doctor's office), and some were blank to allow participants to add new ones if needed ([Multimedia Appendix 6](#)). The interactions between the tokens were represented by arrows drawn on the surface (horizontal white paper) with colored markers. The completed business origami model was displayed throughout the session.

Empathy Mapping

An empathy map is a collaborative design tool for discovering deeper insights about users, customers, or stakeholders [24].

The aim of empathy mapping is for participants to put themselves in the place of another person and understand their motivations and frustrations. The structure of an empathy map canvas often includes 4 quadrants representing the user's external, observable world, and internal mindset.

For our session, the facilitator placed a large outline of a human head onto a flipchart. This head represented the patient in the case. (The name of the patient and several of his/her characteristics were written on the canvas.) Then, 4 quadrants were drawn out from the head representing the following: seeing, saying/doing, hearing, and thinking/feeling. Participants were asked to write down on sticky notes what they think the patient might be seeing, saying/doing, hearing, and/or thinking/feeling during the medical appointment where deintensification was being discussed. The facilitator placed the sticky notes on the appropriate quadrant of the map ([Multimedia Appendix 6](#)). Pains (fears, frustrations, and anxieties) and gains (wants, needs, hopes, and dreams) were also articulated and written at the bottom of the canvas. This activity was repeated with a second human head representing the doctor in the case. The canvases were displayed throughout the session.

Identifying Strategies Card Game

We developed recommendation-specific scenarios about different patients and their primary care providers. The scenarios were designed so patients and clinicians in the scenarios varied along a spectrum of combinations of *degree of resistance to deintensification*, from highly resistant to deintensification, somewhat resistant to deintensification, or not at all resistant to deintensification. Scenarios covered all combinations of patient and clinician types. Each of the scenarios included the following 5 pieces of information: (1) a brief patient description, (2) a brief clinician description, (3) wants/needs of the patient and/or clinician, (4) motivations/reasoning of the patient and/or clinician, and (5) barriers (patient, clinician, and/or system-level) to deintensification. Put together, these pieces expressed a *problem statement* that participants reviewed together [25]. Following the review, participants brainstormed solutions that could help solve the problem as they saw it for that scenario.

The following is an example of a deintensification scenario where the patient is highly resistant to deintensification and the provider is not at all resistant to successful deintensification:

- 1. Patient description: Arik is 74 years old and retired from the army, suffers from diabetes, recently transferred to the VA, with several prescriptions including insulin; most recent HbA_{1c} level is low.
- 2. Provider description: Dr. Stokes is a physician at a large VA Medical Center, has been seeing Arik for 1 year.
- 3-5. Problem statement: Dr. Stokes wants Arik to reduce his insulin (wants or needs information) because Arik's HbA_{1c} level is low and current evidence suggests that a low HbA_{1c} can be harmful in older adults (motivation information) but Arik has been on insulin for many years and is scared his blood sugars will rise if he stops or reduces it, so Arik refuses (barriers information).

[Multimedia Appendix 7](#) provides the full set of patient-clinician scenarios that the participants reviewed. Participants worked in pairs or trios to work through a card game where they were taken through each scenario one-at-a-time in a structured fashion, to identify barriers that might prevent the doctor or patient from scaling back, and to brainstorm solutions (ie, strategies) to overcome those barriers. The pairs/trios were asked to brainstorm as many strategies as possible, then work together to select the best 1 to 3 strategies from all those brainstormed. Participants were prompted with the following instructions as they worked through each scenario using a worksheet (see worksheet template in [Multimedia Appendix 8](#)): Solution 1 - The big problem that would prevent scaling back is (insert text); A solution that can solve the problem is (insert text). This was repeated for up to 2 additional solutions (ie, solutions 2 and 3) as desired by the participants.

Participants repeated the above until they finished all the scenarios or until time for the activity ran out.

Dot Voting

Dot voting is one of the simplest ways to collaboratively prioritize and converge upon agreed solutions [23].

Table 1. Deintensification super strategy categories from phase 1.

| Super strategy category | Example |
|---|---|
| Provide patient education through outreach ^a | Offer a group class to educate patients about deintensification |
| Educate patients using mass/social media ^a | Educate the public about deintensification using billboards, newspapers, or magazines |
| Provide education to providers ^a | Have mandatory trainings for clinic staff (eg, providers and nurses) on the newest overuse recommendations |
| Provide patient-centered care ^b | “Treat the patient as a person and not as a number” |
| Educate patients during an appointment ^b | Use decision aids to help a patient better understand the risks and benefits of scaling back |
| Offer alternatives to care ^b | Have providers consider doing more up front to build rapport and trust with the patient to help ensure success during future scaling back efforts |

^aGroups focusing on this strategy: diabetes treatment in high-risk patients; Screening for carotid artery stenosis in asymptomatic patients.

^bGroup focusing on this strategy: screening for colorectal cancer in older adults.

Phase 2: Patient-Clinician Design Charrette

Patient Recruitment

A staff member mailed patients, who participated in phase 1 and met other inclusion criteria (see [Multimedia Appendix 1](#) for inclusion and exclusion criteria), a recruitment letter explaining the patient-clinician design charrette and informing them that a study team member would be calling to invite them to participate. A copy of the study consent form was included with the mailing. Approximately 1 week after the mailing, the staff called the patient to ascertain their interest in participating (the staff attempted to contact a patient up to 3 times). Once a patient indicated they were interested in participating, the staff member reviewed the consent form with the patient and answered any questions they had.

Two weeks before the session, relevant materials were mailed to the patients who agreed to participate. These materials included information on the goals of the full research study, a summary of the patient-only session (including a table outlining

Following the card game, all scenario worksheets generated by the group were displayed on a nearby wall and read aloud by the group’s facilitator. Each participant in the group was given 6 dot stickers and asked to place dots on the 6 strategies they felt were most important.

Charrette Wrap-Up

At the end of the charrette, participants completed a postsession survey. The survey was similar to the baseline survey but included questions related to the participant’s willingness to participate in phase 2 of the study. Participants received a US \$125 gift card for taking part in the session.

Analysis

Following both patient design charrettes, project staff rapidly reviewed all prioritized deintensification strategies, along with the related facilitator notes and audio recordings. The team followed a consensus process to identify themes and group similar themes together. The resultant 6 themes were termed *super strategies* and used to guide the phase 2 patient-clinician design charrette ([Table 1](#)).

3 of the *super* (deintensification) strategies identified during that session), a description of what to expect during the patient-clinician session, and directions to the session. In addition, patients received an index card titled *Personal Experience with Deintensification*. The index card stated:

Describe a time when you went to your doctor wanting a specific test/treatment, your doctor persuaded you that NOT getting the test/treatment was the best thing to do, and in the end, you felt good about it.

Patients were instructed to complete the card before the session and bring it with them to the session.

Provider Recruitment

A staff member emailed providers a recruitment letter explaining the patient-clinician design charrette. The study consent form was attached to the email. Providers were instructed to review the consent form and reply to the email if they were interested

in participating in the session (the staff sent up to 3 recruitment emails to providers).

Two weeks before the session, relevant materials were hand delivered to the providers who agreed to participate. These materials included information on the goals of the full research study, a summary of the initial patient sessions (including a table outlining 3 of the *super* (deintensification) strategies identified during that session), a description of what to expect during the patient-clinician session, and directions to the session. In addition, providers received an index card titled *Personal Experience with Deintensification*. The index card stated:

Describe a time when a patient came to the clinic wanting a specific test or treatment, but after some discussion you were able to persuade the patient that it really wasn't in their best interest. Then, describe a few ways that patients have made these deintensification conversations easier for you in the past.

Providers were instructed to complete the card before the session and bring it with them to the session.

Design Charrette Overview

The 4-hour session took place at the VA Center for Clinical Management Research in Ann Arbor, Michigan. The registration process began by obtaining written informed consent. Once consent was obtained, participants were directed to their assigned group, which was led by a trained facilitator (see [Multimedia Appendix 9](#) for the facilitator's guide). As in phase 1, each group focused on 1 of the 3 deintensification recommendations mentioned in the study design overview section. In addition, each group concentrated on 3 of the 6 deintensification *super* strategies identified in phase 1 ([Table 1](#)).

To begin, all participants completed a baseline survey. Following a brief presentation by a study investigator to outline the agenda and goals for the day and to summarize the high-level deintensification strategies generated during the phase 1 session, each participant shared their personal experience(s) with deintensification using the prompts introduced on the previously mailed index card, as described above. (If a participant forgot their card, they were instructed to simply share any experience they have had in scaling back or stopping tests or treatments.) After this, each facilitator briefly reviewed the 3 *super* strategies that their group would be focusing on during the remainder of the session, answered any questions participants had about the strategies, and discussed the goal of the primary charrette activity, WhoDo. WhoDo was used in this study to help participants develop concrete actions that specific stakeholders can take to support deintensification efforts. Portions of the charrette activities were audiotaped.

Charrette Activities

WhoDo is a tool that helps to brainstorm, plan, and prioritize actions (see [Multimedia Appendix 4](#)).

We modified the tool to create a *WhoDo matrix* (see [Multimedia Appendix 6](#)) [23]. This matrix collected information not only on the stakeholders (*Who*) and their actions (*Do*), but also on

potential obstacles to the action (*Barriers*) and approaches to overcome the barriers (*How to Overcome*).

Specific questions that were to be considered included the following:

1. Who: Who is involved in making deintensification happen? Who is the decision maker? Who has the needed resources? Whose support is needed?
2. Do: What do they need to do or do differently? What actions will build toward the big goal? (Each Do (action) had to be concrete and measurable.)
3. Barrier: What could get in the way of getting this (Do) done? What potential problems exist?
4. How to Overcome: What needs to happen to be able to overcome the barrier(s)?

In addition, we asked participants to consider stakeholders (*Who*) at 3 different levels. These levels included the primary care team level, the local VA level, and the national VA level. A list of potential stakeholders and/or their role at each level (eg, primary care team—provider, patient, and nurse; local VA level—director [leadership], pharmacists [specialists], social workers [support services], and clerk [administration]; national VA level—National Office to promote health or prevent disease, Veterans Service Organizations) was provided to each of the 3 groups. Facilitators stressed to participants that for deintensification efforts to be successful at any 1 level, they often need to be supported by other levels of the health care system. Each facilitator gave a brief example, at 1 of the levels, as a demonstration.

Step 1: Brainstorming of Who and Do

The initial step of the activity was a simple 30-min brainstorming session. Facilitators instructed participants to consider, within the 3 *super* strategy areas assigned to their group, what could be done to support deintensification (*Do*) and who would be needed to make it happen (*Who*). (Note: We refer to these collectively as *WhoDo*.) Facilitator 1 asked participants to write their *WhoDo* ideas on sticky notes and then share with the entire group, facilitator 2 collected information directly on a whiteboard as they were brainstormed by participants, and facilitator 3 used both of the above techniques to collect information. Facilitators worked to ensure that ideas were generated in each of the 3 *super* strategy areas.

Step 2: Selection of the Most Important WhoDo

Following the brainstorming, participants were asked to work together to identify the actions that would be most effective in supporting appropriate deintensification. Each group was instructed to identify the top 1 to 3 actions and to select the 1 action that they would like to use to start their first *WhoDo* matrix.

Step 3: Identification of Barriers (Barriers) and Solutions for Overcoming the Barriers (How to Overcome)

Participants selected the level (ie, primary care team, local VA, and national VA) for the top 1 to 3 actions, and the facilitator copied the prioritized action into a *WhoDo matrix*, which was presented on large sheets of white paper. Facilitators then asked

participants to brainstorm potential barriers (*Barriers*) that could get in the way of the action (*Do*) actually happening. All barriers were documented within the WhoDo matrix. Once participants felt like their list of barriers was complete, they were instructed to select the one barrier that was likely the most important obstacle to making the *Who* and *Do* happen, and the facilitator highlighted this barrier in the matrix. Following that, participants were instructed to discuss solutions (*How to Overcome*) that could help overcome the biggest barrier. Again, all solutions were documented within the WhoDo matrix. Once the list of solutions was felt to be complete, participants were instructed to select the best solution, and the facilitator highlighted this solution in the matrix. The facilitator asked participants to then consider how the most important solution could be supported by the other 2 levels of the health care system. The participants completed the same steps as above (ie, determining *Who*, *Do*, *Barriers*, and *How to Overcome*) for one or both remaining levels.

Step 4: Selection of the Most Valuable WhoDo

Groups were instructed to select the most valuable *WhoDo* from all completed matrices. Participants were asked to consider the following 3 questions when making their decision: (1) *Which is most likely to lead to appropriate deintensification?* (2) *Which is most sustainable?* (3) *Which would be most acceptable to all stakeholders?* Once the most valuable *WhoDo* was identified, each facilitator shared it with all session participants.

Charrette Wrap-Up

At the end of the charrette, participants completed a postsession survey. Patient participants received a US \$75 gift card for taking part in the session.

Analysis Plan (phase 1 and phase 2)

Categorizing Strategies

The first step in our analysis will be to categorize the strategies that were developed by participants during phase 1. Our analytic team (LD, JS, TC, MK, and SK) will use an inductive coding approach to create categories for the prioritized phase 1 strategies. The categories will focus on the actor or entity responsible for initiating the deintensification strategies. We list the categories here to convey the breadth of responses across different levels: doctor, patient, other staff, multilevel (within

a health system), health system, and national. The team will refine the definitions for the categories while coding the prioritized phase 2 strategies. We will reconcile any outdated codes from phase 1 with our phase 2 codes to ensure continuity in our coding application. Once we finalize our coding scheme, we will follow a deductive approach to categorize the remaining (ie, nonprioritized) strategies for phases 1 and 2.

Developing Themes

Building on our initial work, members of the analytic team will independently review the strategies within each level and create a list of ideas for patterns across the strategies. The team will consider several questions while reviewing the strategies in each level, such as What are the similarities across the strategies? What is the common thread in all these ideas? For example, do the commonalities lie in *who* participants think should be involved, or *how* this process should happen? Finally, we will review the ideas as a group and distill them into themes to capture what we heard from participants in each phase.

Examining the Survey Data

Analysis of the survey data will include basic descriptive statistics of the main variables of interest.

Results

Recruitment

In phase 1, study staff sent recruitment letters and made at least one phone call attempt to 316 eligible patients (Figure 2).

Staff were unable to reach 78 patients via phone, and an additional 179 patients declined to participate in the study. Of the 59 patients verbally agreeing to participate, 35 provided written informed consent and participated in the study.

In phase 2, 18 eligible patients and 29 eligible providers received a study recruitment letter/email (Figure 3).

One patient could not be reached via phone, and 5 patients declined to participate; 14 providers did not respond to the recruitment email, and 7 providers declined to participate. Of the 12 patients who agreed to participate, 9 provided written informed consent and participated in the study. Of the 8 providers who agreed to participate, 7 provided written informed consent and participated in the study.

Figure 2. Recruitment for the two patient-only design charrettes (phase 1).

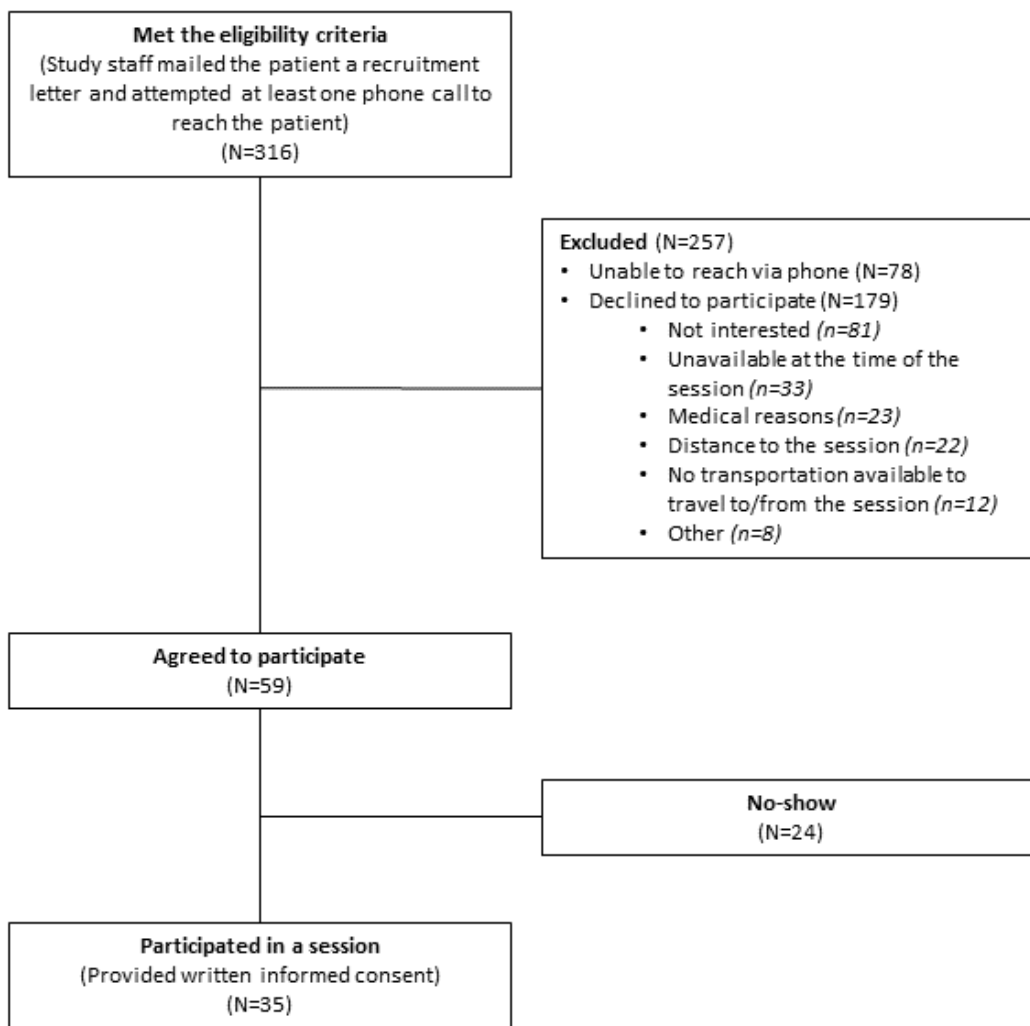
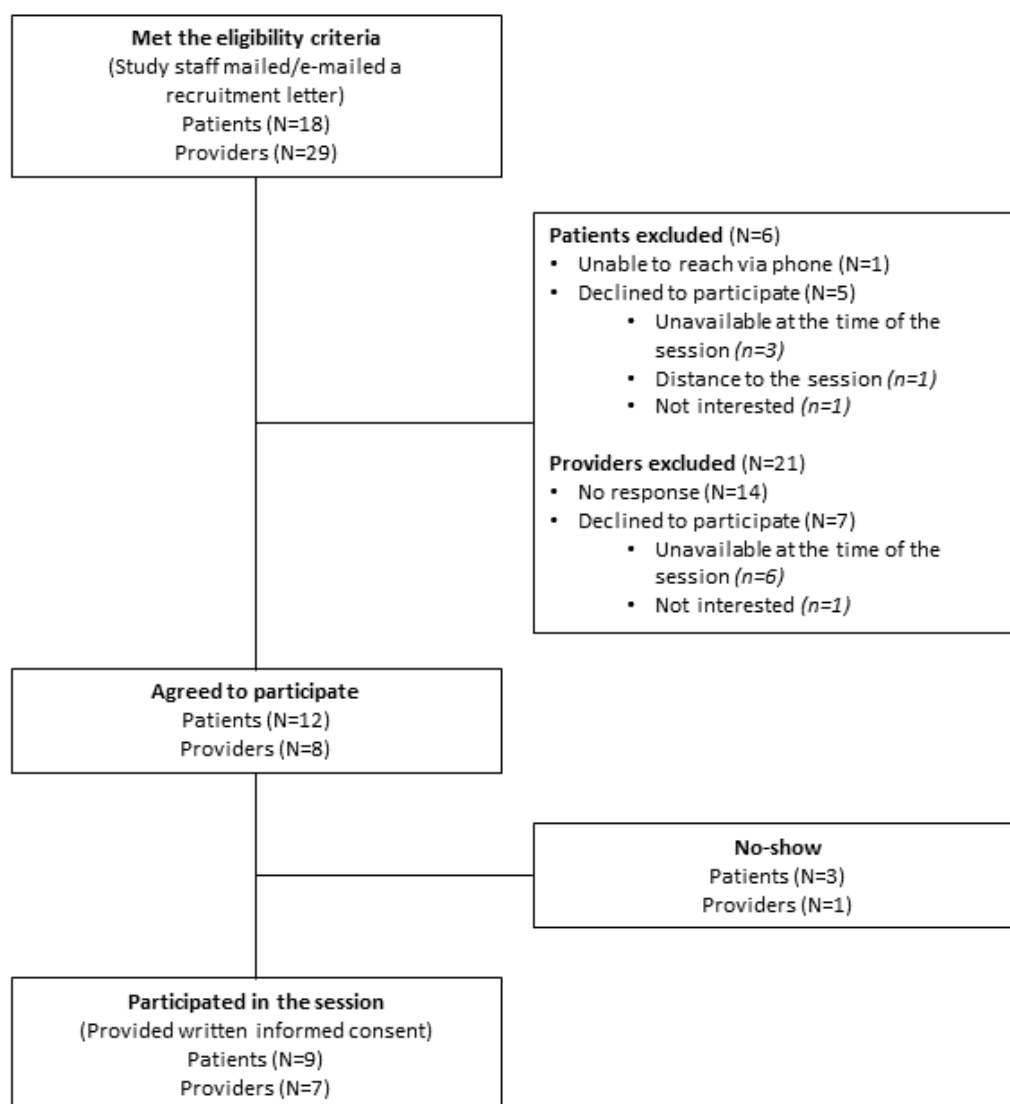


Figure 3. Recruitment for the patient-clinician design charrette (phase 2).

Data Analysis

The categorization of deintensification strategies, development of themes, and analysis of survey data are currently underway. The results are expected to be submitted for publication in early 2020.

Discussion

Our study protocol employs a novel method, design charrettes, to bring providers and patients with differing backgrounds and with different expectations together to cocreate solutions to the complex issue of deintensification. To our knowledge, this is the first study to use design charrettes, a collaborative session consisting of UCD activities guided by a UCD process model, to engage patients and providers in cocreating strategies to support successful deintensification in primary care.

Deintensification is closely connected to the concept of deimplementation. Deintensification occurs when a test or treatment is scaled back or stopped. This project focused on deintensification of routine services as exemplified in practice

recommendations. Deimplementation is a similar concept that focuses on the broader need to develop system approaches to stop low-value practices [26] and can be seen as an implicit part of implementation and organizational change [27]. In the future, there may be deimplementation projects that focus on deintensification recommendations.

Design approaches have only recently been employed in health care, and the wide array of existing design processes have roots in disparate fields such as architecture, engineering, and business [28]. These approaches are now being taught in medical schools and are being used directly by doctors and nurses to improve patient care and patient's experiences [29-31]. A concrete example of how design activities can have a real-world impact is the following: administrators at the Rotterdam Eye Hospital in the Netherlands wanted to transform the patient's experience from an often anxiety-riddled episode into something more reliably pleasant and personal [32]. To do this, they incorporated UCD principles into their planning process. First, hospital staff set out to better understand their target user (ie, patients coming into the hospital for treatment). They found that most patients were scared about losing their eyesight; therefore, their primary

goal was to reduce patients' fears. The team brainstormed potential solutions. They sought insight from both inside and outside the health care field (eg, airlines, supermarkets, and other medical organizations). The most promising ideas were presented to the leadership of the hospital. Small-scale prototypes were tested, and the best ideas spread naturally. By using a design approach, the hospital was able to improve user experience. Patient intake increased by 47%, and the hospital has since won several awards for safety, quality, and design.

Other UCD success stories are summarized in a systematic review by Altman et al [15]. The authors examined how design has been used to plan interventions in health care settings and assessed whether the interventions were effective. They

identified 26 papers, representing 24 interventions that used UCD in intervention development, intervention implementation, or both. A total of 19 of the interventions focused on physical health, 2 on mental health, and 3 on system processes. Although there were variable design activities employed across studies, all but one of the interventions showed positive effects on one or more outcomes.

By directly engaging patients and clinicians in the design process, the uncertainties and risks involved with innovation may be substantially minimized. Our study employs design to increase the chances that the resultant deintensification strategies are acceptable, effective, and sustainable in a primary care setting.

Acknowledgments

This study is funded by the Department of Veterans Affairs Health Services Research and Development (Grant No IIR 15-131). TC is supported by a VA Career Development Award (CDA 16-151). The content is solely the responsibility of the authors and does not necessarily represent the official views of the Department of Veterans Affairs.

Conflicts of Interest

TJC was co-investigator on a completed research grant from Genentech's Corporate Giving Scientific Project Support Program that is outside the scope of this work and unrelated to any Genentech or Roche products. EAK serves on the Clinical Advisory Board for Bind Insurance.

Multimedia Appendix 1

Inclusion and Exclusion Criteria (phase 1 and phase 2).

[\[DOCX File, 14 KB - resprot_v8i11e15618_app1.docx\]](#)

Multimedia Appendix 2

Phase 1 Facilitator Guide.

[\[DOCX File, 863 KB - resprot_v8i11e15618_app2.docx\]](#)

Multimedia Appendix 3

Phase 1 Survey.

[\[DOCX File, 828 KB - resprot_v8i11e15618_app3.docx\]](#)

Multimedia Appendix 4

User-Centered Design Charrette Activities and Associated Model Stage.

[\[DOCX File, 15 KB - resprot_v8i11e15618_app4.docx\]](#)

Multimedia Appendix 5

Case example.

[\[DOCX File, 372 KB - resprot_v8i11e15618_app5.docx\]](#)

Multimedia Appendix 6

Pictures of mind mapping, business origami, and empathy mapping.

[\[DOCX File, 2247 KB - resprot_v8i11e15618_app6.docx\]](#)

Multimedia Appendix 7

Patient-clinician scenarios for the Identifying strategies card game.

[\[DOCX File, 50 KB - resprot_v8i11e15618_app7.docx\]](#)

Multimedia Appendix 8

Identifying strategies card game worksheet example.

[[DOCX File , 750 KB - resprot_v8i11e15618_app8.docx](#)]

Multimedia Appendix 9
Phase 2 Facilitator Guide.

[[DOCX File , 807 KB - resprot_v8i11e15618_app9.docx](#)]

Multimedia Appendix 10

Previous peer-review reports from the funder, the Department of Veterans Affairs.

[[PDF File \(Adobe PDF File\), 106 KB - resprot_v8i11e15618_app10.pdf](#)]

References

1. Colla CH, Mainor AJ, Hargreaves C, Sequist T, Morden N. Interventions aimed at reducing use of low-value health services: a systematic review. *Med Care Res Rev* 2017 Oct;74(5):507-550. [doi: [10.1177/1077558716656970](#)] [Medline: [27402662](#)]
2. Kerr EA, Hofer TP. Deintensification of routine medical services: the next frontier for improving care quality. *JAMA Intern Med* 2016 Jul 1;176(7):978-980. [doi: [10.1001/jamainternmed.2016.2292](#)] [Medline: [27272959](#)]
3. Kale MS, Korenstein D. Overdiagnosis in primary care: framing the problem and finding solutions. *Br Med J* 2018 Aug 14;362:k2820. [doi: [10.1136/bmj.k2820](#)] [Medline: [30108054](#)]
4. Maciejewski ML, Mi X, Sussman J, Greiner M, Curtis LH, Ng J, et al. Overtreatment and deintensification of diabetic therapy among medicare beneficiaries. *J Gen Intern Med* 2018 Jan;33(1):34-41 [FREE Full text] [doi: [10.1007/s11606-017-4167-y](#)] [Medline: [28905179](#)]
5. McAlister FA, Youngson E, Eurich DT. Treatment deintensification is uncommon in adults with type 2 diabetes mellitus: a retrospective cohort study. *Circ Cardiovasc Qual Outcomes* 2017 Apr;10(4). [doi: [10.1161/CIRCOUTCOMES.116.003514](#)] [Medline: [28416531](#)]
6. Sussman JB, Kerr EA, Saini SD, Holleman RG, Klamerus ML, Min LC, et al. Rates of deintensification of blood pressure and glycemic medication treatment based on levels of control and life expectancy in older patients with diabetes mellitus. *JAMA Intern Med* 2015 Dec;175(12):1942-1949. [doi: [10.1001/jamainternmed.2015.5110](#)] [Medline: [26502220](#)]
7. Rittel HW, Webber MM. Dilemmas in a general theory of planning. *Policy Sci* 1973;4(2):155-169. [doi: [10.1007/bf01405730](#)]
8. Schwitzer G. A guide to reading health care news stories. *JAMA Intern Med* 2014 Jul;174(7):1183-1186. [doi: [10.1001/jamainternmed.2014.1359](#)] [Medline: [24796314](#)]
9. Squiers LB, Bann CM, Dolina SE, Tzeng J, McCormack L, Kamerow D. Prostate-specific antigen testing: men's responses to 2012 recommendation against screening. *Am J Prev Med* 2013 Aug;45(2):182-189. [doi: [10.1016/j.amepre.2013.04.005](#)] [Medline: [23867025](#)]
10. Torke AM, Schwartz PH, Holtz LR, Montz K, Sachs GA. Older adults and forgoing cancer screening: 'I think it would be strange'. *JAMA Intern Med* 2013 Apr 8;173(7):526-531 [FREE Full text] [doi: [10.1001/jamainternmed.2013.2903](#)] [Medline: [23478883](#)]
11. Morgan DJ, Brownlee S, Leppin AL, Kressin N, Dhruva SS, Levin L, et al. Setting a research agenda for medical overuse. *Br Med J* 2015 Aug 25;351:h4534 [FREE Full text] [doi: [10.1136/bmj.h4534](#)] [Medline: [26306661](#)]
12. Powell AA, Bloomfield HE, Burgess DJ, Wilt TJ, Partin MR. A conceptual framework for understanding and reducing overuse by primary care providers. *Med Care Res Rev* 2013 Oct;70(5):451-472. [doi: [10.1177/1077558713496166](#)] [Medline: [23916984](#)]
13. Sirovich BE, Woloshin S, Schwartz LM. Too Little? Too Much? Primary care physicians' views on US health care: a brief report. *Arch Intern Med* 2011 Sep 26;171(17):1582-1585 [FREE Full text] [doi: [10.1001/archinternmed.2011.437](#)] [Medline: [21949169](#)]
14. Bartels LM. Democracy with attitudes. In: MacKuen MB, Rabinowitz G, editors. *Electoral Democracy*. Ann Arbor, MI: University of Michigan Press; 2003:48-82.
15. Altman M, Huang TT, Breland JY. Design thinking in health care. *Prev Chronic Dis* 2018 Sep 27;15:E117 [FREE Full text] [doi: [10.5888/pcd15.180128](#)] [Medline: [30264690](#)]
16. Dopp AR, Parisi KE, Munson SA, Lyon AR. A glossary of user-centered design strategies for implementation experts. *Transl Behav Med* 2018 Dec 7. [doi: [10.1093/tbm/iby119](#)] [Medline: [30535343](#)]
17. Martin B, Hanington BM. *Universal Methods of Design: 100 Ways to Research Complex Problems, Develop Innovative Ideas, and Design Effective Solutions*. Beverly, MA: Rockport Publishers; 2012.
18. Lennertz B, Lutzenhiser A. *The Charrette Handbook: The Essential Guide for Accelerated, Collaborative Community Planning*. Chicago, IL: APA/Planners Press; 2006.
19. University of Michigan STAMPS School of Art and Design. URL: <https://stamps.umich.edu/> [accessed 2019-07-24]
20. Roberts JP, Fisher TR, Trowbridge MJ, Bent C. A design thinking framework for healthcare management and innovation. *Healthc (Amst)* 2016 Mar;4(1):11-14. [doi: [10.1016/j.hjdsi.2015.12.002](#)] [Medline: [27001093](#)]
21. Stanford d.school. Design Thinking Bootcamp Bootleg URL: <https://dschool.stanford.edu/resources/the-bootcamp-bootleg> [accessed 2019-07-24]

22. Fitch K, Bernstein S, Aguillar M, Burnand B, LaCalle J, Lazaro P, et al. The RAND/UCLA Appropriateness Method User's Manual. Santa Monica, CA: RAND; 2001.
23. Gray D, Brown S, Macanujo J. Gamestorming: A Playbook for Innovators, Rulebreakers, and Changemakers. Sebastopol, CA: O'Reilly Media Inc; 2012.
24. XPLANE. Empathy Map Worksheet URL: <https://x.xplane.com/empathymap> [accessed 2019-06-24]
25. Devos J. Toptal. Design Problem Statements - What They Are and How to Frame Them URL: <https://www.toptal.com/designers/product-design/design-problem-statement> [accessed 2019-06-24]
26. Niven DJ, Mrklas KJ, Holodinsky JK, Straus SE, Hemmelgarn BR, Jeffs LP, et al. Towards understanding the de-adoption of low-value clinical practices: a scoping review. *BMC Med* 2015 Oct 6;13:255 [FREE Full text] [doi: [10.1186/s12916-015-0488-z](https://doi.org/10.1186/s12916-015-0488-z)] [Medline: [26444862](https://pubmed.ncbi.nlm.nih.gov/26444862/)]
27. Wang V, Maciejewski ML, Helfrich CD, Weiner BJ. Working smarter not harder: coupling implementation to de-implementation. *Healthc (Amst)* 2018 Jun;6(2):104-107 [FREE Full text] [doi: [10.1016/j.hjdsi.2017.12.004](https://doi.org/10.1016/j.hjdsi.2017.12.004)] [Medline: [29279297](https://pubmed.ncbi.nlm.nih.gov/29279297/)]
28. Dam R, Siang T. Interaction Design Foundation. Design Thinking: Get a Quick Overview of the History URL: <https://www.interaction-design.org/literature/article/design-thinking-get-a-quick-overview-of-the-history> [accessed 2019-06-24]
29. McLaughlin JE, Wolcott MD, Hubbard D, Umstead K, Rider TR. A qualitative review of the design thinking framework in health professions education. *BMC Med Educ* 2019 Apr 4;19(1):98 [FREE Full text] [doi: [10.1186/s12909-019-1528-8](https://doi.org/10.1186/s12909-019-1528-8)] [Medline: [30947748](https://pubmed.ncbi.nlm.nih.gov/30947748/)]
30. Kalaichandran A. The New York Times. 2017 Aug 3. Design Thinking for Doctors and Nurses URL: <https://www.nytimes.com/2017/08/03/well/live/design-thinking-for-doctors-and-nurses.html> [accessed 2019-06-24]
31. Trowbridge M, Chen D, Gregor A. Teaching design thinking to medical students. *Med Educ* 2018 Nov;52(11):1199-1200. [doi: [10.1111/medu.13699](https://doi.org/10.1111/medu.13699)] [Medline: [30345675](https://pubmed.ncbi.nlm.nih.gov/30345675/)]
32. van der Heijde R, Deichmann D. Harvard Business Review. 2016 Dec 2. How Design Thinking Turned One Hospital into a Bright and Comforting Place URL: <https://hbr.org/2016/12/how-design-thinking-turned-one-hospital-into-a-bright-and-comforting-place> [accessed 2019-06-24]

Abbreviations

HbA_{1c}: hemoglobin A1c

UCD: user-centered design

VA: veterans affairs

Edited by G Eysenbach; submitted 25.07.19; peer-reviewed by A Lyon, A Dopp, C Tuvey; comments to author 30.09.19; revised version received 04.10.19; accepted 08.10.19; published 26.11.19.

Please cite as:

Klamerus ML, Damschroder LJ, Sparks JB, Skurla SE, Kerr EA, Hofer TP, Caverly TJ

Developing Strategies to Reduce Unnecessary Services in Primary Care: Protocol for User-Centered Design Charrettes

JMIR Res Protoc 2019;8(11):e15618

URL: <http://www.researchprotocols.org/2019/11/e15618/>

doi: [10.2196/15618](https://doi.org/10.2196/15618)

PMID: [31769764](https://pubmed.ncbi.nlm.nih.gov/31769764/)

©Mandi L Klamerus, Laura J Damschroder, Jordan B Sparks, Sarah E Skurla, Eve A Kerr, Timothy P Hofer, Tanner J Caverly. Originally published in JMIR Research Protocols (<http://www.researchprotocols.org>), 26.11.2019. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in JMIR Research Protocols, is properly cited. The complete bibliographic information, a link to the original publication on <http://www.researchprotocols.org>, as well as this copyright and license information must be included.

Original Paper

Impact of Perinatal Different Intrauterine Environments on Child Growth and Development: Planning and Baseline Data for a Cohort Study

Isabel Cristina Ribas Werlang^{1*}, PhD; Juliana Rombaldi Bernardi^{1,2,3*}, PhD; Marina Nunes¹, PhD; Thiago Beltram Marcelino^{1,2}, MSc; Vera Lucia Bosa³, PhD; Mariana Bohns Michalowski¹, MD, PhD; Clécio Homrich da Silva^{1,2}, MD, PhD; Marcelo Zubaran Goldani^{1,2}, MD, PhD

¹Laboratório de Pediatria Translacional, Centro de Pesquisa Experimental, Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil

²Programa de Pós-Graduação em Saúde da Criança e do Adolescente, Departamento de Pediatria, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil

³Programa de Pós Graduação em Alimentação, Nutrição e Saúde, Departamento de Nutrição, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil

*these authors contributed equally

Corresponding Author:

Isabel Cristina Ribas Werlang, PhD
Laboratório de Pediatria Translacional
Centro de Pesquisa Experimental
Hospital de Clínicas de Porto Alegre
Ramiro Barcelos, 2350
Porto Alegre, 90035-007
Brazil
Phone: 55 5133598019
Email: iverlang@yahoo.com.br

Abstract

Background: Several studies have shown that exposure of the fetus and newborn to prenatal and perinatal events, respectively, may influence the health outcomes of the child throughout their life cycle.

Objective: This study aimed to increase the knowledge on the impact of different intrauterine environments on child growth and development, as we know that pregnancy and early years are a window of opportunity for health promotion and prevention interventions of diseases.

Methods: The recruitment occurred 24 to 48 hours after delivery and involved mothers and their newborns in 2 public hospitals in Porto Alegre, Brazil, from December 2011 to January 2016. The mothers-newborns dyads were allocated to 5 groups: diabetes mellitus, mothers with a clinical diagnosis of diabetes; systemic arterial hypertension (SAH), mothers with a clinical diagnosis of systematic arterial hypertensive disease during pregnancy; maternal smoking, mothers who smoked at any moment of gestation; small for gestational age (SGA), mothers with SGA newborns because of intrauterine growth restriction; and control, mothers without the clinical characteristics previously mentioned. Several protocols and anthropometric measurements were applied in the interviews at immediate postpartum and 7 and 15 days and 1, 3, and 6 months after birth. For this study, we analyzed only data collected during postpartum interviews. The statistical analyses were performed using Pearson chi-square test, Mann-Whitney test, or Kruskal-Wallis test with Dunn post hoc. The significance level was set at 5%. The Hospital Ethics and Research Committees approved the study.

Results: Of the 485 eligible mothers-newborns dyads, 400 agreed to participate (82.5%, 400/485). As expected, newborns from the SGA group had significantly lower birth weight, smaller stature, and lower cephalic perimeter ($P < .001$). This group also had the highest percentage of primiparous women in comparison with other groups ($P = .005$) except for control. Mothers from the SAH group had the highest mean age, the highest percentage of cesarean sections, and presented greater gestational weight gain.

Conclusions: In this study, we describe the planning and structure for the systematic follow-up of mother-newborn dyads in the first 6 months after birth, considering the important demographic and epidemiological transition scenario in Brazil. The results of this prospective longitudinal study may provide a better understanding of the causal mechanisms involved in health and life course disease related to different adverse intrauterine environments.

KEYWORDS

observational study; growth; development; fetal development child health; maternal health

Introduction

Background

Several studies have described the influence of intra- and extrauterine environment changes on human growth and development, leading to a particular health-disease pattern during life course [1,2]. Metabolic variation during the gestational period can provide an unfavorable environment to fetal growth, triggering structural and functional adaptations with permanent effects on organs and tissues of the individual [3,4].

Fetal exposure to high glucose concentrations can lead to changes in neuroendocrine metabolism, acting on metabolic programming and potentially contributing to the development of type 2 diabetes mellitus (DM) in adulthood [5]. Intrauterine hypoxia associated with hypertension during pregnancy also contributes to perinatal morbidity and mortality, and to the possibility of cognitive deficit in offspring, exemplifying the concept of transgenerational risk of cardiovascular disease [6,7].

In the same way, maternal smoking (MS) causes changes in immunity and lung function during the neonatal period [8]. Other effects include attention deficit hyperactivity disorder, motor function problems, cognitive deficits [9], increased incidence of asthma [10], and increased risk of developing obstructive pulmonary chronic disease [11].

On the contrary, small for gestational age (SGA) infants per se have been associated with changes in the metabolism of fetal glucose and insulin homeostasis, altering metabolic mechanisms essential for short-term and long-term postnatal health and disease outcomes [12].

Thus, the analysis of the impact of those adverse intrauterine environments mentioned on infant growth and development can contribute to new insights on mechanisms related to health and disease, and in the development of early interventions, which are decisive for chronic diseases prevention [4].

Objectives

The impact of perinatal environment variations on health of the newborn at first 6 months of life (IVAPSA) study aimed to identify the effects of the intrauterine and perinatal environmental variations on infant growth and development during the first 6 months of life. The study has offered a remarkable approach to the theme and increased the knowledge upon the impact of different intrauterine environments on health and disease outcomes during childhood and adulthood.

Methods

Design and Population

The participant recruitment occurred from December 2011 to January 2016 in 2 public hospitals in Porto Alegre, Brazil: Hospital de Clínicas de Porto Alegre (HCPA) and Grupo

Hospitalar Conceição (GHC). We invited mothers delivering between 37 and 42 weeks of gestation to participate; they should fit into the following groups:

- DM: clinical diagnosis of diabetes, considering any disease classification (gestational, type 1 and 2).
- Systemic arterial hypertension (SAH): presence of hypertensive disease during pregnancy (chronic, preeclampsia, eclampsia and overlapping diseases).
- MS: mothers who confirmed in a specific questionnaire that had smoked at any moment of gestation, regardless of the number of cigarettes.
- SGA: mothers of SGA newborns—categories below the fifth percentile of the Alexander curve [13] because of intrauterine growth restriction.
- Control: group without the clinical characteristics previously mentioned. Mothers without confounding comorbidities were prioritized in the recruitment, that is, those without the coexistence of other factors previously mentioned.

Those excluded from the analysis were the following participants:

- HIV positive: intrauterine exposure to the virus, use of antiretroviral drugs, and contraindication to breastfeeding.
- Twin or preterm newborns: born with low birth weight, may present greater neonatal vulnerability and also develop catch-up growth during the first year of life.
- Newborns with congenital malformations: more vulnerable to diseases and are likely to require neonatal hospitalization.
- Newborns who require early hospitalization: generally become more vulnerable and adversely affect their growth and development.

The definition of these exclusion criteria was based on the fact that they possibly contribute to changes in the growth and development of the newborn and infant within the first 6 months of life and affect their future health and disease outcomes.

The Research and Ethics Committees of the HCPA (protocol No. 11/0097) and the GHC (protocol No. 11/027) approved our study. All participants were recruited after written informed consent. All methods were performed in accordance with the latest current guidelines and regulations of the National Health Council of the Brazilian Ministry of Health (resolutions No. 466/2012 and No. 580/2018).

Assessment of Participant Characteristics

Mothers-newborns dyads were recruited 24 to 48 hours after delivery. The follow-up was conducted at 7 and 15 days and at 1, 3, and 6 months of the infant's life (Table 1). During the follow-up, through various protocols, information was obtained on (1) the family: demographic and socioeconomic characteristics; (2) the mother: age, schooling, profession, stress, domestic violence, postpartum depression, and confidence; (3) during gestation: prenatal care and parity; (4) the perinatal period: type of delivery, gestational age, Apgar score, gender,

weight, height, and cephalic perimeter of newborn; (5) the infant: growth, development, and sleep; (6) maternal and infant feeding; and (7) maternal and infant anthropometric measures. Mothers agreed to provide breast milk in the postpartum period and at 1 month after birth. Saliva from mothers and their newborns were collected in the postpartum period for DNA extraction. More detailed information about the assessments, protocols, and the IVAPSA study can also be verified in a previous publication [14].

Specifically, for this study, we analyzed only data collected during postpartum recruitment. The maternal variables evaluated were age (years), schooling (years), number of previous

pregnancies and parity, pregestational body mass index (BMI), and weight gain during pregnancy (kg). The gestational assistance variables used were delivery mode and number of prenatal consultations. Newborn variables included gender, weight (g), length (cm), cephalic perimeter (cm), and Apgar index.

In addition, we promoted an active search in social networks (basic health units, schools, markets, and commercial establishments) and used the post office system to access the most distant or unsafe neighborhoods and interviews previously scheduled by telephone on weekends and holidays.

Table 1. Variables, protocols, and collected sample performed in the study of impact of perinatal environment variations on health of the newborn at first 6 months of life (2011-2016).

| Interviews | Postpartum | 7 days | 15 days | 1 month | 3 months | 6 months |
|---|------------|----------------|------------------|---------|-----------|----------|
| Location | Hospital | Home care | CRC ^a | CRC | Home care | CRC |
| Variables | | | | | | |
| Gestational | X | — ^b | — | — | — | — |
| Demographic and socioeconomic characteristics | X | — | — | — | — | — |
| Perinatal | X | — | — | — | — | — |
| Environmental | X | X | X | X | X | X |
| Maternal, newborn, and infant feeding practices | — | X | X | X | X | X |
| Protocols | | | | | | |
| Maternal violence | — | — | — | X | — | X |
| Maternal care | — | X | X | — | — | — |
| Maternal confidence | — | — | X | — | — | — |
| Maternal perception | — | — | X | — | — | — |
| Maternal perceived stress | — | — | — | X | — | — |
| Postpartum depression | — | — | — | X | X | X |
| Breastfeeding observation | X | — | — | — | — | — |
| Parental care | — | — | — | — | X | — |
| Child development | — | X | — | X | X | X |
| Child's sleep | — | — | — | X | X | X |
| Mother-child bond | — | — | — | — | X | X |
| Collected samples | | | | | | |
| Saliva | X | — | — | — | — | — |
| Breast milk | X | — | — | X | — | — |
| Anthropometry | — | X | X | X | X | X |

^aCRC: Clinical Research Center, Hospital de Clínicas de Porto Alegre.

^bData were not collected.

Statistical Analysis

Database processing and analysis were performed using SPSS software (version 18.0; SPSS Inc, Chicago, IL). The descriptive statistical analysis verified the absolute and relative frequency of categorical variables. For continuous variables, central tendency measurements were obtained according to the variable distribution. The Pearson chi-square test or Mann-Whitney test

was used to analyze the differences between the group of participating mothers and the refusals. To evaluate the differences between the study groups, Pearson chi-square test or Kruskal-Wallis test with Dunn post hoc was used.

Results

Recruitment

Before the recruitment, from September to December 2011, a pilot study was conducted, which covered 17 mothers-newborns dyads. Finally, the study presented a total of 485 eligible mothers-newborns from which 85 were refusals, leading to a total sample of 400 pairs (82.5%, 400/485). The characteristics of participants and refusals in the recruitment are presented in [Table 2](#).

Considering differences between participants and nonparticipants, there was a significant distinction for delivery

mode (higher incidence of vaginal delivery among mothers who agreed to participate, $P<.001$) and for the number of pregnancies (greater number of pregnancies among participating mothers, $P<.001$). On the contrary, it was observed that other maternal and newborn characteristics were similar.

Of mothers who participated in the postnatal study ($n=400$), 58.8% (235/400) were interviewed at 7 days, 66.0% (264/400) at 15 days, 66.8% (267/400) with 1 month, 67.0% (268/400) with 3 months, and 58.8% (235/400) with 6 months of life of the child. The profile of refusals, losses of tracking, and data recovered by each interview by groups can be verified in [Table 3](#).

Table 2. Characteristics of mother-newborn dyads who accepted and refused to participate in the initial study interview (2011-2016).

| Variables | Participants (N ^a =400) | Refusals (N ^a =85) | P value |
|------------------------------------|------------------------------------|-------------------------------|--------------------|
| Mother | | | |
| Age (years), mean (SD) | 26.15 (6.60) | 27.90 (7.01) | .30 |
| Education (years), mean (SD) | 9.26 (2.73) | 10.00 (7.10) | .66 |
| White, n (%) | 209 (54.9) | 53 (62) | .21 |
| Vaginal delivery, n (%) | 248 (65.1) | 32 (35) | <.001 ^b |
| Number of pregnancies, mean (SD) | 3.10 (1.43) | 2.07 (1.46) | <.001 ^c |
| Newborn | | | |
| Weight (g), mean (SD) | 3234.01 (499.85) | 3287.23 (497.38) | .46 |
| Length (cm), mean (SD) | 48.56 (2.25) | 48.69 (2.05) | .78 |
| Cephalic perimeter (cm), mean (SD) | 33.79 (1.54) | 34.10 (1.36) | .07 |
| Apgar 1st min, mean (SD) | 8.39 (1.33) | 8.39 (1.33) | .92 |
| Apgar 5th min, mean (SD) | 9.45 (0.63) | 9.48 (0.80) | .25 |

^aN refers to the entire population under study.

^bPearson chi-square test.

^cMann Whitney test.

Table 3. Frequency of interviewed participants, recovered data, losses of follow-up, and refusals during the study (2011-2016).

| Interviews | DM ^a | SAH ^b | MS ^c | SGA ^d | Control | Total |
|------------------------|-----------------|------------------|-----------------|------------------|------------|-------------|
| 7 days, n (%) | | | | | | |
| Conducted | 46 (59) | 24 (64) | 49 (56) | 26 (70) | 90 (55) | 235 (58.8) |
| Recovered data | 13 (16) | 9 (24) | 17 (19) | 7 (18) | 29 (18) | 75 (18) |
| Losses | 17 (21) | 4 (10) | 20 (23) | 4 (10) | 38 (23) | 83 (21) |
| Refusals | 2 (2) | 0 (0) | 1 (1) | 0 (0) | 4 (2) | 7 (2) |
| Total | 78 (19) | 37 (9) | 87 (22) | 37 (9) | 161 (40.3) | 400 (100.0) |
| 15 days, n (%) | | | | | | |
| Conducted | 54 (69) | 30 (81) | 53 (60) | 25 (67) | 102 (63.4) | 264 (66.0) |
| Recovered data | 0 (0) | 1 (3) | 4 (4) | 1 (3) | 8 (5) | 14 (3) |
| Losses | 21 (26) | 5 (13) | 27 (31) | 11 (29) | 50 (31) | 114 (28.5) |
| Refusals | 3 (4) | 1 (3) | 3 (3) | 0 (0) | 1 (16) | 8 (2) |
| Total | 78 (19) | 37 (9) | 87 (22) | 37 (9) | 161 (40.3) | 400 (100.0) |
| 1 month, n (%) | | | | | | |
| Conducted | 50 (64) | 26 (70) | 55 (63) | 27 (73) | 109 (67.7) | 267 (66.8) |
| Recovered data | 0 (0) | 1 (3) | 2 (2) | 0 (0) | 4 (2) | 7 (2) |
| Losses | 19 (24) | 9 (24) | 21 (24) | 10 (27) | 36 (22) | 95 (23) |
| Refusals | 9 (11) | 1 (3) | 9 (10) | 0 (0) | 12 (7) | 31 (8) |
| Total | 78 (19) | 37 (9) | 87 (22) | 37 (9) | 161 (40.3) | 400 (100.0) |
| 3 months, n (%) | | | | | | |
| Conducted | 51 (65) | 26 (70) | 58 (66) | 26 (70) | 107 (66.5) | 268 (67.0) |
| Recovered data | 1 (1) | 1 (3) | 0 (0) | 0 (0) | 1 (1) | 3 (1) |
| Losses | 19 (24) | 8 (22) | 20 (23) | 10 (27) | 35 (22) | 92 (23) |
| Refusals | 7 (9) | 2 (5) | 9 (10) | 1 (3) | 18 (11) | 37 (9) |
| Total | 78 (19) | 37 (9) | 87 (22) | 37 (9) | 161 (40.3) | 400 (100.0) |
| 6 months, n (%) | | | | | | |
| Conducted | 48 (61) | 25 (68) | 43 (49) | 25 (68) | 94 (58) | 235 (58.8) |
| Losses | 23 (29) | 10 (27) | 32 (37) | 10 (27) | 47 (29) | 122 (30.5) |
| Refusals | 7 (9) | 2 (5) | 12 (14) | 2 (5) | 20 (12) | 43 (11) |
| Total | 78 (19) | 37 (9) | 87 (22) | 37 (9) | 161 (40.3) | 400 (100.0) |

^aDM: diabetes mellitus.

^bSAH: systemic arterial hypertension.

^cMS: maternal smoking.

^dSGA: small for gestational age.

Analysis of Variables From Newborns

As expected, newborns from the SGA group had significantly low birth weight, height, and head circumference ($P < .001$). Despite the different intrauterine environments, there was no statistically significant difference in the Apgar 1 and 5 indexes, and in the gender distribution (Table 4).

Analysis of Maternal and Health Care Variables

Mothers from the SAH group had the highest median age and a higher percentage of cesareans. In addition, these mothers

presented greater gestational weight gain. Mothers from the DM group had the highest values of pregestational BMI. The educational level of women smokers was statistically lower when compared with DM and control ($P = .005$). In addition, the MS group presented a higher percentage of mothers who did less than 7 prenatal consultations. Mothers of the SGA group had the lowest median age, and a lower median pregestational BMI and lower weight gain during gestation. This group also had the highest percentage of primiparous women compared with other groups ($P = .005$), with the exception of control (Table 4).

Table 4. Characteristics of the newborn and mothers related to study groups.

| Variables | DM ^a (N ^b =78) | SAH ^c (N ^b =37) | MS ^d (N ^b =87) | SGA ^e (N ^b =37) | Control (N ^b =161) | P value |
|---|--------------------------------------|---------------------------------------|--------------------------------------|---------------------------------------|-------------------------------|--------------------|
| Newborn | | | | | | |
| Gender (female), n (%) | 39 (50) | 19 (51) | 43 (49) | 22 (59) | 89 (55.2) | .78 |
| Weight at birth (g), median (range) | 3416.60 (2475 to 4760) | 3182.84 (2125 to 4630) | 3114.88 (2260 to 4000) | 2517.46 (2090 to 2760) | 3380.59 (2400 to 4965) | <.001 ^f |
| Length at birth (cm), median (range) | 48.95 (45 to 53) | 48.08 (44 to 53) | 48.04 (42 to 53) | 46.07 (42 to 49.5) | 49.33 (43.5 to 59) | <.001 ^f |
| Cephalic perimeter (cm), median (range) | 34.12 (31 to 37) | 34.00 (32 to 36.5) | 33.73 (31 to 37) | 31.92 (30 to 34.5) | 34.04 (30.5 to 38) | <.001 ^f |
| Apgar 1st min, median (range) | 8.31 (3 to 10) | 8.29 (3 to 10) | 8.51 (2 to 10) | 8.35 (4 to 10) | 8.37 (3 to 10) | .61 |
| Apgar 5th min, median (range) | 9.29 (7 to 10) | 9.49 (8 to 10) | 9.51 (7 to 10) | 9.58 (9 to 10) | 9.43 (7 to 10) | .19 |
| Mothers | | | | | | |
| Age (years), median (range) | 28.15 (17 to 40) | 29.05 (14 to 42) | 24.60 (16 to 39) | 23.84 (13 to 41) | 25.73 (15 to 42) | <.001 ^f |
| Maternal education (years), median (range) | 9.62 (1 to 17) | 9.32 (3 to 17) | 8.37 (3 to 15) | 9.72 (5 to 15) | 9.49 (0 to 17) | .005 ^f |
| Number of pregnancies, median (range) | 3.37 (2 to 8) | 3.08 (1 to 7) | 3.06 (1 to 8) | 2.69 (2 to 6) | 3.05 (1 to 9) | .56 |
| Primiparous, n (%) | 27 (35) | 10 (27) | 25 (29) | 21 (57) | 74 (45.9) | .005 ^g |
| Number prenatal consultations, n (%), <7 consultations | 13 (17) | 5 (13) | 49 (56) | 14 (38) | 50 (31.0) | <.001 ^g |
| Type of delivery, n (%) vaginal | 46 (59) | 11 (30) | 65 (75) | 24 (65) | 114 (70.8) | <.001 ^g |
| Pregestational BMI (kg/m ²), median (range) | 28.49 (19.8 to 55.9) | 27.92 (18.3 to 41.5) | 24.79 (15.4 to 43.3) | 22.78 (16.9 to 35.3) | 24.51 (18.0 to 41.6) | <.001 ^f |
| Gestational weight gain (kg), median (range) | 13.05 (-3 to 36.0) | 16.42 (0 to 31.5) | 13.81 (-2.6 to 30.8) | 11.48 (-3.0 to 25.8) | 13.64 (-9.0 to 33.5) | .02 ^f |

^aDM: diabetes mellitus.

^bN: refers to the entire population under study.

^cSAH: systemic arterial hypertension.

^dMS: maternal smoking.

^eSGA: small for gestational age.

^fKruskal-Wallis test with Dunn post hoc.

^gPearson chi-square test.

Discussion

Principal Findings

This study presented an original methodological prospective longitudinal design [14], focusing on maternal and infant clinical trajectory during the first 6 months of life. It was conducted in a city with 1.5 million inhabitants in a vast geographic area. The follow-up strategy performed a high number of interventions in a short period, leading to several methodological challenges [14]. Initially, a pilot study was conducted to investigate the feasibility of the research and to consolidate the methodology and logistics in this study. Strategies were applied to improve the mothers' adherence throughout the study, such as home visits. Interviews at 7 and 15 days and at 3 months were chosen because they do not include protocols that are difficult to execute or need specific devices, whereas postpartum 1 month and 6 months were carried out at the Clinical Research Center.

Usually, the follow-up is planned with larger intervals between interventions in the classical longitudinal studies carried out in Brazil. In the Pelotas cohort, the steps were at 3, 12, 24, and 48 months of age of the child [15]. In the IVAPSA study, the purpose was to establish several interventions in closer intervals up to 6 months of age [14]. Some protocols related to the mother's psychological parameters and the child's gross motor development contributed to the establishment of the selected periods [16,17].

Refusals to participate and dropouts and follow-up lost are expected in all cohort studies [18]. However, they can be minimized by consolidating an adequate relationship between the participants and the researchers, making the first contact very decisive for follow-up. In this study, most of the characteristics of the mothers and their newborns who refused to participate did not differ from those who consented to.

As expected, the SGA newborn group showed lower birth weight, length, and cephalic perimeter [19,20]. In a study published by our group, we found that, in addition to these

characteristics, mothers from the SGA group have shown low levels of leptin and insulin in the transition from colostrum to mature milk [21]. This finding can be associated with the rapid weight gain of these newborns in the first month of life. Another publication by our research team has shown that newborns from the SGA group had a greater impact on the growth trajectory in the first 6 months in comparison with MS and control groups, even considering factors such as MS or diet [22].

The mothers from the DM group had a higher pregestational BMI and delivered heavier newborns in relation to the other intrauterine groups. This result corroborates previous findings that also detected an association between pregestational BMI greater than 25 kg/m² and fetal macrosomia [23,24]. As demonstrated in other studies, lower birth weight medians were observed in the HAS, MS, and SGA groups [6,25-27]. All these intrauterine environments can be related to reduction in the placental perfusion, owing to increased blood pressure and constriction vasa, causing a deficit in fetal growth [25,27]. Regardless of this reduction in the placental perfusion that can also affect birth conditions [27], the Apgar index was similar among the groups in this study. Besides, some factors have been associated with the birth of SGA children, such as preterm delivery, short maternal stature, mother's low weight, maternal age, and unfavorable socioeconomic conditions [28]. Factors such as age or pregestational BMI were not different in the SGA group compared with the control group, in which children were not SGA.

The mothers of the SAH group had older age, higher median for gestational weight gain, and high pregestational BMI, results that were also observed by other authors [29]. According to the guidelines of the Institute of Medicine from the United States, the recommendation is that women with a BMI between 25 and 29.9 kg/m² should have gestational weight gain between 7 to 11.5 kg [30].

Mothers from the smoking group had lower educational level and lower total number of prenatal consultations, demonstrating an environment of social vulnerability. The pregnant woman's knowledge of her health condition (DM or SAH) may determine the demand for more frequent care than the others. A study published with data from this cohort, using MS and control groups, found that the number of prenatal consultations was negatively influenced by MS during pregnancy and by the number of children, along with a positive correlation regarding maternal age [31]. In the general analysis of groups, a higher frequency of more than 7 visits (67%) was observed, which corroborates with data observed in a previous study, evidencing an increase in prenatal coverage in Porto Alegre [32]. Currently, the World Health Organization recommends a minimum of 8 prenatal consultations to reduce perinatal mortality and improve the experience of care for women [33]. In the southern region of Brazil, the number of births from pregnant women with more

than 6 prenatal visits between the years 2000 and 2010 increased from 53.2% to 75.5%, and the demand for prenatal care was higher among women over 25 years of age [34,35].

Vaginal delivery was performed in most of the samples, except in the SAH group owing to obstetric peculiarities that usually require surgical delivery. Referring to the number of previous pregnancies, comparative data between the years 2004 and 2014 showed a decrease in the total fertility rate in Brazil from 2.14 to 1.74 [36]. In this study, it was found that all groups had a higher number of gestations when compared with the last Brazilian average.

Limitations

The random distribution of the participants' home, the vast distance traveled by the research team, and the high level of insecurity in some areas were some difficulties to conduct a longitudinal study in a large city in Brazil, different from classic cohort studies in small or medium-size cities such as Pelotas [15] and Ribeirão Preto [37]. Other important issues include obtaining financial support for the transportation of participants and researchers, permanent training of the research team, high frequency of changes at participants' addresses, and duration of the interview because of many questionnaires, ranging from 1 to 2.5 hours. Regarding the collection of biological materials, the main difficulty was the extraction of breast milk (colostrum) during the postpartum visit.

Strengths

In this study, the main strengths were the planning and structuring of a birth follow-up, considering the scenario of demographic and epidemiological transition in Brazil [36,38]. This process is characterized by an intense change in the pattern of health and disease throughout the population with an increased number of pregnant women with high obstetric risk. The adoption of a convenience sample from public hospitals and exclusion criteria were necessary to overcome difficulties in sample recruitment and allowed to control possible confounding such as gestational age, social class, and perinatal and prenatal interferences, facilitating the analysis of different outcomes between groups.

Conclusions

Considering the influence of intrauterine environments on the health outcomes in children and adults, and the potential interventions during pregnancy and at the newborn's first years of life, it is essential to understand the patterns of growth and development related to maternal clinical background. Therefore, this prospective longitudinal study with innovative design can bring new insights about causal mechanisms involved in health and illness of individual process and provides opportunities for public health promotion with prevention strategies.

Acknowledgments

The authors are especially grateful to the participating families for the availability and participation in the research.

Conflicts of Interest

None declared.

References

1. Calkins K, Devaskar SU. Fetal origins of adult disease. *Curr Probl Pediatr Adolesc Health Care* 2011 Jul;41(6):158-176 [FREE Full text] [doi: [10.1016/j.cppeds.2011.01.001](https://doi.org/10.1016/j.cppeds.2011.01.001)] [Medline: [21684471](https://pubmed.ncbi.nlm.nih.gov/21684471/)]
2. Simeoni U, Armengaud J, Siddeek B, Tolsa J. Perinatal origins of adult disease. *Neonatology* 2018;113(4):393-399. [doi: [10.1159/000487618](https://doi.org/10.1159/000487618)] [Medline: [29852488](https://pubmed.ncbi.nlm.nih.gov/29852488/)]
3. Barker DJ, Eriksson JG, Forsén T, Osmond C. Fetal origins of adult disease: strength of effects and biological basis. *Int J Epidemiol* 2002 Dec;31(6):1235-1239. [doi: [10.1093/ije/31.6.1235](https://doi.org/10.1093/ije/31.6.1235)] [Medline: [12540728](https://pubmed.ncbi.nlm.nih.gov/12540728/)]
4. Gluckman PD, Hanson MA. Developmental plasticity and human disease: research directions. *J Intern Med* 2007 May;261(5):461-471 [FREE Full text] [doi: [10.1111/j.1365-2796.2007.01802.x](https://doi.org/10.1111/j.1365-2796.2007.01802.x)] [Medline: [17444885](https://pubmed.ncbi.nlm.nih.gov/17444885/)]
5. Chandler-Laney P. Possible link between mothers' high blood sugar during pregnancy and children's reduced insulin sensitivity? *Pediatric Heal* 2010 Dec;4(6):561-563. [doi: [10.2217/phe.10.55](https://doi.org/10.2217/phe.10.55)]
6. Kvehaugen AS, Dechend R, Ramstad HB, Troisi R, Fugelseth D, Staff AC. Endothelial function and circulating biomarkers are disturbed in women and children after preeclampsia. *Hypertension* 2011 Jul;58(1):63-69. [doi: [10.1161/HYPERTENSIONAHA.111.172387](https://doi.org/10.1161/HYPERTENSIONAHA.111.172387)] [Medline: [21606387](https://pubmed.ncbi.nlm.nih.gov/21606387/)]
7. Pinheiro TV, Brunetto S, Ramos JG, Bernardi JR, Goldani MZ. Hypertensive disorders during pregnancy and health outcomes in the offspring: a systematic review. *J Dev Orig Health Dis* 2016 Aug;7(4):391-407. [doi: [10.1017/S2040174416000209](https://doi.org/10.1017/S2040174416000209)] [Medline: [27168118](https://pubmed.ncbi.nlm.nih.gov/27168118/)]
8. Aagaard-Tillery KM, Porter TF, Lane RH, Varner MW, Lacoursiere DY. In utero tobacco exposure is associated with modified effects of maternal factors on fetal growth. *Am J Obstet Gynecol* 2008 Jan;198(1):66.e1-66.e6. [doi: [10.1016/j.ajog.2007.06.078](https://doi.org/10.1016/j.ajog.2007.06.078)] [Medline: [18166310](https://pubmed.ncbi.nlm.nih.gov/18166310/)]
9. Pagani LS. Environmental tobacco smoke exposure and brain development: the case of attention deficit/hyperactivity disorder. *Neurosci Biobehav Rev* 2014 Jul;44:195-205. [doi: [10.1016/j.neubiorev.2013.03.008](https://doi.org/10.1016/j.neubiorev.2013.03.008)] [Medline: [23545330](https://pubmed.ncbi.nlm.nih.gov/23545330/)]
10. Burke H, Leonardi-Bee J, Hashim A, Pine-Abata H, Chen Y, Cook DG, et al. Prenatal and passive smoke exposure and incidence of asthma and wheeze: systematic review and meta-analysis. *Pediatrics* 2012 Apr;129(4):735-744. [doi: [10.1542/peds.2011-2196](https://doi.org/10.1542/peds.2011-2196)] [Medline: [22430451](https://pubmed.ncbi.nlm.nih.gov/22430451/)]
11. Stocks J, Sonnappa S. Early life influences on the development of chronic obstructive pulmonary disease. *Thorax* 2013 Jun;73(3):161-173 [FREE Full text] [doi: [10.1177/1753465813479428](https://doi.org/10.1177/1753465813479428)] [Medline: [23439689](https://pubmed.ncbi.nlm.nih.gov/23439689/)]
12. Devaskar SU, Chu A. Intrauterine growth restriction: hungry for an answer. *Physiology (Bethesda)* 2016 Mar;31(2):131-146 [FREE Full text] [doi: [10.1152/physiol.00033.2015](https://doi.org/10.1152/physiol.00033.2015)] [Medline: [26889018](https://pubmed.ncbi.nlm.nih.gov/26889018/)]
13. Alexander GR, Himes JH, Kaufman RB, Mor J, Kogan M. A United States national reference for fetal growth. *Obstet Gynecol* 1996 Feb;87(2):163-168. [doi: [10.1016/0029-7844\(95\)00386-X](https://doi.org/10.1016/0029-7844(95)00386-X)] [Medline: [8559516](https://pubmed.ncbi.nlm.nih.gov/8559516/)]
14. Bernardi JR, Ferreira CF, Nunes M, da Silva CH, Bosa VL, Silveira PP, et al. Impact of perinatal different intrauterine environments on child growth and development in the first six months of life--IVAPSA birth cohort: rationale, design, and methods. *BMC Pregnancy Childbirth* 2012 Apr 2;12:25 [FREE Full text] [doi: [10.1186/1471-2393-12-25](https://doi.org/10.1186/1471-2393-12-25)] [Medline: [22471837](https://pubmed.ncbi.nlm.nih.gov/22471837/)]
15. Santos IS, Barros AJ, Matijasevich A, Domingues MR, Barros FC, Victora CG. Cohort profile: the 2004 Pelotas (Brazil) birth cohort study. *Int J Epidemiol* 2011 Dec;40(6):1461-1468 [FREE Full text] [doi: [10.1093/ije/dyq130](https://doi.org/10.1093/ije/dyq130)] [Medline: [20702597](https://pubmed.ncbi.nlm.nih.gov/20702597/)]
16. Pridham KF, Chang AS. What being the parent of a new baby is like: revision of an instrument. *Res Nurs Health* 1989 Oct;12(5):323-329. [Medline: [2798953](https://pubmed.ncbi.nlm.nih.gov/2798953/)]
17. Liao PJ, Campbell SK. Examination of the item structure of the Alberta infant motor scale. *Pediatr Phys Ther* 2004;16(1):31-38. [doi: [10.1097/01.PEP.0000114843.92102.98](https://doi.org/10.1097/01.PEP.0000114843.92102.98)] [Medline: [17057469](https://pubmed.ncbi.nlm.nih.gov/17057469/)]
18. Coeli C, Faerstein E. Estudos de coorte. In: *Epidemiologia*. Second edition. São Paulo, SP, Brazil: Atheneu; 2008.
19. Dacaj R, Izetbegovic S, Stojkanovic G, Gjocaj C. Hepato - Cephalic index as a predictor of Intrauterine Growth Restriction. *Acta Inform Med* 2016 Feb;24(1):12-15 [FREE Full text] [doi: [10.5455/aim.2016.24.12-15](https://doi.org/10.5455/aim.2016.24.12-15)] [Medline: [27046941](https://pubmed.ncbi.nlm.nih.gov/27046941/)]
20. Castanys-Muñoz E, Kennedy K, Castañeda-Gutiérrez E, Forsyth S, Godfrey KM, Koletzko B, et al. Systematic review indicates postnatal growth in term infants born small-for-gestational-age being associated with later neurocognitive and metabolic outcomes. *Acta Paediatr* 2017 Aug;106(8):1230-1238. [doi: [10.1111/apa.13868](https://doi.org/10.1111/apa.13868)] [Medline: [28382722](https://pubmed.ncbi.nlm.nih.gov/28382722/)]
21. Nunes M, da Silva CH, Bosa VL, Bernardi JR, Werlang IC, Goldani MZ, NESCA Group. Could a remarkable decrease in leptin and insulin levels from colostrum to mature milk contribute to early growth catch-up of SGA infants? *BMC Pregnancy Childbirth* 2017 Dec 6;17(1):410 [FREE Full text] [doi: [10.1186/s12884-017-1593-0](https://doi.org/10.1186/s12884-017-1593-0)] [Medline: [29212463](https://pubmed.ncbi.nlm.nih.gov/29212463/)]
22. de Brito ML, Nunes M, Bernardi JR, Bosa VL, Goldani MZ, da Silva CH. Somatic growth in the first six months of life of infants exposed to maternal smoking in pregnancy. *BMC Pediatr* 2017 Mar 9;17(1):67 [FREE Full text] [doi: [10.1186/s12887-017-0819-7](https://doi.org/10.1186/s12887-017-0819-7)] [Medline: [28279149](https://pubmed.ncbi.nlm.nih.gov/28279149/)]

23. Ben-Haroush A, Hadar E, Chen R, Hod M, Yogev Y. Maternal obesity is a major risk factor for large-for-gestational-infants in pregnancies complicated by gestational diabetes. *Arch Gynecol Obstet* 2009 Apr;279(4):539-543. [doi: [10.1007/s00404-008-0767-4](https://doi.org/10.1007/s00404-008-0767-4)] [Medline: [18758799](https://pubmed.ncbi.nlm.nih.gov/18758799/)]
24. Gaudet L, Ferraro ZM, Wen SW, Walker M. Maternal obesity and occurrence of fetal macrosomia: a systematic review and meta-analysis. *Biomed Res Int* 2014;2014:640291 [FREE Full text] [doi: [10.1155/2014/640291](https://doi.org/10.1155/2014/640291)] [Medline: [25544943](https://pubmed.ncbi.nlm.nih.gov/25544943/)]
25. Bakker H, Jaddoe VW. Cardiovascular and metabolic influences of fetal smoke exposure. *Eur J Epidemiol* 2011 Oct;26(10):763-770 [FREE Full text] [doi: [10.1007/s10654-011-9621-2](https://doi.org/10.1007/s10654-011-9621-2)] [Medline: [21994150](https://pubmed.ncbi.nlm.nih.gov/21994150/)]
26. Chelchowska M, Ambroszkiewicz J, Jablonka-Salach K, Gajewska J, Maciejewski TM, Bulska E, et al. Tobacco smoke exposure during pregnancy increases maternal blood lead levels affecting neonate birth weight. *Biol Trace Elem Res* 2013 Nov;155(2):169-175 [FREE Full text] [doi: [10.1007/s12011-013-9775-8](https://doi.org/10.1007/s12011-013-9775-8)] [Medline: [23934137](https://pubmed.ncbi.nlm.nih.gov/23934137/)]
27. Oliveira C, Lins CP, Sá R, Netto HC, Bornia RG, Silva N, et al. Síndromes hipertensivas da gestação e repercussões perinatais. *Rev Bras Saude Mater Infant* 2006 Mar;6(1):93-98 [FREE Full text] [doi: [10.1590/S1519-38292006000100011](https://doi.org/10.1590/S1519-38292006000100011)]
28. Eickmann SH, Lima M, Motta M, Romani S, Lira P. Crescimento de nascidos a termo com peso baixo e adequado nos dois primeiros anos de vida. *Rev Saúde Pública* 2006 Dec;40(6):1073-1081. [doi: [10.1590/S0034-89102006000700016](https://doi.org/10.1590/S0034-89102006000700016)]
29. Macdonald-Wallis C, Tilling K, Fraser A, Nelson SM, Lawlor DA. Gestational weight gain as a risk factor for hypertensive disorders of pregnancy. *Am J Obstet Gynecol* 2013 Oct;209(4):327.e1-327.17 [FREE Full text] [doi: [10.1016/j.ajog.2013.05.042](https://doi.org/10.1016/j.ajog.2013.05.042)] [Medline: [23711667](https://pubmed.ncbi.nlm.nih.gov/23711667/)]
30. National Research Council, Institute of Medicine, Board on Children, Youth, and Families, Food and Nutrition Board, Committee to Reexamine IOM Pregnancy Weight Guidelines. Gestational weight gain as a risk factor for hypertensive disorders of pregnancy. In: Rasmussen KM, Yaktine AL, editors. *Weight Gain During Pregnancy: Reexamining The Guidelines*. Washington (DC): National Academies Press; 2009.
31. Ferreira AP, Bernardi JR, Ferreira CF, Santos D, Santos KF, Pereira LW, et al. Fatores associados ao número de consultas pré-natais de mulheres tabagistas e não tabagistas atendidas em hospitais de porto alegre (RS), Brasil. *Saúde em Redes* 2016 Aug;2(2):161-178. [doi: [10.18310/2446-4813.2016v2n2p167-178](https://doi.org/10.18310/2446-4813.2016v2n2p167-178)]
32. Galão A, Soder A, Gerhardt M, Faertes T, Kruger M, Pereira M, et al. SEER UFRGS. Effects of maternal smoking during pregnancy and perinatal complications URL: <https://seer.ufrgs.br/hcpa/article/view/10669/7002> [accessed 2019-09-23]
33. World Health Organization. WHO Recommendations on Antenatal Care for a Positive Pregnancy Experience. Geneva, Switzerland: World Health Organization; 2016.
34. IBGE, Coordenação de População e Indicadores Sociais. Síntese de indicadores sociais: uma análise das condições de vida da população brasileira. In: *Estudos e Pesquisas - Informação Demográfica e Socioeconômica*. Rio de Janeiro, RJ, Brazil: IBGE; 2015.
35. Buriol VC, Hirakata V, Goldani MZ, da Silva CH. Temporal evolution of the risk factors associated with low birth weight rates in Brazilian capitals (1996-2011). *Popul Health Metr* 2016;14:15 [FREE Full text] [doi: [10.1186/s12963-016-0086-0](https://doi.org/10.1186/s12963-016-0086-0)] [Medline: [27147908](https://pubmed.ncbi.nlm.nih.gov/27147908/)]
36. Schramm JM, Oliveira AF, Leite I, Valente JG, Gadelha AJ, Portela MC. Epidemiological transition and the study of burden of disease in Brazil. *Ciência & Saúde Coletiva* 2004;9(4):897-908. [doi: [10.1590/S1413-81232004000400011](https://doi.org/10.1590/S1413-81232004000400011)]
37. Barbieri MA, Bettiol H, Silva AA, Cardoso VC, Simões VM, Gutierrez MR, et al. Health in early adulthood: the contribution of the 1978/79 Ribeirão Preto birth cohort. *Braz J Med Biol Res* 2006 Aug;39(8):1041-1055 [FREE Full text] [doi: [10.1590/s0100-879x2006000800007](https://doi.org/10.1590/s0100-879x2006000800007)] [Medline: [16906279](https://pubmed.ncbi.nlm.nih.gov/16906279/)]
38. Mendes A, Sá DA, Miranda G, Lyra T, Tavares R. [The public healthcare system in the context of Brazil's demographic transition: current and future demands]. *Cad Saude Publica* 2012 May;28(5):955-964 [FREE Full text] [doi: [10.1590/s0102-311x2012000500014](https://doi.org/10.1590/s0102-311x2012000500014)] [Medline: [22641518](https://pubmed.ncbi.nlm.nih.gov/22641518/)]

Abbreviations

BMI: body mass index

DM: diabetes mellitus

GHC: Grupo Hospitalar Conceição

HCPA: Hospital de Clínicas de Porto Alegre

IVAPSA: impact of perinatal environment variations on health of the newborn at first 6 months of life

MS: maternal smoking

SAH: systemic arterial hypertension

SGA: small for gestational age

Edited by G Eysenbach; submitted 03.12.18; peer-reviewed by S Shorey, J van den Heuvel; comments to author 08.04.19; revised version received 05.08.19; accepted 21.08.19; published 12.11.19.

Please cite as:

Werlang ICR, Bernardi JR, Nunes M, Marcelino TB, Bosa VL, Michalowski MB, da Silva CH, Goldani MZ

Impact of Perinatal Different Intrauterine Environments on Child Growth and Development: Planning and Baseline Data for a Cohort Study

JMIR Res Protoc 2019;8(11):e12970

URL: <http://www.researchprotocols.org/2019/11/e12970/>

doi: [10.2196/12970](https://doi.org/10.2196/12970)

PMID: [31714249](https://pubmed.ncbi.nlm.nih.gov/31714249/)

©Isabel Cristina Ribas Werlang, Juliana Rombaldi Bernardi, Marina Nunes, Thiago Beltram Marcelino, Vera Lucia Bosa, Mariana Bohns Michalowski, Clécio Homrich da Silva, Marcelo Zubarán Goldani. Originally published in JMIR Research Protocols (<http://www.researchprotocols.org>), 12.11.2019. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in JMIR Research Protocols, is properly cited. The complete bibliographic information, a link to the original publication on <http://www.researchprotocols.org>, as well as this copyright and license information must be included.

Protocol

Monitoring of Vedolizumab Infusion Therapy (MOVE-IT) Response With Fecal Inflammation Markers, Ultrasound, and Trough Serum Level in Patients With Ulcerative Colitis: Protocol for a Multicentric, Prospective, Noninterventional Study

Jimmi Cording^{1*}, PhD; Margit Blömacher^{1*}, PhD; Berit Inga Wiebe¹, MSc; Jost Langhorst², PhD, MD; Torsten Kucharzik³, MD, PhD; Andreas Sturm⁴, MD, PhD; Stefan Schreiber⁵, MD, PhD; Ulf Helwig^{5,6}, MD, PhD

¹Kompetenznetz Darmerkrankungen eV, Kiel, Germany

²Klinikum Bamberg, Bamberg, Germany

³Klinikum Lüneburg, Lüneburg, Germany

⁴DRK Kliniken Berlin | Westend, Berlin, Germany

⁵University of Kiel, Kiel, Germany

⁶Medical Practice for Internal Medicine Oldenburg, Oldenburg, Germany

*these authors contributed equally

Corresponding Author:

Jimmi Cording, PhD

Kompetenznetz Darmerkrankungen eV

Hopfenstraße 60

Kiel, 24103

Germany

Phone: 49 15129110689

Email: j.cording@kompetenznetz-ced.de

Abstract

Background: Vedolizumab has been shown to induce clinical remission in patients with active ulcerative colitis. Treatment with anti-integrin vedolizumab leads to clinical remission in 16.9% and clinical response in 47.1% of cases after 6 weeks. However, in clinical practice, no decision to discontinue or continue vedolizumab therapy is made until 14 weeks at the earliest.

Objective: The aim of this study is to develop an algorithm for optimizing vedolizumab administration in patients with moderate-to-severe ulcerative colitis by calculating the probability of clinical response at week 14, on the basis of the data from week 6.

Methods: This is a prospective, single-arm, multicentric, noninterventional, observational study with no interim analyses and a sample size of 35 evaluable patients.

Results: The enrollment started in August 2018 and was still open at the date of submission. The study is expected to complete in September 2020.

Conclusions: The early identification of patients who are responding to an integrin antibody is therapeutically beneficial. At the same time, patients who are not responding can be identified earlier. The development of a therapeutic algorithm for identifying patients as responders or nonresponders can thus help prescribing physicians avoid ineffective treatments and stop these very early.

(*JMIR Res Protoc* 2019;8(11):e14335) doi:[10.2196/14335](https://doi.org/10.2196/14335)

KEYWORDS

ulcerative colitis; vedolizumab; ultrasound

Introduction

Background

Ulcerative colitis (UC) belongs to the group of chronic inflammatory bowel diseases (IBD), with a chronic recurrent course of disease. Vedolizumab has been shown to induce clinical remission in patients with active UC [1]. Treatment with anti-integrin vedolizumab leads to clinical remission in 16.9% and clinical response in 47.1% of cases after 6 weeks [1]. However, in clinical practice no decision to discontinue or continue vedolizumab therapy is made until 14 weeks at the earliest. Sometimes, clinical response could be improved by an additional infusion at week 10. The decision to perform this infusion has not been defined yet.

Early identification of patients responding to an anti-integrin antibody would result in a therapeutic benefit, whereas patients who would not respond could be identified earlier than usual. This approach would lead to a safer anti-integrin antibody application; consequently, this would lead to an increased penetration rate of biological treatment in IBD patients.

Objective

This study aims to create a decision algorithm for the optimized use of vedolizumab. The algorithm is based on measurements of early changes in noninvasive clinical markers, such as fecal calprotectin, intestinal ultrasound (IUS), and drug levels.

In interventional pivotal studies, the partial Mayo score, as used in the GEMINI study [1,2], is often regarded as the gold standard.

Here, we also seek to use IUS to determine the course of IBD disease. In the last decade, IUS has emerged as an important imaging modality in the diagnosis of Crohn disease (CD), as well as for monitoring disease progression, and in the therapeutic response to CD and UC. The technique is of growing importance in IBD [3].

Methods

Trial Design

The study is being carried out in conformity with the German Medicinal Products Act (*Arzneimittelgesetz*, AMG) and is a noninterventional study in accordance with the Medicinal Products Act (§ 4 section 23 p. 3 AMG). The study is designed as a prospective, single-arm, multicentric, noninterventional, observational study, with no interim analyses and a sample size of 35 evaluable patients, for which 50 patients need to be recruited.

Outcomes

Primary

The aim of the study is to show that a change in selected parameters—positive drug levels ≥ 24 $\mu\text{g/mL}$, fecal calprotectin $\geq 50\%$, and changes in abdominal ultrasound properties ($\geq 25\%$ reduction in wall thickness)—compared with the baseline value at week 6 are reliable predictors of clinical response at week 14.

Trough Serum Level

We assume that early measurable positive trough level might have a predictive value for the clinical response. Data from studies involving vedolizumab showed predictive interpretation on trough serum levels of vedolizumab. It was shown that 87.67% of patients at week 6 responded in a trough-level-dependent manner. In addition, studies on antitumor necrosis factor (TNF) agents have shown that the early drug level is important to predict response to therapy [1,4].

Secondary

To predict the probability of a clinical response to a therapy with the integrin antibody vedolizumab at week 22, we monitored the elevation of the fecal calprotectin level in week 6, of the abdominal ultrasound, and the drug level. In addition, it is being investigated whether other stool markers (lactoferrin, S100A12, or Polymorphonuclear-(PMN) elastase) can be used as predictors for a clinical response to a vedolizumab therapy.

In addition to the primary study goal, the following secondary outcomes are being analyzed:

- The different markers (combinations of markers), regarding their correlation with the clinical response (eg, receiver operating characteristic curves or chi-square);
- At which time point a 50% reduction of fecal inflammation markers and ultrasound are reliable predictors of response (other than at 6 weeks);
- Whether antidrug antibodies (ADA) formation at week 6 correlates with clinical response, at least in anti-TNF treatment, and is an important marker [5]; the presence of ADA will be determined using the Vedolizumab free ADA enzyme-linked immunosorbent assay kit (Immundiagnostik AG);
- Whether ADA and vedolizumab levels correlate with any levels of fecal inflammation markers—calprotectin assay (TechLab, Inc);
- Ultrasound (which stool marker has the best sensitivity);
- Whether the following parameters are associated with clinical response—serum C-reactive protein (CRP) level, number of leukocytes, number of thrombocytes, hemoglobin level, and if applicable, ferritin level;
- The rates of adverse events are documented and evaluated; and
- The therapy maintenance is measured by at a follow-up visit at week 52.

Statistics

Statistical Analysis

The hypothesis for the primary endpoint of predicting clinical response at week 14 by at least 2 improved markers (drug level, intestinal ultrasound, and calprotectin level) at week 6 is as follows:

H_0 : The probability of response $P_1 = n_{11}/n_{1+}$ and $P_2 = n_{21}/n_{2+}$ is the same for both groups (improved markers vs nonimproved markers).

H_0 : $P_1 = P_2$

vs

H1: The probability of response is not the same.

$H_1: P_1 \neq P_2$

The sample size calculation will be done with a chi-square test.

The secondary endpoints will be analyzed with suitable statistical methods, such as receiver operating characteristic

curves or rank correlation for correlations. To analyze parameters associated with clinical response, a regression analysis will be performed. The analysis of adverse events will be done with appropriate descriptive methods.

There will be no interims analysis; there will be only 1 analysis at the end of the study (Table 1).

Table 1. Calculation of response rate to vedolizumab infusion therapy.

| At least 2 improved markers (week 6) | Clinical response (week 14) | | Total |
|--------------------------------------|-----------------------------|----------|------------------|
| | Yes | No | |
| Yes | n_{11} | n_{12} | n_{1+} |
| No | n_{21} | n_{22} | n_{2+} |
| Total | n_{+1} | n_{+2} | N/A ^a |

^aNot applicable.

Sample Size Calculation

The following assumptions were used to calculate the sample size (Table 2):

- The rate of clinical response at week 14 is 0.57 [6].
- The assumptions for clinical response rates at week 14 for the changed markers at week 6 are that 80% of patients with at least two improved markers at week 6 will have a clinical response at week 14, and 25% of patients who have less than 2 improved markers at week 6 will have a clinical response at week 14.

The clinical response in week 14 is measured with the partial Mayo score:

- Reduction of <2 points (clinical response)
- Partial Mayo score of ≤ 2 points (remission)

These assumptions result in a sample size of 36 patients (calculated with the R function Basic Functions for Power Analysis [pwr] chi-square test, significance level=0.05, and power=0.9). With a dropout rate of 35%, the sample size is 50 patients.

Table 2. Sample size calculation based on a clinical response rate of 0.57.

| At least 2 improved markers (week 6) | Clinical response (week 14) | |
|--------------------------------------|-----------------------------|---------------|
| | Yes | No |
| Yes | $p_{11}=0.8$ | $p_{12}=0.2$ |
| No | $p_{21}=0.25$ | $p_{22}=0.75$ |
| Total | $p_{2+1}=0.57$ | $p_{+2}=0.43$ |

Definition of Study Population

The primary and secondary evaluation criteria are assessed according to the intention-to-treat principle (ITT). The corresponding collective includes all patients included in the study, regardless of possible protocol violations (eg, study terminations). In addition to the ITT analyses, sensitivity analyses are being carried out according to the per-protocol principle. Relevant protocol violations that lead to exclusion from the per-protocol collective are defined in the statistical analysis plan.

Selection of Study Centers

All study centers are part of the German IBD Study Group, and they are chosen according to their main area of focus and their experience in the treatment of UC. Regarding the results of the IUS examinations, no differences in the diagnostic quality of IUS measurements were found among gastroenterologists [7,8]. By signing the investigator agreement, each study center selected confirms its fulfilment of all formal requirements for inclusion in the study and guarantees its compliance with data privacy

laws and any other regulations pertaining to the execution of this observational study.

Participant Criteria

The inclusion criteria for the study include (1) clinically and endoscopically confirmed diagnosis of UC (3 months before participation in the study); (2) secured disease by increased fecal calprotectin $\geq 100 \mu\text{g/g}$ and/or endoscopic score: Ulcerative Colitis Endoscopic Index of Severity ≥ 3 , 3 weeks before the baseline visit; (3) ultrasound detectable disease; sonographic sign of active inflammation, determined by the bowel wall thickness $>4 \text{ mm}$ (sigmoidum), $>3 \text{ mm}$ (colon); (4) if an independent treatment with vedolizumab according to the routine medical practice is done, there should a break of at least 12 weeks between the end of the treatment and the beginning of the participation in the study; (5) age ≥ 18 years and <80 years; (6) signed consent form; (7) start of a study-independent vedolizumab therapy according to medical practice; (8) sufficient German language communication skills; and (9) ability of the patient to understand the nature, significance, and scope

of the clinical trial and make an independent decision on the basis of this knowledge.

The exclusion criteria include (1) pregnancy and lactation; (2) off-label treatment with vedolizumab; (3) contraindications for treatment with vedolizumab (according to product information); (4) ileostoma or ileoanal pouch; (5) infectious colitis (eg, *Clostridium difficile* colitis and *Cytomegalovirus* colitis); (6) obesity \geq grade I (body mass index >30): insufficient, sonographic intestinal wall imaging; (7) proctitis; (8) participation in an intervention study within the last 30 days before the start of the vedolizumab therapy; and (9) other medical reasons.

Study-Specific Interventions

No medical interventions are performed in the course of the study other than those required by the standard medical procedure. When taking routine blood samples, vedolizumab serum levels and anti-vedolizumab antibody levels should also be monitored, if possible. Only the natural progress of the disease in UC patients is monitored and evaluated.

Schedule of Visits

There are no defined study visits. In the course of the study, the only clinical and laboratory data recorded are those corresponding to the standard medical procedure. Data are recorded in the following observational weeks: baseline/screening, 6, (10, optional), 14, 22, and 52. Deviations of ± 5 days from this documentation schedule fall within the scope of the study protocol. The period until the next examination is subsequently shortened or lengthened accordingly to compensate for deviations and maintain the examination rhythm.

The following data are recorded at the initial screening examination: date of consent, screening date, inclusion and exclusion criteria, personal information (date of birth, sex, height, weight, and smoker status), date of initial UC diagnosis, first symptoms, duration of acute symptoms (in days), Montreal classification, and information regarding previous medication (anti-TNF, aminosalicylates, budesonide, systemic corticosteroids, and azathioprine).

During the follow-up visits (baseline, weeks 6, 14, and 22), data on the following parameters are collected: current medication (vedolizumab [time and dose], aminosalicylate, budesonide, systemic corticosteroids, and azathioprine); partial Mayo score; laboratory tests (hemoglobin, CRP, leukocytes, calprotectin, lactoferrin, PMN elastase, S100A12, vedolizumab trough serum levels, anti-vedolizumab antibodies); and IUS parameters.

At week 10 (optional visit), current medication, partial Mayo score, laboratory tests (hemoglobin, CRP, and leukocytes), current disease activity, notification of serious adverse event/adverse drug reactions events, and special situations are reported. A week 10 infusion is approved in Germany, and it cannot be prevented in an observational study. We assume that this infusion at week 10 will have no influence on the overall result (nor on our predictability). In addition, the intestinal ultrasound is measured. In the follow-up visit (week 52), the

maintenance of the therapy is assessed by determining the partial Mayo score.

Documentation

Data are recorded using case report forms (CRFs). The investigator is responsible for the timely, correct, complete, and legible recording of study data in the CRF and confirms recording by signature. CRFs are completed with a black ballpoint pen. Corrections are documented as follows: The wrong entry is crossed out with a single line, and corrections are entered next to the crossed-out text and verified by date and initials, stating the reason for the change, if necessary. Instructions for use (entry and corrections) are included in each CRF. Source data, according to the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use E6 guideline on good clinical practice (GCP), are original documents in patient files, as well as doctors' letters, certified copies of original records, and laboratory printouts. Study data are to be recorded from patient files.

Patient Identification

All patient data are pseudonymized. Each patient will be clearly identified by a patient identification number assigned at each study center. The investigator will keep a patient identification list, documenting the patient identification number with the patient's full name, date of birth, sex, and date of informed consent.

The patient identification list is part of the investigator file, and it will remain at the site. The patient identification number comprises a 2-digit clinic number, as well as a running 2-digit number of recruited patients per study site.

Trial

Start of Patient Participation

Any patient with a clinically and endoscopically confirmed diagnosis of UC and qualified for vedolizumab treatment according to routine medical practice is a potential study candidate. All potential candidates who come to the attention of the investigator will be informed regarding the possibility of participating in the study.

End of Patient Participation

The observation of each patient ends according to the schedule with the last study visit. A patient's participation in the study will be terminated prematurely if at least one of the following criteria is met: (1) withdrawal of informed consent, (2) termination of vedolizumab treatment, (3) lack of medical justification for further participation in the study, (4) premature termination of the complete trial, or (5) subsequent discovery that not all inclusion criteria are met and/or that any exclusion criteria are met.

Trial Duration/End of Trial

The recruiting phase has a planned duration of 24 months. The observational phase has a planned duration of 52 weeks. The complete trial is considered to have ended after all queries from the study coordination center have been answered by each

individual study center, at the latest, 4 months after the last visit of the last patient.

Study centers that grossly violate the AMG, data protection regulations, or the GCP guidelines can be excluded from the further recruitment and observation of study patients. Premature termination of the study as a whole will be taken into consideration if ethical or scientific justification for the trial is compromised or no longer valid, errors or violations significantly compromise the scientific integrity of the data collected for the study with regard to the study aims, or the requirements for a successful execution of the study are no longer fulfilled for other reasons. The principal investigator will consult the corresponding biometrician regarding any possible premature termination of the trial. The minutes of the aforementioned consultation meeting will be recorded and subjected to the approval of both parties. Any decision regarding the premature termination of the trial will be taken jointly by the principal investigator and the corresponding biometrician.

Data Quality Assurance

Upon receipt at the study coordination center, CRF will be checked for completeness and consistency (in-house review). Queries will be generated for missing or implausible entries and sent to the corresponding study centers. After the clarification of implausible entries and completion of missing data, CRF will be handed over to the corresponding data management department for data entry.

Quality Control and Assurance

The principal investigator and/or auditors designated by the principal investigator are entitled to conduct audits at the study centers and any other facilities participating in the study. They are entitled to inspect and review all study-relevant documents. This right also applies to regulatory inspectors.

Ethical and Regulatory Aspects

The study is conducted in compliance with the current version of the Declaration of Helsinki (October 2013, Fortaleza, Brazil). This study cannot begin before approval has been obtained from the corresponding ethics committee. Before inclusion in the study, the investigator will inform each patient about the nature, significance, risks, and scope of the study, as well as the patient's right to withdraw from the study at any time without prejudice. An informed consent form is handed to the patient, describing the study in nonscientific and generally understandable language. Each patient must consent to study participation in writing. The patient must be provided with adequate time to decide with the opportunity to ask any questions before the consent form is signed.

In accordance with AMG, § 40 Abs. 2a, patients are informed that the data related to their disease will be stored with a pseudonym and analyzed for scientific purposes. Patients must consent to the use of their pseudonymized data in writing. Informed consent forms are to be signed and dated by the patient and the treating physician.

This clinical study is carried out in conformity with the requirements of the current German Medicinal Products Act, as well as all applicable legal provisions regarding data

protection and the GCP guidelines. The general notification requirement as per § 67 AMG will be complied with.

Results

The enrollment started in August 2018 and was still open at the date of submission. The study is expected to complete in August 2020.

Discussion

Rationale for the Trial

In this study, a prospective study approach was chosen, as the probability of a clinical response at week 14 is to be calculated on the basis of the data from week 6. A single cohort is needed to answer this question. It is not necessary to compare groups with the same structure.

Justifications for Trial Design

To achieve a higher representativeness of the study statement for the population as a whole, the study will be conducted nationwide and multicentrally, with specially selected study sites. The treatment and diagnosis do not follow a predefined test plan, but they exclusively follow the medical practice. A vedolizumab infusion at week 10 is approved in Germany, and this cannot be prevented in an observational study. We assume that this infusion at week 10 will have no influence on the overall result (nor on our predictability). This noninterventional approach is intended to strengthen the representativeness of the study statement for everyday medical practice, as no reduction in the dispersion of the target parameters is achieved through different experimental approaches.

Trough Serum Level

Trough serum levels above 24 µg/mL of vedolizumab at week 6 are associated with clinical remission and clinical response [1]. Early low trough serum level and antibody detection toward the therapeutic drug antibody are at least documented for TNF-alpha antibodies, and they are associated with a poor response [5]. Therefore, an early measurable high trough serum level and the absence of antibodies might have a predictive value on the clinical response [1].

Stool Marker

Fecal calprotectin reflects the mucosal inflammation status. The good correlation between high fecal calprotectin and mucosal inflammation is described previously [9,10]. We assume a clear activity, measured by fecal calprotectin and/or endoscopic score. Therefore, the Mayo score was chosen as the inclusion criterion. Furthermore, there is no doubt, that fecal calprotectin is diminished during a valuable therapeutic response. At least in the UC trial, calprotectin was significantly diminished in the verum arm versus placebo arm [1]. The median calprotectin level showed a reduction of 50% (from 1000 µg/g to 500 µg/g) [1]. Different stool markers have diverse sensitivity [11]. Therefore, a different determination of stool markers might be useful to distinguish between responders and nonresponders. The prediction of response is shown for fecal calprotectin [12], lactoferrin [13], and S100A12 [11,14].

Intestinal Ultrasound

The detection of intestinal inflammation by ultrasound is a well-established but underused method [3]. Recently, we have shown that the reduction of ultrasound features correlates with clinical response in CD [7,8]. Similar data were presented at the United European Gastroenterology week 2017 in Barcelona

for UC [15]. Furthermore, early response was seen in UC by rectal ultrasound [16].

This early monitoring of response study aims to achieve a more thorough understanding of therapeutic development in patients with moderate-to-severe UC, receiving regular doses of vedolizumab, by developing an algorithm for optimizing vedolizumab administration.

Acknowledgments

This study is supported by Takeda Pharmaceuticals International AG (Glattpark-Opfikon, Zurich) and the German IBD Study Group (Kiel, Germany). The authors are grateful to all parties involved in the study, the study coordinating center German IBD Study Group, the sites, and the participants.

Authors' Contributions

All authors contributed to design of the study protocol, revision of the draft, and final approval of the version to be published.

Conflicts of Interest

UH, TK, SS, and JL received lecture and consulting fees from Takeda.

References

1. Feagan BG, Rutgeerts P, Sands BE, Hanauer S, Colombel JF, Sandborn WJ, GEMINI 1 Study Group. Vedolizumab as induction and maintenance therapy for ulcerative colitis. *N Engl J Med* 2013 Aug 22;369(8):699-710. [doi: [10.1056/NEJMoa1215734](https://doi.org/10.1056/NEJMoa1215734)] [Medline: [23964932](https://pubmed.ncbi.nlm.nih.gov/23964932/)]
2. de Vos M, Dewit O, D'Haens G, Baert F, Fontaine F, Vermeire S, Behalf of BIRD. Fast and sharp decrease in calprotectin predicts remission by infliximab in anti-TNF naïve patients with ulcerative colitis. *J Crohns Colitis* 2012 Jun;6(5):557-562. [doi: [10.1016/j.crohns.2011.11.002](https://doi.org/10.1016/j.crohns.2011.11.002)] [Medline: [22398050](https://pubmed.ncbi.nlm.nih.gov/22398050/)]
3. Bryant RV, Friedman AB, Wright EK, Taylor KM, Begun J, Macconi G, et al. Gastrointestinal ultrasound in inflammatory bowel disease: an underused resource with potential paradigm-changing application. *Gut* 2018 May;67(5):973-985. [doi: [10.1136/gutjnl-2017-315655](https://doi.org/10.1136/gutjnl-2017-315655)] [Medline: [29437914](https://pubmed.ncbi.nlm.nih.gov/29437914/)]
4. Schulze H, Esters P, Hartmann F, Stein J, Christ C, Zorn M, et al. A prospective cohort study to assess the relevance of vedolizumab drug level monitoring in IBD patients. *Scand J Gastroenterol* 2018 Jun;53(6):670-676. [doi: [10.1080/00365521.2018.1452974](https://doi.org/10.1080/00365521.2018.1452974)] [Medline: [29560811](https://pubmed.ncbi.nlm.nih.gov/29560811/)]
5. Cornillie F, Hanauer SB, Diamond RH, Wang J, Tang KL, Xu Z, et al. Postinduction serum infliximab trough level and decrease of C-reactive protein level are associated with durable sustained response to infliximab: a retrospective analysis of the ACCENT I trial. *Gut* 2014 Nov;63(11):1721-1727 [FREE Full text] [doi: [10.1136/gutjnl-2012-304094](https://doi.org/10.1136/gutjnl-2012-304094)] [Medline: [24474383](https://pubmed.ncbi.nlm.nih.gov/24474383/)]
6. Amiot A, Grimaud J, Peyrin-Biroulet L, Filippi J, Pariente B, Roblin X, Observatory on Efficacy of Vedolizumab in Patients With Inflammatory Bowel Disease Study Group, Groupe d'Etude Therapeutique des Affections Inflammatoires du tube Digestif. Effectiveness and safety of vedolizumab induction therapy for patients with inflammatory bowel disease. *Clin Gastroenterol Hepatol* 2016 Nov;14(11):1593-601.e2. [doi: [10.1016/j.cgh.2016.02.016](https://doi.org/10.1016/j.cgh.2016.02.016)] [Medline: [26917043](https://pubmed.ncbi.nlm.nih.gov/26917043/)]
7. Kucharzik T, Wittig BM, Helwig U, Börner N, Rössler A, Rath S, TRUST Study Group. Use of intestinal ultrasound to monitor Crohn's disease activity. *Clin Gastroenterol Hepatol* 2017 Apr;15(4):535-42.e2. [doi: [10.1016/j.cgh.2016.10.040](https://doi.org/10.1016/j.cgh.2016.10.040)] [Medline: [27856365](https://pubmed.ncbi.nlm.nih.gov/27856365/)]
8. Kucharzik T, Wittig BM, Helwig U, Roessler A, Rath S, Maaser C. Bowel ultrasound is useful in Crohn's disease monitoring: analysis from the TRUST study in Germany. *J Crohns Colitis* 2015 Jan 19;9(Suppl 1):S336. [doi: [10.1093/ecco-jcc/jju027.630](https://doi.org/10.1093/ecco-jcc/jju027.630)]
9. Reinisch W, Bressler B, Curtis R, Parikh A, Yang H, Rosario M, et al. Fecal calprotectin responses following induction therapy with vedolizumab in moderate to severe ulcerative colitis: a post Hoc analysis of GEMINI 1. *Inflamm Bowel Dis* 2019 Mar 14;25(4):803-810 [FREE Full text] [doi: [10.1093/ibd/izy304](https://doi.org/10.1093/ibd/izy304)] [Medline: [30295811](https://pubmed.ncbi.nlm.nih.gov/30295811/)]
10. Walsham NE, Sherwood RA. Fecal calprotectin in inflammatory bowel disease. *Clin Exp Gastroenterol* 2016;9:21-29 [FREE Full text] [doi: [10.2147/CEG.S51902](https://doi.org/10.2147/CEG.S51902)] [Medline: [26869808](https://pubmed.ncbi.nlm.nih.gov/26869808/)]
11. Barnes EL, Burakoff R. New biomarkers for diagnosing inflammatory bowel disease and assessing treatment outcomes. *Inflamm Bowel Dis* 2016 Dec;22(12):2956-2965 [FREE Full text] [doi: [10.1097/MIB.0000000000000903](https://doi.org/10.1097/MIB.0000000000000903)] [Medline: [27763951](https://pubmed.ncbi.nlm.nih.gov/27763951/)]
12. Langhorst J, Boone J, Lauche R, Rueffer A, Dobos G. Faecal Lactoferrin, Calprotectin, PMN-elastase, CRP, and white blood cell count as indicators for mucosal healing and clinical course of disease in patients with mild to moderate ulcerative

- colitis: post Hoc analysis of a prospective clinical trial. *J Crohns Colitis* 2016 Jul;10(7):786-794. [doi: [10.1093/ecco-jcc/jjw044](https://doi.org/10.1093/ecco-jcc/jjw044)] [Medline: [26874351](https://pubmed.ncbi.nlm.nih.gov/26874351/)]
13. Langhorst J, Elsenbruch S, Koelzer J, Rueffer A, Michalsen A, Dobos GJ. Noninvasive markers in the assessment of intestinal inflammation in inflammatory bowel diseases: performance of fecal lactoferrin, calprotectin, and PMN-elastase, CRP, and clinical indices. *Am J Gastroenterol* 2008 Jan;103(1):162-169. [doi: [10.1111/j.1572-0241.2007.01556.x](https://doi.org/10.1111/j.1572-0241.2007.01556.x)] [Medline: [17916108](https://pubmed.ncbi.nlm.nih.gov/17916108/)]
 14. Däbritz J, Langhorst J, Lügering A, Heidemann J, Mohr M, Wittkowski H, et al. Improving relapse prediction in inflammatory bowel disease by neutrophil-derived S100A12. *Inflamm Bowel Dis* 2013 May;19(6):1130-1138. [doi: [10.1097/MIB.0b013e318280b1cd](https://doi.org/10.1097/MIB.0b013e318280b1cd)] [Medline: [23377171](https://pubmed.ncbi.nlm.nih.gov/23377171/)]
 15. Maaser C, Petersen F, Helwig U, Rössler A, Lang D, Rath S, et al. Bowel ultrasound is useful in disease monitoring of ulcerative colitis patients: first analysis from the TRUST&UC study in Germany. 2017 Apr 1 Presented at: Protoc Natl DGVS Congr; 2017; Dresden URL: <https://tinyurl.com/yxon5rlh>
 16. Ellrichmann M, Bethge J, Zeissig S, Brandt B, Arlt A, Nikolaus S, et al. Changes of the colonic wall structure precede mucosal healing in patients with acute inflammatory bowel disease undergoing anti-integrin therapy - preliminary results of a prospective study. *United Eur Gastroenterol J* 2015 Apr;148(4):S-193-S-194. [doi: [10.1016/s0016-5085\(15\)30643-0](https://doi.org/10.1016/s0016-5085(15)30643-0)]

Abbreviations

ADA: antidrug antibodies
AMG: Arzneimittelgesetz, German Medicinal Products Act
CD: Crohn disease
CRF: case report form
CRP: C-reactive protein
GCP: good clinical practice
IBD: inflammatory bowel disease
ITT: intention-to-treat
IUS: intestinal ultrasound
PMN: Polymorphonuklear
TNF: tumor necrosis factor
UC: ulcerative colitis

Edited by G Eysenbach; submitted 10.04.19; peer-reviewed by E Dreesen, E Lippert; comments to author 09.08.19; revised version received 23.08.19; accepted 27.08.19; published 08.11.19.

Please cite as:

Cording J, Blömacher M, Wiebe BI, Langhorst J, Kucharzik T, Sturm A, Schreiber S, Helwig U
Monitoring of Vedolizumab Infusion Therapy (MOVE-IT) Response With Fecal Inflammation Markers, Ultrasound, and Trough Serum Level in Patients With Ulcerative Colitis: Protocol for a Multicentric, Prospective, Noninterventional Study
JMIR Res Protoc 2019;8(11):e14335
URL: <https://www.researchprotocols.org/2019/11/e14335>
doi: [10.2196/14335](https://doi.org/10.2196/14335)
PMID: [31702563](https://pubmed.ncbi.nlm.nih.gov/31702563/)

©Jimmi Cording, Margit Blömacher, Berit Inga Wiebe, Jost Langhorst, Torsten Kucharzik, Andreas Sturm, Stefan Schreiber, Ulf Helwig. Originally published in *JMIR Research Protocols* (<http://www.researchprotocols.org>), 08.11.2019. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in *JMIR Research Protocols*, is properly cited. The complete bibliographic information, a link to the original publication on <http://www.researchprotocols.org>, as well as this copyright and license information must be included.

Protocol

A National Behavioral and Clinical Surveillance System of Adults With Diagnosed HIV (The Medical Monitoring Project): Protocol for an Annual Cross-Sectional Interview and Medical Record Abstraction Survey

Linda Beer¹, PhD; Christopher H Johnson¹, MS; Jennifer L Fagan¹, MA; Emma L Frazier¹, PhD; Margaret Nyaku¹, MPH; Jason A Craw¹, MPH; Catherine C Sanders¹, MA; Ruth E Luna-Gierke¹, MPH; R Luke Shouse¹, MD

Centers for Disease Control and Prevention, Atlanta, GA, United States

Corresponding Author:

Linda Beer, PhD
Centers for Disease Control and Prevention
1600 Clifton Rd NE MS E-46
Atlanta, GA, 30329
United States
Phone: 1 404 639 5268
Email: LBeer@cdc.gov

Abstract

Background: The Medical Monitoring Project (MMP) is a national population-based behavioral and clinical surveillance system of adults with diagnosed HIV in the United States, and it is sponsored by the Centers for Disease Control and Prevention (CDC). Its purpose is to provide locally and nationally representative estimates of factors affecting HIV transmission risk and clinical outcomes.

Objective: This study aimed to describe the rationale for and methodology of the MMP, in addition to its contribution to evaluating and monitoring HIV prevention, care, and treatment efforts in the United States.

Methods: MMP employs a stratified 2-stage sample design to select annual samples of persons living with diagnosed HIV from the National HIV Surveillance System and conducts interviews and medical record abstractions with participating persons.

Results: MMP data are published routinely via annual reports, conference presentations, and scientific publications. Data may be accessed upon request from the CDC, contingent on the guidelines established for the security and confidentiality of HIV surveillance data.

Conclusions: MMP is the only source of annual population-based data on the behaviors and clinical care of persons with diagnosed HIV in the United States. It provides essential information for monitoring progress toward national treatment and prevention goals and guiding efforts to improve the health of persons with diagnosed HIV and prevent HIV transmission.

International Registered Report Identifier (IRRID): RR1-10.2196/15453

(*JMIR Res Protoc* 2019;8(11):e15453) doi:[10.2196/15453](https://doi.org/10.2196/15453)

KEYWORDS

HIV; public health surveillance; population surveillance; epidemiological monitoring; epidemiology

Introduction

The Medical Monitoring Project

The Medical Monitoring Project (MMP) is a national population-based behavioral and clinical surveillance system of adults with diagnosed HIV in the United States. It is sponsored by the Centers for Disease Control and Prevention (CDC) and conducted in health departments in 16 states and

Puerto Rico, including 6 separately funded cities located within the states. MMP project areas include the following jurisdictions: California; Chicago, Illinois; Delaware; Florida; Georgia; Houston, Texas; Illinois; Indiana; Los Angeles County, California; Michigan; Mississippi; New Jersey; New York City, New York; New York State; North Carolina; Oregon; Pennsylvania; Philadelphia, Pennsylvania; Puerto Rico; San Francisco, California; Texas; Virginia; and Washington.

The primary objectives of MMP are to provide locally and nationally representative estimates of HIV transmission risk behaviors and clinical outcomes among persons with diagnosed HIV; describe health-related behaviors; determine accessibility and use of prevention, care, and support services; increase understanding of care and treatment provided; and examine variations of these factors by respondent characteristics.

Background

From 2007 to 2014, MMP's study design relied on a multistage probability sample of persons with diagnosed HIV who were receiving HIV medical care to generate locally and nationally representative estimates of clinical outcomes and HIV-related behaviors [1-4]. With this design, MMP provided data for important national HIV prevention indicators among persons in care for HIV, such as the proportion of those who were prescribed HIV antiretroviral therapy (ART), were adherent to ART, and achieved viral suppression.

Although the importance of ART for reducing morbidity and mortality for persons living with HIV has long been established [5,6], in recent years, the role of ART in HIV prevention has grown more central. When taken as prescribed, ART can reduce the amount of HIV in the blood (viral load) to undetectable levels [7-11]. A person living with HIV who has an undetectable viral load has effectively no risk of transmitting HIV to their HIV-negative sexual partners [12]. Mathematical models show the potential for halting the spread of HIV through an aggressive program of universal testing and immediate ART initiation, a strategy initially dubbed *test and treat* and now more generally known as *treatment as prevention* (TasP) [13-15]. National HIV prevention goals identify 2 areas for critical focus: *broad support for people living with HIV to remain engaged in comprehensive care, including support for treatment adherence and universal viral suppression among people living with HIV* [16].

However, from 2007 to 2014, MMP's design excluded persons with diagnosed HIV who were not receiving HIV medical care, which is necessary to initiate ART and maintain an undetectable viral load. This design limited MMP's capacity to monitor progress toward linkage to and retention in care objectives and its ability to elucidate barriers to receipt of HIV medical care. In a 2012 report discussing implementation of the US National HIV/AIDS Strategy, the National Academy of Medicine (formerly known as the Institute of Medicine) concluded, "Primary barriers to optimal outcomes for people living with HIV include late diagnosis, delayed linkage to care for HIV, poor retention in care, delayed initiation of ART, and poor adherence to ART..." and recommended MMP expands its population of inference to include HIV-positive persons not receiving medical care [17]. Fortunately, by this time, the National HIV Surveillance System (NHSS)—a CDC-funded surveillance system that monitors national trends in HIV infection diagnoses [18]—had established name-based HIV case reporting in all US jurisdictions and could be used as a source for sampling persons with diagnosed HIV.

Therefore, to address the information gaps described above and enhance the usefulness of the data collected, in 2015, MMP implemented revised methods and began to sample persons directly from the NHSS [18] to represent all persons with

diagnosed HIV regardless of receipt of HIV medical care. This increased MMP's capacity to monitor and guide efforts to prevent HIV infection and improve clinical outcomes through available treatment and other interventions.

Methods

Design

Beginning with the 2015 cycle, MMP employed a 2-stage sample design to produce annual representative estimates of the sociodemographic, behavioral, and clinical characteristics of adults with diagnosed HIV in the United States. With this design, participating project areas can produce annual representative estimates of these characteristics among persons in their jurisdictions (ie, states, territory, county, and cities), and the national dataset can be used to produce annual nationally representative estimates.

The first stage of sampling involved a one-time geographically stratified random sampling of US states and territories with probability proportional to size based on the estimated total number of persons living with AIDS as reported to the NHSS at the end of 2002. Although the target population for MMP is all persons diagnosed with HIV in the United States, when the first-stage sample was initially drawn, HIV non-AIDS diagnoses were not reportable in all the states; therefore, the estimated number of persons living with AIDS was used as the best available proxy. Using an indirect measure of size at any given sampling stage does not necessarily affect the validity of the statistical estimates derived from the overall sample if the measure is closely correlated with the desired characteristic, as is the case for AIDS and HIV cases.

On the basis of available funding, 20 primary sampling units were selected during the first stage of sampling in 2004. All 20 state/territory health departments selected for the first-stage sample agreed to participate in MMP. In 5 of the selected states, HIV surveillance activities in 6 large cities are funded separately from the rest of the state, and MMP chose to do the same—resulting in a total of 26 MMP project areas. States with separately funded cities collect data from persons sampled in the state who are living outside of the funded cities; these states receive state-level MMP datasets that combine the state and city data to produce estimates that represent the state as a whole. Owing to budget restrictions, beginning in 2009, 3 areas (Massachusetts, South Carolina, and Maryland) were dropped from the MMP project area sample through a random selection process, resulting in 23 project areas representing 16 states and Puerto Rico. MMP has retained a 100% response rate at this first stage of sampling (ie, all sampled jurisdictions participated) since the inception of this surveillance system.

MMP periodically evaluates the continued validity of the first-stage sample of states and territories. An analysis of counts of reported diagnoses of HIV for 2011 showed that the proportional contribution of states to the burden of HIV had not changed considerably from the distribution of AIDS cases on which the initial sample was based, and this relationship still holds for 2015 HIV diagnosis counts. Thus, the design weights reflecting states' original sampling probabilities were still

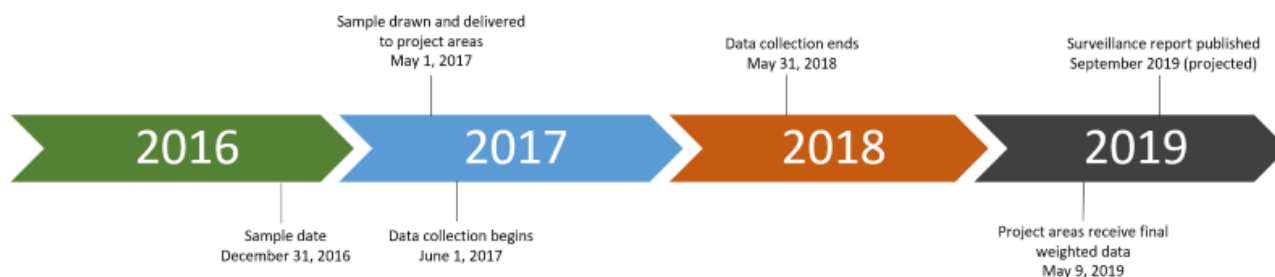
reasonably close to what they would have been if sampled using reported HIV diagnoses. On the basis of these findings, we concluded that selecting a new first-stage sample was not warranted, and we retained the original sample, thereby preserving operational efficiencies and the ability of participating states to continue generating local estimates of indicators of HIV care and treatment in their jurisdictions. The 23 participating MMP project areas included approximately 72.80% (732,827/1,006,691) of all persons with diagnosed HIV in the United States during 2016.

The second stage of sampling involves annual random sampling of eligible persons directly from the NHSS. A pilot test of these methods was conducted during 2012 to 2014, and findings from that pilot informed the methods used in this study [19,20]. Eligible persons are those who, on the date of sampling, were

alive, living with diagnosed HIV, aged ≥ 18 years, and a resident of an MMP project area. The date of sampling is December 31 of the year before the data collection cycle (eg, December 31, 2014, for the 2015 data collection cycle). Every year, a total of 9700 persons (with minimum state/territory sample size of 400 persons) are selected (Table 1), which allows for estimates of sufficient precision at both the national and local levels. The sample is drawn in March/April of the data collection cycle year to allow time for NHSS reporting delays, and data collection begins in June of the cycle year and ends the following May. For example, the data collection period for the 2015 data collection cycle was from June 2015 to May 2016. Figure 1 presents MMP's timeline from the date of sampling to the publication of the cycle's surveillance data report, using outcomes from the 2017 data collection cycle.

Table 1. Medical Monitoring Project's sample sizes by project area.

| Project area | Number of persons sampled |
|---|---------------------------|
| California (excluding Los Angeles County and San Francisco) | 500 |
| Chicago, Illinois | 400 |
| Delaware | 400 |
| Florida | 800 |
| Georgia | 500 |
| Houston, Texas | 400 |
| Illinois (excluding Chicago) | 200 |
| Indiana | 400 |
| Los Angeles County, California | 400 |
| Michigan | 400 |
| Mississippi | 400 |
| New Jersey | 500 |
| New York City, New York | 800 |
| New York State (excluding New York City) | 200 |
| North Carolina | 400 |
| Oregon | 400 |
| Pennsylvania (excluding Philadelphia) | 200 |
| Philadelphia, Pennsylvania | 400 |
| Puerto Rico | 400 |
| San Francisco, California | 400 |
| Texas (excluding Houston) | 400 |
| Virginia | 400 |
| Washington | 400 |
| Total | 9700 |

Figure 1. Medical Monitoring Project 2017 cycle timeline.

Health department staff in participating project areas locate and recruit sampled persons using information contained in local health department NHSS records and other available sources such as surveillance databases for other conditions, social services records, and people search engines (eg, Lexis-Nexis, TLO), as permitted by local regulations. Questionnaire data are collected via 45-min telephone or in-person interviews with participating persons, following which a matched medical record abstraction of clinical data is performed for persons who received medical care for their HIV. Questionnaire topics include sociodemographics, HIV treatment and adherence, barriers to care and services, sexual behaviors, alcohol and drug use, stigma and discrimination, met and unmet needs for medical and ancillary services, gynecological and reproductive history, and use of HIV/STD prevention services. Medical record abstraction topics include inpatient and outpatient health care encounters, diagnoses, medications, and laboratory testing and screening. Questionnaires and medical record abstraction instruments are updated approximately every 3 years to improve the quality and accuracy of the data collected and to respond to emerging trends in HIV epidemiology and public health. Participants are given a token of appreciation of approximately US \$50 in cash or cash equivalent (eg, gift card), depending on local standards. All sampled persons are offered linkage or reengagement to HIV medical care services, as well as information and referrals for other medical, prevention, and ancillary services, if needed.

As a part of routine public health surveillance, MMP is determined to be nonresearch [21]. Participating states or territories obtain local institutional review board approval to collect data, when required. Informed consent to participate in the project is obtained from all interviewed participants.

The second stage (person-level) response rate for the 2015 cycle, the first year in which new MMP methods were implemented, was 39.8% (3654/9179) after adjustment for eligibility. The response rate for the 2016 MMP cycle was 44.3% (4038/9107), and the response rate for the 2017 MMP cycle was 46.3% (4229/9126). These improvements were because of multiple factors, including the development of more efficient MMP processes and establishment of cooperative relationships needed to successfully find and recruit sampled persons. Although MMP staff work continuously to increase response rates from cycle to cycle, low response rates are not necessarily indicative of nonresponse bias when probabilistic samples are drawn from frames that can provide key information on all sampled persons that can be used to adjust for nonresponse [22], as is the case for the NHSS frame used by MMP. Regardless, as the system

matures, we expect improvements in response rates, as was seen in prior years under MMP's old design.

Weighting and Data Security

MMP data are first weighted on the basis of known probabilities of selection at the project area and person levels. Then, data are weighted to adjust for nonresponse using known predictors of response based on the NHSS frame. Information available from the NHSS includes age, sex at birth, race/ethnicity, indication of receipt of HIV care as evidenced by laboratory test (CD4 or viral load) results, length of time since HIV diagnosis, completeness of address and phone number information derived from local health department HIV surveillance databases, and mode of HIV acquisition. Using the NHSS as a frame is beneficial because the data are continually updated. An updated frame with the same specifications as the initial frame is drawn 1 year after the construction of the initial frame, which allows MMP data to be adjusted for noncoverage of the population of interest, multiplicity, and updated information on eligibility and HIV care receipt at time of sampling. As a final step in the weighting process, data are poststratified to NHSS population totals for various demographic factors (ie, sex at birth, age, and race/ethnicity) to ensure the data are representative of the population of inference.

MMP data are subject to the CDC's Data Security and Confidentiality Guidelines for HIV, Viral Hepatitis, Sexually Transmitted Disease, and Tuberculosis programs [23]. These protocols are followed at the project area and national level to ensure the integrity, confidentiality, and security of MMP data. Although local health departments maintain names and contact information for persons with diagnosed HIV reported to the NHSS, no contact information for sampled persons is ever sent to the CDC. MMP itself collects no directly personally identifiable information in its data systems. The software used to collect interview and medical record data has password-protected access so that unauthorized users are unable to view, export, or modify collected data. The security of the system meets all Federal Information Systems Management Act, Office of Management and Budget, Health and Human Services, and CDC Information Technology Security requirements, which ensure the confidentiality, integrity, and availability of data on federal information systems.

MMP collects and monitors data related to core national HIV prevention goals of preventing new HIV infections, increasing access to care, and improving health outcomes for persons living with HIV [16,24]. As MMP includes a range of gender, racial, ethnic, and sexual minority populations, the data collected are

also used to assess disparities between groups in these factors. Key MMP estimates used to inform national HIV prevention efforts include ART prescription and adherence, as well as other factors that can affect HIV transmission such as HIV stigma and sexual behaviors. The quality of data collected is maintained by ongoing national and local training of data collectors, the use of electronic data collection systems with built-in logic checks to prevent data entry errors, required data quality assurance activities for MMP project areas, and extensive data quality protocols that govern the processing and cleaning of MMP data.

Results

Data Analysis

As mentioned above, in 2015, MMP expanded its population of inference from adults receiving HIV care to all adults with diagnosed HIV regardless of receipt of medical care. This expansion necessitated substantial modification of sampling and weighting methods. As a result of these changes, MMP estimates for 2015 onward are not comparable with those derived using the prior design, and the CDC recommends that analysts do not combine 2015 data with data from prior years or assess trends across the pre- and post-2015 data collection cycles. This recommendation is consistent with the approach of other large national health surveys following methodological changes, such as the Behavioral Risk Factor Surveillance System and the National Survey on Drug Use and Health, which advised against comparing results before and after the implementation of such changes [25,26].

One benefit of MMP's change to direct sampling of persons from the NHSS is that MMP data are designed to be linkable to NHSS data. This ability to link MMP data to NHSS data allows for additional analyses that can be beneficial for public health programming and service delivery, such as assessing at the individual level whether behaviors that resulted in HIV acquisition continue to be present at the time of interview, which may inform development of tailored HIV prevention interventions among persons living with HIV. In addition, participating state and local health departments can prospectively monitor care access and HIV viral load test results among persons who received linkage or reengagement assistance following the MMP interview.

Owing to MMP's design, specialized statistical analysis procedures must be used for analysis. When analyzing complex sample data, analysts must consider unequal selection probabilities, nonresponse, and other adjustment factors. Weighted survey procedures in software packages such as SAS and SUDAAN, which require the analyst to specify the design characteristics of MMP, should be used to analyze weighted MMP data. The CDC has prepared documentation for analysts that provides guidelines and sample code for weighted analysis of MMP data.

National MMP data are not publicly available because of the need for specialized technical assistance for working with the large and complex datasets and the security and confidentiality guidelines for the release of HIV surveillance data. However,

the CDC will grant access to MMP data in accordance with security and confidentiality guidelines on a case-by-case basis. Researchers may submit analysis concept proposals that are reviewed and prioritized based on their importance for public health, their scientific merit, and on the needs and current workload of the team that oversees MMP at the CDC. There are currently no fees associated with accessing or receiving MMP data, but release is subject to the availability of CDC resources to complete such requests. More information on the appropriate procedures for concept proposals can be obtained by contacting the CDC [27].

For state- or city-level analyses, researchers should coordinate directly with the state or city health departments that conduct MMP in the area(s) of interest. Contact information for the local MMP principal investigators is available on the MMP website [28].

Furthermore, the MMP website provides detailed project information by cycle year, including protocols and data collection instruments [29].

Data Dissemination

Aggregate national MMP data are published for each data collection cycle in HIV Surveillance Special Reports [30]. These reports provide national estimates of key sociodemographic, clinical, and behavioral characteristics, in addition to information on methods and variable definitions. State and local health departments also regularly publish MMP data via health department reports.

The CDC uses MMP data to guide efforts designed to achieve national goals and objectives set forth in the Division of HIV/AIDS Prevention (DHAP) Strategic Plan and other federal directives [16,24]. Specifically, MMP is the data source used by the CDC to monitor homelessness, HIV stigma, and sexual behaviors that increase the risk of HIV transmission among persons with diagnosed HIV. MMP data are also used by the CDC to inform HIV communication campaigns and educational materials (eg, [31,32]).

At the state and city level, MMP data are used to inform the jurisdictions' Integrated HIV Prevention and Care Plans. These plans are mandatory for certain CDC/DHAP and Health Resources and Services Administration's HIV/AIDS Bureau grantees and are used to guide HIV prevention and care planning. Specifically, MMP data are used to describe the needs of persons with diagnosed HIV; existing gaps in HIV prevention and care services; and the sociodemographic, behavioral, and clinical characteristics of persons with diagnosed HIV. MMP data inform establishment of priorities, allocation of HIV prevention and care resources, and evaluation of existing programs and policies through its use in local planning processes.

Numerous national and local analyses of MMP data have been disseminated through peer-reviewed scientific journals, through reports, and at national meetings [29]. Publication highlights from recent years include documenting significant improvements in ART prescription and viral suppression among HIV patients [33], increased sexually transmitted disease testing among sexually active HIV patients [34], and an assessment of service

delivery and patient outcomes in different medical care settings [35]. In addition, MMP was used as a data source for an influential publication that estimated HIV transmission at each step of the care continuum in the United States, which was published in the *Journal of the American Medical Association Internal Medicine* [36].

Discussion

MMP is the only source of annual population-based estimates of certain key characteristics among persons with diagnosed HIV needed to assess national and local progress toward US

treatment and prevention goals. To advance the CDC's High Impact Prevention approach to HIV prevention and realize the clinical and prevention benefits of TasP at the population and individual levels, it is critical to ensure that everyone living with HIV is engaged in medical care and virally suppressed. MMP contributes essential information on barriers to treatment and care, use of and adherence to ART, viral suppression, and sexual behaviors that could increase the risk of HIV transmission. National and local MMP data inform geographically tailored approaches to improve HIV treatment and prevention.

Acknowledgments

The authors thank participating MMP providers, facilities, and project areas. The authors also acknowledge the contributions of the Clinical Outcomes Team and the Behavioral and Clinical Surveillance Branch at the CDC and the MMP Project Area Group Members. The findings and conclusions in this protocol are those of the authors and do not necessarily represent the official position of the CDC. Funding for MMP is provided by a cooperative agreement (PS09-937) from the CDC.

Conflicts of Interest

None declared.

References

1. Blair JM, Fagan JL, Frazier EL, Do A, Bradley H, Valverde EE, National Center for HIV/AIDS, Viral Hepatitis, STD, TB Prevention, CDC. Behavioral and clinical characteristics of persons receiving medical care for HIV infection - Medical Monitoring Project, United States, 2009. *MMWR Suppl* 2014 Jun 20;63(5):1-22. [Medline: [24941443](#)]
2. Frankel MR, McNaghten AD, Shapiro MF, Sullivan PS, Berry SH, Johnson CH, et al. A probability sample for monitoring the HIV-infected population in care in the US and in selected states. *Open AIDS J* 2012;6:67-76 [FREE Full text] [doi: [10.2174/1874613601206010067](#)] [Medline: [23049655](#)]
3. Iachan R, Johnson CH, Harding RL, Kyle T, Saavedra P, Frazier EL, et al. Design and weighting methods for a nationally representative sample of HIV-infected adults receiving medical care in the United States-medical monitoring project. *Open AIDS J* 2016;10:164-181 [FREE Full text] [doi: [10.2174/1874613601610010164](#)] [Medline: [27651851](#)]
4. McNaghten AD, Wolfe MI, Onorato I, Nakashima AK, Valdiserri RO, Mokotoff E, et al. Improving the representativeness of behavioral and clinical surveillance for persons with HIV in the United States: the rationale for developing a population-based approach. *PLoS One* 2007 Jun 20;2(6):e550 [FREE Full text] [doi: [10.1371/journal.pone.0000550](#)] [Medline: [17579722](#)]
5. Egger M, May M, Chêne G, Phillips AN, Ledergerber B, Dabis F, et al. Prognosis of HIV-1-infected patients starting highly active antiretroviral therapy: a collaborative analysis of prospective studies. *Lancet* 2002 Jul 13;360(9327):119-129. [doi: [10.1016/S0140-6736\(02\)09411-4](#)] [Medline: [12126821](#)]
6. Mellors JW, Muñoz A, Giorgi JV, Margolick JB, Tassoni CJ, Gupta P, et al. Plasma viral load and CD4+ lymphocytes as prognostic markers of HIV-1 infection. *Ann Intern Med* 1997 Jun 15;126(12):946-954. [doi: [10.7326/0003-4819-126-12-199706150-00003](#)] [Medline: [9182471](#)]
7. Cohen J. Breakthrough of the year. HIV treatment as prevention. *Science* 2011 Dec 23;334(6063):1628. [doi: [10.1126/science.334.6063.1628](#)] [Medline: [22194547](#)]
8. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, HPTN 052 Study Team. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med* 2011 Aug 11;365(6):493-505 [FREE Full text] [doi: [10.1056/NEJMoa1105243](#)] [Medline: [21767103](#)]
9. Gray RH, Wawer MJ, Brookmeyer R, Sewankambo NK, Serwadda D, Wabwire-Mangen F, Rakai Project Team. Probability of HIV-1 transmission per coital act in monogamous, heterosexual, HIV-1-discordant couples in Rakai, Uganda. *Lancet* 2001 Apr 14;357(9263):1149-1153. [doi: [10.1016/S0140-6736\(00\)04331-2](#)] [Medline: [11323041](#)]
10. Quinn TC, Wawer MJ, Sewankambo N, Serwadda D, Li C, Wabwire-Mangen F, et al. Viral load and heterosexual transmission of human immunodeficiency virus type 1. Rakai Project Study Group. *N Engl J Med* 2000 Mar 30;342(13):921-929. [doi: [10.1056/NEJM200003303421303](#)] [Medline: [10738050](#)]
11. Wawer MJ, Gray RH, Sewankambo NK, Serwadda D, Li X, Laeyendecker O, et al. Rates of HIV-1 transmission per coital act, by stage of HIV-1 infection, in Rakai, Uganda. *J Infect Dis* 2005 May 1;191(9):1403-1409. [doi: [10.1086/429411](#)] [Medline: [15809897](#)]

12. Centers for Disease Control and Prevention. Evidence of HIV Treatment and Viral Suppression in Preventing the Sexual Transmission of HIV URL: <https://www.cdc.gov/hiv/pdf/risk/art/cdc-hiv-art-viral-suppression.pdf> [accessed 2019-07-11]
13. Dieffenbach CW, Fauci AS. Universal voluntary testing and treatment for prevention of HIV transmission. *J Am Med Assoc* 2009 Jun 10;301(22):2380-2382. [doi: [10.1001/jama.2009.828](https://doi.org/10.1001/jama.2009.828)] [Medline: [19509386](https://pubmed.ncbi.nlm.nih.gov/19509386/)]
14. Granich RM, Gilks CF, Dye C, de Cock KM, Williams BG. Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model. *Lancet* 2009 Jan 3;373(9657):48-57. [doi: [10.1016/S0140-6736\(08\)61697-9](https://doi.org/10.1016/S0140-6736(08)61697-9)] [Medline: [19038438](https://pubmed.ncbi.nlm.nih.gov/19038438/)]
15. Montaner JS, Hogg R, Wood E, Kerr T, Tyndall M, Levy AR, et al. The case for expanding access to highly active antiretroviral therapy to curb the growth of the HIV epidemic. *Lancet* 2006 Aug 5;368(9534):531-536. [doi: [10.1016/S0140-6736\(06\)69162-9](https://doi.org/10.1016/S0140-6736(06)69162-9)] [Medline: [16890841](https://pubmed.ncbi.nlm.nih.gov/16890841/)]
16. White House Office of National AIDS Policy. National HIV/AIDS Strategy: Updated to 2020 URL: <https://www.hiv.gov/federal-response/national-hiv-aids-strategy/nhas-update> [accessed 2015-12-17]
17. Institute of Medicine. Monitoring HIV Care In The United States: A Strategy For Generating National Estimates Of HIV Care And Coverage. Washington, DC: National Academies Press; 2012.
18. Centers for Disease Control and Prevention. HIV Surveillance Systems URL: <https://www.cdc.gov/hiv/statistics/surveillance/systems/index.html> [accessed 2019-07-11]
19. Padilla M, Mattson CL, Scheer S, Udeagu CN, Buskin SE, Hughes AJ, et al. Locating people diagnosed with HIV for public health action: utility of HIV case surveillance and other data sources. *Public Health Rep* 2018;133(2):147-154 [FREE Full text] [doi: [10.1177/0033354918754541](https://doi.org/10.1177/0033354918754541)] [Medline: [29486143](https://pubmed.ncbi.nlm.nih.gov/29486143/)]
20. Wei SC, Messina L, Hood J, Hughes A, Jaenicke T, Johnson K, et al. Methods to include persons living with HIV not receiving HIV care in the Medical Monitoring Project. *PLoS One* 2019;14(8):e0219996 [FREE Full text] [doi: [10.1371/journal.pone.0219996](https://doi.org/10.1371/journal.pone.0219996)] [Medline: [31369574](https://pubmed.ncbi.nlm.nih.gov/31369574/)]
21. Centers for Disease Control and Prevention. 2010. Distinguishing Public Health Research and Public Health Nonresearch URL: <http://www.cdc.gov/od/science/integrity/docs/cdc-policy-distinguishing-public-health-research-nonresearch.pdf> [accessed 2019-09-20]
22. Groves R. Nonresponse rates and nonresponse bias in household surveys. *Public Opin Q* 2006;70(5):646-674. [doi: [10.1093/poq/nfl033](https://doi.org/10.1093/poq/nfl033)]
23. Centers for Disease Control and Prevention. Data Security and Confidentiality Guidelines for HIV, Viral Hepatitis, Sexually Transmitted Disease, and Tuberculosis Programs URL: <https://www.cdc.gov/nchhstp/programintegration/docs/pcsdatabasecurityguidelines.pdf> [accessed 2019-07-11]
24. Centers for Disease Control and Prevention. Division of HIV/AIDS Prevention Strategic Plan 2017-2020 URL: <https://www.cdc.gov/hiv/pdf/dhap/cdc-hiv-dhap-external-strategic-plan.pdf> [accessed 2019-09-20]
25. Centers for Disease Control and Prevention (CDC). Methodologic changes in the Behavioral Risk Factor Surveillance System in 2011 and potential effects on prevalence estimates. *MMWR Morb Mortal Wkly Rep* 2012 Jun 8;61(22):410-413 [FREE Full text] [Medline: [22672976](https://pubmed.ncbi.nlm.nih.gov/22672976/)]
26. Kennet J, Gfroerer J. Evaluating and Improving Methods Used in the National Survey on Drug Use and Health. Rockville, MD: Substance Abuse and Mental Health Services Administration, Office of Applied Studies; 2005.
27. Centers for Disease Control and Prevention. Contacting the Medical Monitoring Project URL: <https://www.cdc.gov/hiv/statistics/systems/mmp/contact.html> [accessed 2019-07-11]
28. Centers for Disease Control and Prevention. Medical Monitoring Project Project Areas URL: <https://www.cdc.gov/hiv/statistics/systems/mmp/projectareas.html> [accessed 2019-07-11]
29. Centers for Disease Control and Prevention. Medical Monitoring Project Resources URL: <https://www.cdc.gov/hiv/statistics/systems/mmp/resources.html> [accessed 2019-07-11]
30. Centers for Disease Control and Prevention. HIV Surveillance Reports URL: <https://www.cdc.gov/hiv/library/reports/hiv-surveillance.html> [accessed 2019-07-11]
31. Centers for Disease Control and Prevention. HIV and Gay and Bisexual Men URL: <https://www.cdc.gov/hiv/group/msm/index.html> [accessed 2019-09-24]
32. Centers for Disease Control and Prevention. HIV and Transgender People URL: <https://www.cdc.gov/hiv/group/gender/transgender/index.html> [accessed 2019-09-24]
33. Bradley H, Mattson CL, Beer L, Huang P, Shouse RL, Medical Monitoring Project. Increased antiretroviral therapy prescription and HIV viral suppression among persons receiving clinical care for HIV infection. *AIDS* 2016 Aug 24;30(13):2117-2124 [FREE Full text] [doi: [10.1097/QAD.0000000000001164](https://doi.org/10.1097/QAD.0000000000001164)] [Medline: [27465279](https://pubmed.ncbi.nlm.nih.gov/27465279/)]
34. Mattson CL, Bradley H, Beer L, Johnson C, Pearson WS, Shouse RL, Medical Monitoring Project. Increased sexually transmitted disease testing among sexually active persons receiving medical care for human immunodeficiency virus infection in the United States, 2009-2013. *Clin Infect Dis* 2017 Mar 1;64(5):629-634 [FREE Full text] [doi: [10.1093/cid/ciw834](https://doi.org/10.1093/cid/ciw834)] [Medline: [27940947](https://pubmed.ncbi.nlm.nih.gov/27940947/)]
35. Weiser J, Beer L, Frazier EL, Patel R, Dempsey A, Hauck H, et al. Service delivery and patient outcomes in Ryan White HIV/AIDS Program-funded and -nonfunded health care facilities in the United States. *JAMA Intern Med* 2015 Oct;175(10):1650-1659 [FREE Full text] [doi: [10.1001/jamainternmed.2015.4095](https://doi.org/10.1001/jamainternmed.2015.4095)] [Medline: [26322677](https://pubmed.ncbi.nlm.nih.gov/26322677/)]

36. Skarbinski J, Rosenberg E, Paz-Bailey G, Hall HI, Rose CE, Viall AH, et al. Human immunodeficiency virus transmission at each step of the care continuum in the United States. *JAMA Intern Med* 2015 Apr;175(4):588-596. [doi: [10.1001/jamainternmed.2014.8180](https://doi.org/10.1001/jamainternmed.2014.8180)] [Medline: [25706928](https://pubmed.ncbi.nlm.nih.gov/25706928/)]

Abbreviations

ART: antiretroviral therapy
CDC: Centers for Disease Control and Prevention
DHAP: Division of HIV/AIDS Prevention
MMP: Medical Monitoring Project
NHSS: National HIV Surveillance System
TasP: treatment as prevention

Edited by G Eysenbach; submitted 11.07.19; peer-reviewed by E Mokotoff, A Lansky, S Scheer; comments to author 17.08.19; revised version received 23.08.19; accepted 27.08.19; published 18.11.19.

Please cite as:

Beer L, Johnson CH, Fagan JL, Frazier EL, Nyaku M, Craw JA, Sanders CC, Luna-Gierke RE, Shouse RL

A National Behavioral and Clinical Surveillance System of Adults With Diagnosed HIV (The Medical Monitoring Project): Protocol for an Annual Cross-Sectional Interview and Medical Record Abstraction Survey

JMIR Res Protoc 2019;8(11):e15453

URL: <http://www.researchprotocols.org/2019/11/e15453/>

doi: [10.2196/15453](https://doi.org/10.2196/15453)

PMID: [31738178](https://pubmed.ncbi.nlm.nih.gov/31738178/)

©Linda Beer, Christopher H Johnson, Jennifer L Fagan, Emma L Frazier, Margaret Nyaku, Jason A Craw, Catherine C Sanders, Ruth E Luna-Gierke, R Luke Shouse. Originally published in *JMIR Research Protocols* (<http://www.researchprotocols.org>), 18.11.2019. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in *JMIR Research Protocols*, is properly cited. The complete bibliographic information, a link to the original publication on <http://www.researchprotocols.org>, as well as this copyright and license information must be included.

Protocol

Action Ethnography of Community Reintegration for Veterans and Military Service Members With Traumatic Brain Injury: Protocol for a Mixed Methods Study

Christine Melillo¹, MPH, RN, PhD; Kiersten Downs¹, PhD; Christina Dillahunt-Aspillaga^{1,2}, PhD; Jason Lind¹, PhD; Karen Besterman-Dahan¹, PhD; Bridget Hahm¹, MA, MPH; Nicole Antinori¹, MBA; Christine Elnitsky³, RN, PhD; Angelle M Sander^{4,5}, PhD; Heather G Belanger⁶, PhD; Peter Toyinbo¹, MBChB, CPH, PhD; Gail Powell-Cope¹, FAAN, ARNP, PhD

¹Research and Development Service, James A Haley Veterans' Hospital, Veterans Health Administration, Tampa, FL, United States

²Rehabilitation and Mental Health Counseling Program, College of Behavioral and Community Sciences, University of South Florida, Tampa, FL, United States

³School of Nursing, College of Health and Human Services, University of North Carolina at Charlotte, Charlotte, NC, United States

⁴Brain Injury Research Center, TIRR Memorial Hermann, Houston, TX, United States

⁵H Ben Taub Department of Physical Medicine and Rehabilitation, Baylor College of Medicine, Houston, TX, United States

⁶Defense and Veterans Brain Injury Center, US Special Operations Command, Tampa, FL, United States

Corresponding Author:

Christine Melillo, MPH, RN, PhD
Research and Development Service
James A Haley Veterans' Hospital
Veterans Health Administration
8900 Grand Oak Circle
Tampa, FL, 33637
United States
Phone: 1 813 558 3938
Fax: 1 813 558 3990
Email: christine.melillo@va.gov

Abstract

Background: Numerous studies of community reintegration (CR) in traumatic brain injury (TBI) have been conducted in civilian populations, but research is limited in veteran and military service member populations. Little is known about how knowledge from civilian studies translates into veterans' experiences and needs. The US Department of Veterans Health Administration (VHA) recognizes the distinctive health care needs of post-9/11 veteran and military service members, particularly with TBI, including the need to bridge health and rehabilitation-related services from acute care and inpatient settings to veteran and military service members' homes and communities to facilitate CR.

Objective: The goal of this study is to better understand the experiences of veterans with complicated mild, moderate, or severe TBI; their families; and CR workers as veterans and servicemembers transition to and sustain living in communities. This paper describes the rationale, design, and methods used to reach this goal.

Methods: This five-year longitudinal mixed methods study uses both a community-engaged research (CEnR) approach and an ethnographic approach. The sample includes 30 veterans and service members with TBI, 13 family caregivers, 11 CR specialists, 16 key stakeholders, and 82 community events. Interviews and observations are coded and analyzed using hierarchical coding schemes and thematic analysis. Analyses include data from surveys, interviews, and participant observations. Content analysis is used to highlight the complex social context of reintegration and to triangulate quantitative data. Egocentric (personal) social network analysis is used to examine the support system a veteran or service member has in place to facilitate reintegration.

Results: Study enrollment and data collection are completed. Data analyses are underway.

Conclusions: The results of this study may provide a heightened understanding of environmental factors affecting CR in complicated mild, moderate, or severe TBI. Veteran, servicemember and family voices and insights provide VHA clinicians and policy makers with an ecological view of CR that is grounded in the life experiences of veterans, military service members, and

families. The results of this study provide a roadmap for designing and testing interventions to maximize CR in a variety of domains. The longitudinal ethnographic approach allows for capturing detailed experiences within the naturalistic context. CEnR allows collaborative assessment of the social context of reintegration with community members.

International Registered Report Identifier (IRRID): DERR1-10.2196/14170

(*JMIR Res Protoc* 2019;8(11):e14170) doi:[10.2196/14170](https://doi.org/10.2196/14170)

KEYWORDS

ethnography; veteran; traumatic brain injury; community; military; social networks

Introduction

Community Reintegration

Leading disability and rehabilitation organizations, researchers and clinicians recognize the importance of community reintegration (CR) to the health, quality of life, and well-being of persons with disabilities [1-3]. CR is defined as “the assumption or resumption of culturally and developmentally appropriate social roles following disability” [1]. Key components of CR emphasized by researchers, clinicians, and consumers include independence in daily life, involvement in productive or meaningful activities, and engagement in satisfying social relationships [4,5].

The Veterans Health Administration (VHA) recognizes the importance of CR in relation to the overall health and well-being of veterans. VHA programs exist to support CR, including vocational rehabilitation [6], community partnerships, and educational benefits [7-9]. Many of these programs tend to be medically based and disparate from one VHA facility to another VHA facility. The limited scope of and variation among these programs motivated the development of this study. The VHA is charged to effectively assist veterans with living healthy, meaningful, and productive lives. Neurological conditions, including traumatic brain injury (TBI), are leading causes of serious, long-term disability [10]. Since 2001, nearly 400,000 service members have been diagnosed with a brain injury [11], and more than 1.2 million newly separated veterans have accessed VHA health services [12]. In addition, complex comorbidities, such as mental health disorders, pain, and irritability, are likely to interfere with work, social functioning, and independent living and affect disability long-term CR outcomes [13,14]. Despite the heightened attention on TBI due to recent conflicts (Operation Enduring Freedom, Operation Iraqi Freedom, and Operation New Dawn [OEF/OIF/OND]) and associated deployments, stateside injuries account for the majority of severe TBIs in veteran and military service members [11]. These injuries pose unique challenges to the current generation of veterans returning to prior relationships, living situations, work, and social roles [15,16]. Most research on CR for veterans and servicemembers has focused on return to work and family life, with little examination of the social, physical, and environmental factors that affect CR [17,18].

To address these research gaps, the VHA Rehabilitation Research and Development Service convened a state-of-the-art conference in 2010 to advance the science of measurement for important outcomes for rehabilitation. One workgroup reported on directions for conceptualization and measurement of CR [5].

The workgroup acknowledged that the concepts of activity and participation in life roles (International Classification of Functioning concepts) and reintegration overlap and that CR is multidimensional and complex. The workgroup identified 11 key dimensions of CR for veterans with TBI, which were further distilled by Sanders to 3 dimensions of CR: (1) employment or other productive activity, (2) independent living, and (3) social relationships and activities [17]. In this study, we use Sander's 3 dimensions as a framework for examining CR in this population [17].

Few studies to date have examined the subjective CR experiences of injured post-9/11 V, SMs and their family members [16,19,20]. Significant gaps in evidence of reintegration among veterans and servicemembers with specific health conditions or effective models of service delivery are identified [16]. Furthermore, there is a need to focus research on the intersection of individual, family, and community perspectives to adequately account for the complex context of reintegration. Experiences regarding barriers and facilitators to community resources and services are needed to inform VHA policy and service delivery models.

This research provides current and in-depth knowledge about CR in veterans and servicemembers with TBI from recent conflicts. This study uses a longitudinal design with multiple data collection methods from multiple stakeholder perspectives. The primary objectives of this research are to (1) describe CR experiences as perceived by veterans and servicemembers; (2) compare and contrast barriers and facilitators to CR from multiple perspectives (eg, veterans and servicemembers, families, and providers of CR-related health care and services); (3) describe how personal social networks influence CR; and (4) identify veterans and servicemembers patient-centered strategies needed to improve CR. This paper describes a protocol employing ethnographic research to investigate the experiences of veterans and servicemembers living with a TBI and their caregivers in the context of CR.

Background

CR is an ongoing, complex process [14]. Consideration of individual perspectives helps shape the understanding of the complex interactions between outcomes and associated environmental CR factors [21]. Studying CR through multiple lenses facilitates capturing the rich, layered experiences of participants and addresses the multidimensional nature of reintegration from an intersectional perspective [16]. Study designs and approaches (eg, mixed methods, CEnR, and ethnography) are used to acknowledge this complexity.

Theoretical Background and Ethnographic Approaches in Community Reintegration

Ethnography is the art and science used to describe a group or culture [22]. We use an ethnographic approach to learning about the social and cultural life of communities, institutions, and other settings [23]. Ethnographers use a variety of research methods and rigorous data collection techniques such as interviews, surveys, and participant observation to avoid bias and ensure accuracy of data collection and analyses [24]. This approach employs both inductive and deductive techniques to build culturally valid theories situated in local contexts. Ethnography builds on perspectives of the people situated within settings of interest [23]. The ethnographic approach in this protocol is used as a way to witness events in our participants' world that may be beyond the reach of research approaches that are of more clinical nature [24].

The success of an ethnographic approach is dependent on rapport between participants and researcher [25]. Common techniques used in ethnographies to build a sense of rapport include participant observations and ethnographic interviews [25]. Participant observation involves detailed observation and recording of information about peoples' lives. Ethnographic interviews occur over time, which helps to create a more complete picture of participant experience. This inductive, participant-perceived, and holistic approach of ethnography is ideal for studying veterans and servicemembers with TBI because it allows a diversity of perspectives to be represented.

There is a continuum of approaches to engage the community of interest. Community-engaged research (CEnR) relies on

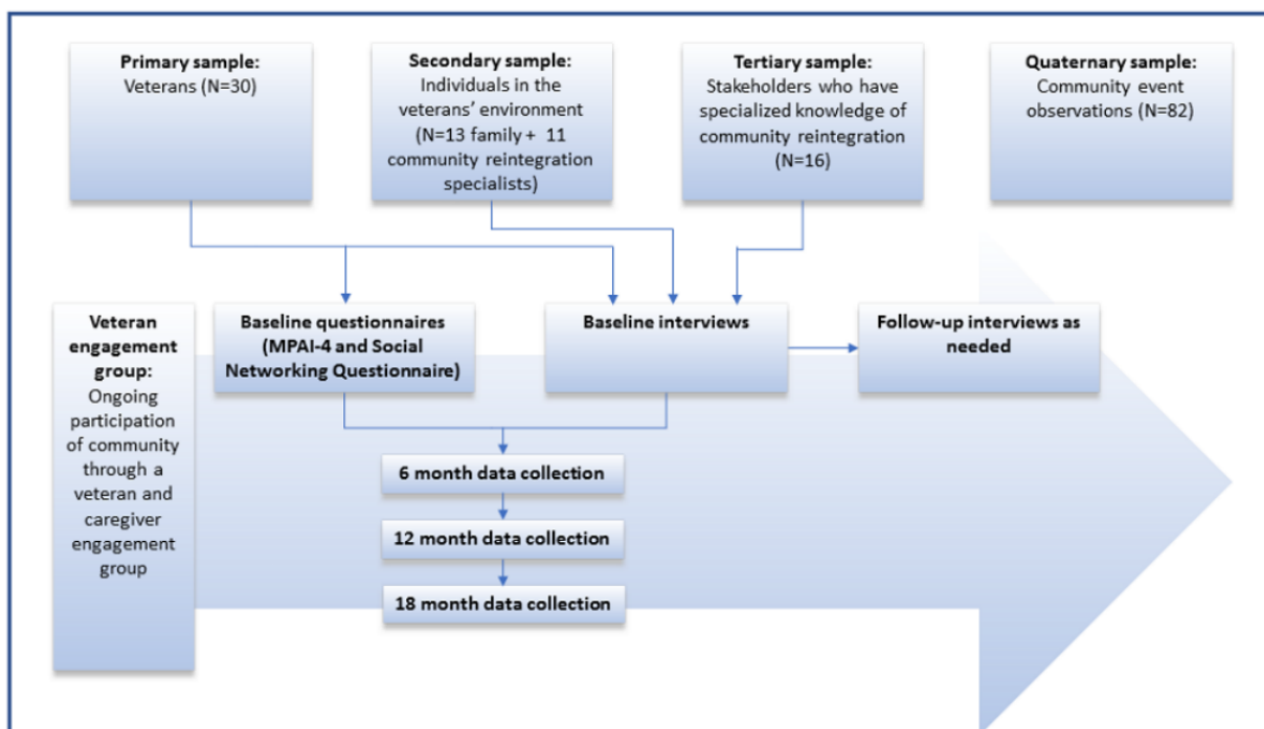
collaborative relationships between communities and researchers and is based on the understanding that communities best know the needs and concerns of their members [26]. This study uses CEnR as a collaborative research approach where the community informs the research process. Specifically, we relied heavily on the CEnR approach to share results of analysis with our community partners to facilitate interpretation and validation of concurrent study findings. Likewise, the community provides opportunities to translate findings into meaningful practice for community members and VHA alike. This approach to research involves all partners in the process and recognizes the unique strengths that each brings [27].

Methods

Design and Overview

This 5-year longitudinal ethnography study uses mixed methods (interviews, questionnaires, and participant observation) from a CEnR perspective (Figure 1). The combination of mixed methods is advantageous as it can provide (1) data and methodological triangulation, (2) a more complete understanding of research problems than either method on its own, (3) strengths that offset the respective weaknesses of both quantitative and qualitative research, and (4) answers questions that cannot be answered by either method alone [28]. Quantitative and qualitative methods can be combined in various ways depending on the timing of the collection of data, the relative weight of each, and how data will be used in analysis. A convergent mixed method design is used in this study [29]. Integration of findings from quantitative and qualitative components occur at the data analysis and interpretation phases.

Figure 1. Schematic of study design data collection. MPAI-4: Mayo-Portland Adaptability Inventory-4.



Triangulation increases the validity, strength, and interpretative potential of the study; decreases investigator biases; and provides multiple perspectives of a given topic [30]. In this study, we employ a triangulation protocol as a strategy to integrate findings from different data sources. Specifically, convergent coding matrices [29] are used to achieve 2 types of methodological triangulation: (1) within-method triangulation (observation and interviews) and (2) across-method triangulation (structured questionnaires, interviews, and participant observations). The convergent coding matrix is used to display qualitative and quantitative findings that emerge in one place. This approach enables consideration of agreement, partial agreement, or dissonance between findings from different data sources [29]. The triangulation protocol facilitates the identification of meta-themes that cut across finding from different methods. After each qualitative data collection point, corresponding data are analyzed, and the results inform subsequent qualitative data collection for further clarification and probing of qualitative findings. When appropriate, triangulation occurs on both the individual and aggregate levels. Qualitative interviews, community observations, and CR surveys are compared and contrasted to determine the extent to which the data triangulate or converge [28]. Qualitative interviews from all 3 participant groups are compared and contrasted. Qualitative interviews and CR surveys are being triangulated with the social network questionnaires.

The collaborative nature of this study is an iterative process. The study incorporates a formal engagement of the target community through the veteran engagement group (VEG). Community engagement exists on a continuum of “community” (eg, immediate family, hospital unit, neighborhood, and city) and “engagement” (eg, transactional, transitional, and transformative) [31]. The VEG engages the community at large, building relationships and transforming the research process, as well as the community at large through information and connection.

Ethical Review and Considerations

This study protocol was reviewed and approved by the affiliated university institutional review board as well as the local Veterans Affairs Research and Development Committee. These oversight entities look specifically for ethical considerations within each submitted protocol. The entities include attorneys, nurses, physicians, and veterans, among others, with expertise in evaluating safety and ethics of research protocols. Given the target population for the study protocol, persons diagnosed with complicated mild, moderate, and severe TBI, we used several measures to assure the protection of participants who consent to participate in the study, some of which are described in further detail in other parts of the protocol. Study staff underwent training and created study-specific procedures for working with participants who might voice thoughts of dying by suicide. Proxy consent and assent to participate were obtained for participants who were not competent to consent themselves [32]. Ongoing communications such as letters sent to participants include more information than would be used in populations without the potential for memory problems. In addition, team meetings often discussed the appropriateness of using data collection tools with this population.

Sampling

Primary Sample

This sample includes veterans and servicemembers from OEF/OIF/OND with complicated mild, moderate, or severe TBI who received acute or transitional rehabilitation. Acute rehabilitation occurs immediately after veterans and servicemembers is medically stable and able to participate in rehabilitation. Transitional rehabilitation typically occurs after acute rehabilitation. Length of stay varies but is often a few months. veterans and servicemembers live in an apartment-style rehabilitation facility with a focus on functional, cognitive, and social goals. Length of stay is typically 1 to 6 months. Patients who have an anticipated or actual discharge from an acute or transitional care rehabilitation program, who are English speaking, and who have access to the internet are included. Patients who have severe substance abuse or severe disruptive behavior that could endanger participants or others, including data collectors, and anticipated discharge to or residence in an institutional facility are excluded. Proxy consent (from the legally authorized representative) is sought for those individuals determined not to be competent based on documentation in the electronic health record. Each veteran and servicemember remains active in the study for approximately 18 months to complete all data collection points.

Initially, the study design called for enrolling patients within 2 months of discharge from the acute or transitional rehabilitation programs. However, admissions of patients with moderate to severe TBI to the acute and transitional rehabilitation programs declined upon the inception of the study, resulting in very few patients eligible to participate in the study. In consultation with clinical coinvestigators and consultants, the study team expanded the inclusion criteria to include patients discharged within the past 12 months from acute or transitional rehabilitation. Ultimately, the decision was made to remove the time since discharge from acute or transitional rehabilitation criterion due to the difficulties stated above.

Secondary Sample

This sample consists of people identified by veterans and servicemembers as being within their social network and providing some level of support such as helping them at home or in the community and being important in their CR process. veterans and servicemembers identify potential participants for this secondary sample and provide contact information. For the purposes of this study, family is defined broadly as a person who provides a substantial amount of support as defined by the veterans and servicemembers and may be from family of origin or family of choice. CR specialists are defined as professionals who have assisted the veterans and servicemembers in their recovery after TBI (eg, case managers and VHA military liaisons) and are identified specifically by the veterans and servicemembers as an important asset to their rehabilitation. People who have involvement in care of the index veteran or servicemember and who are English speaking are included. There are no exclusion criteria. Each secondary sample participant remains active in the study for approximately 18 months to complete data collection.

Tertiary Sample

This sample consists of key community stakeholders who exert influence on the veterans and servicemembers indirectly through professional activities or medical and nonmedical appointments such as directors of community agencies (eg, Team Red, White, and Blue), people who work in relevant agencies such as VHA, State of Florida Department of Veterans' Affairs staff, or local or state rehabilitation organizations. Stakeholders who have specialized knowledge related to care of veterans and servicemembers with TBI who live in the community are included. There are no exclusion criteria.

Quaternary Sample

This sample includes public events and spaces that are relevant to CR for veterans and servicemembers such as job fairs, open houses for organizations who provide veterans' services, public art displays, and artistic performances. The study team uses multiple sources to identify events and resources that would be readily available to veterans and servicemembers and their families following their discharge from acute or transitional rehabilitation. Sources include local hospital outreach calendars; social media sites such as Facebook, Twitter, and Instagram; event calendars and announcements listed through local newspaper and media outlets; and websites for organizations such as veterans service organizations, nonprofit organizations, local cultural and sporting events, and community-based organizations.

Sampling Size

The primary sample includes 30 veterans and servicemembers with complicated mild, moderate, or severe TBI. The secondary sample includes 13 caregivers and 11 CR specialists. The tertiary sample includes 16 key stakeholders. Typically, health services research with veterans and servicemembers with complicated mild, moderate, or severe TBI is limited due to the difficulty in obtaining a statistically powered sample size [33]. This study includes a methodology that capitalizes on small sample sizes. Although generalizability in the statistical sense may not be possible with the small sample size, the external validity of qualitative research will ultimately be determined by the usefulness of the findings in comparable settings with similar veterans and servicemembers [34]. In qualitative research, data saturation is achieved not based on sample size but rather on the depth and breadth of information obtained from participants

related to the phenomena under study [30,35]. Evidence shows that 20-60 knowledgeable people are enough to uncover and understand the key themes in a study of lived experience [36].

Multiple methods are used to recruit veterans and servicemembers who received care from a VHA Polytrauma Rehabilitation Center, either acute or transitional rehabilitation programs for recruitment into the study. Study staff advertise the study in inpatient rehabilitation areas through placement of study brochures and posters and announcements in relevant local newsletters. In addition, clinical partners refer potentially eligible participants to the research study team for screening. Recruitment and enrollment occur both before and after discharge from the acute and transitional rehabilitation programs with baseline data collection initiating after discharge. The study team conducts an eligibility review before enrollment using electronic health records and an internal program evaluation database to determine if a potential participant meets inclusion and exclusion criteria. Potential participants are contacted via United States paper mail if discharged or approached in person if still on site. Follow-up contact to schedule interview and survey data collection visits are conducted by phone calls and US mail.

Snowball sampling, whereby participants refer other people for participation [36], is used to identify the secondary sample. Participants in the secondary sample are contacted after verbal permission from the veterans and servicemembers. The tertiary sample is identified by the study team based on their knowledge of organizations and services relevant to CR; some participants in this sample are referred by other study participants. Telephone-assisted enrollment includes a waiver of documentation of consent. All study participants receive a copy of the informed consent (IC) form and a 1-page summary of consent by US mail as part of the IC process. The quaternary sample is identified by routine reviews of CR-related event sources. All study team members participate in the selection of events by reviewing event information by email or team meeting and identification of the team member(s) who will observe the event.

Measures

Table 1 summarizes variables by sample, data collection instrument, and timing of data collection variables.

Table 1. Variables and measures.

| Variable and definition | Sample | Data collection instrument | Data collection timing |
|---|-----------------------|---|-----------------------------------|
| Demographics | | | |
| Veterans and service members | | | |
| Age, gender, military service history, date of injury, and employment status | Primary | Questionnaire | Baseline |
| Caregiver | | | |
| Relationship to veteran or service member, length of time in relationship and caregiving, age, gender, and employment status | Secondary | Questionnaire | Baseline |
| CR^a specialist and stakeholder | | | |
| occupation, length of time in current role, experience related to CR, or veterans and servicemembers' health | Tertiary | Questionnaire | Baseline |
| Community reintegration | | | |
| Participation in community life that encompasses: (1) employment or other productive activity, (2) independent living, and (3) social relationships and activities. | Primary | Interview guide; Mayo-Portland Adaptability Inventory-4 Participation Index | Baseline and 6, 12, and 18 months |
| | Secondary | Interview guide | Baseline and 6, 12, and 18 months |
| Barriers and facilitators to community reintegration | | | |
| Personal, interpersonal, or environmental factors that prevent or support engagement in employment or other productive activity, independent living, or social relationships and activities | Primary | Interview guide and field notes | Baseline and 6, 12, and 18 months |
| | Secondary | Interview guide | Baseline and 6, 12, and 18 months |
| | Tertiary | Interviews | One time and as needed |
| | Quaternary | Participant observation field notes and document reviews | Monthly and as needed |
| Strategies to improve CR | | | |
| Activities intentionally undertaken by study participants to remove barriers and promote CR | Primary and secondary | Interview guide | Baseline and 6, 12, and 18 months |
| | Tertiary | Interviews | One time and as needed |
| | Quaternary | Participant observation | Monthly and as needed |
| Personal social networks | | | |
| Relationships (ties) between an individual and members of own immediate social environment who interact with one another, and provide tangible social support | Primary | Social network questionnaire | Baseline and 6, 12, and 18 months |

^aCR: community reintegration.

Interview Guide

Investigators employ open-ended, broad interview questions to capture veterans and servicemembers' explanatory models of TBI and perspectives of CR. The research team developed the interview guide based on CR literature and study questions and objectives. Questions are modified as needed based on ongoing data collection and analysis.

Personal Social Network Questionnaire

Investigators collect personal social support network information through the Social Network Questionnaire designed by the

investigators. Veterans and servicemembers are asked to identify up to 5 other persons who provide them with emotional support, small services, large services, financial aid, and companionship.

Veterans and servicemembers also provide information on each identified person such as demographics, how long they have known each other, how often they talk to each other, and how that person is connected to them (eg, spouse, parent, siblings, friends, commander, or counselor). To capture personal social support network cohesion, veterans and servicemembers describe the relative strength of the relationship between each pair of their network contacts as to whether the network alters

are “strangers,” “are as close to each other as I am to them,” or are “neither of these.”

The Mayo-Portland Adaptability Inventory-4, Participation Index

The Mayo-Portland Adaptability Inventory-4 (MPAI-4) consists of 9 items with a 5-point ordinal scale [37]. Raters choose responses that best describe the level at which the person being evaluated experiences problems. Items tap into initiating activities, social contacts with others, leisure and recreation, self-care, independence in living situation, transportation, paid and unpaid employment, and management of finances. Items are summed to yield an overall score. The MPAI-4 has satisfactory internal consistency (Cronbach alpha=.89) and good content validity [38]. Although this instrument does not specifically frame results to our study CR domains. This instrument is designed to capture posthospitalization experiences and can be completed by health care providers, people with TBI, and their significant others. Ratings by different groups can be combined to provide a more reliable assessment.

Data Collection Procedures

Figure 1 shows the data collection procedures and schedule for all samples. Formal in-person or telephone interviews are conducted with veterans and servicemembers (or proxies) every 6 months. Participant observation is conducted at event locations identified by researchers and participants to help researchers better understand CR. A semistructured field note template is used to record observations, interactions, and context by the study team member as soon as possible after attending community events. Photographs are taken as needed to supplement field note data.

Interviews are conducted by telephone or in person at the discretion of the study participant. Follow-up interviews are informed by survey and prior interview data. Interviews are audio recorded with the subjects' consent, and the study investigator documents field notes, noting contextual features of the interview that are not captured in the recording (eg, nonverbal communication and characteristics of the setting). The interviews take a semistructured approach in that they are conducted with a preformulated interview guide, but they allow for answers to those questions to be fully expanded at the discretion of the interviewer and interviewee and enhanced by probes [23]. A flexible and dynamic approach is employed that provides an opportunity to uncover participants' perspectives, using a conversational style to promote a spontaneous flow of information [39].

Web-based survey questionnaires are password protected. Qualtrics, a secure, Web-based survey tool, is used to record questionnaire data [40]. If the participant is unable to complete the Web-based survey, the interviewer assists in person or via telephone interview. Letters are mailed instructing participants on how to log in and access the Web-based survey, and reminder letters are mailed to ensure completion.

The CEnR approach requires meaningful engagement with veterans and servicemembers and family stakeholders. After initial attempts to engage study participants in a Web-based bulletin board forum were unsuccessful, a VEG was developed

as an alternative method for veterans and servicemembers and family stakeholder engagement to assist study team members throughout the research process. Recent recommendations by the Health Services Research and Development Service Veteran Engagement Workgroup Final Report [41] support establishing VEGs to meaningfully engage veterans and servicemembers and significant others into research endeavors, thus ensuring veterans and servicemembers voices are well represented. This study's VEG comprised 6 active volunteers. Members of the engagement group include veterans with a TBI (n=3) and caregivers for veterans with a brain injury (n=3). Participants have used VHA rehabilitation services for themselves or their loved ones. The research team developed the description and recruitment process for VEG members. Interested persons are recruited via word of mouth and via the James A. Haley Veterans' Hospital and Clinics social media outlets—Facebook and Twitter. Of note, VEG participants are not research subjects enrolled in the study, but they serve as consultants to the research team. The VEG meetings vary in frequency from quarterly earlier in the study to bimonthly, as there is more data to share and input to solicit. This partnership yields positive results by providing feedback (eg, interpretation guidance and member checking) on early qualitative data analysis, advice for participant recruitment, and dissemination of early products. For example, the VEG is instrumental in the development of a stakeholder-driven Tip-Sheet derived from interpretation of data from local community event observations. The VEG also provides critical feedback on funded proposals informed by results of this study (eg, Resource Facilitation [42]), provides input on priorities for dissemination of current research findings and future next steps.

Data Analysis

Qualitative

Qualitative insights from data analysis are used to iteratively guide subsequent data collection (eg, choice of next subjects [theoretical sampling], modification of interview questions, and feedback from subjects on researcher interpretations of data and provisional results). All interview audio files, field notes, and documents are transcribed or scanned and stored on a secure VHA server with access only to the research team.

A computer-assisted analysis model known as Noticing things, Collecting things, and Thinking about things (NCT) is employed to analyze the data [43,44]. The analysis process can be linear, starting with noticing interesting things in the data, collecting them (eg, as codes), thinking about them, and then writing interesting insights. However, more often, qualitative analysis requires moving back and forth between noticing, collecting, and thinking about things, as shown by arrows in the middle of the figure (see Figure 1). The NCT model uses coding structures, memoing, process mapping, and diagramming to describe, categorize, and connect the data to determine common themes patterns and inconsistencies relating to participants' experiences, perceptions, and opinions.

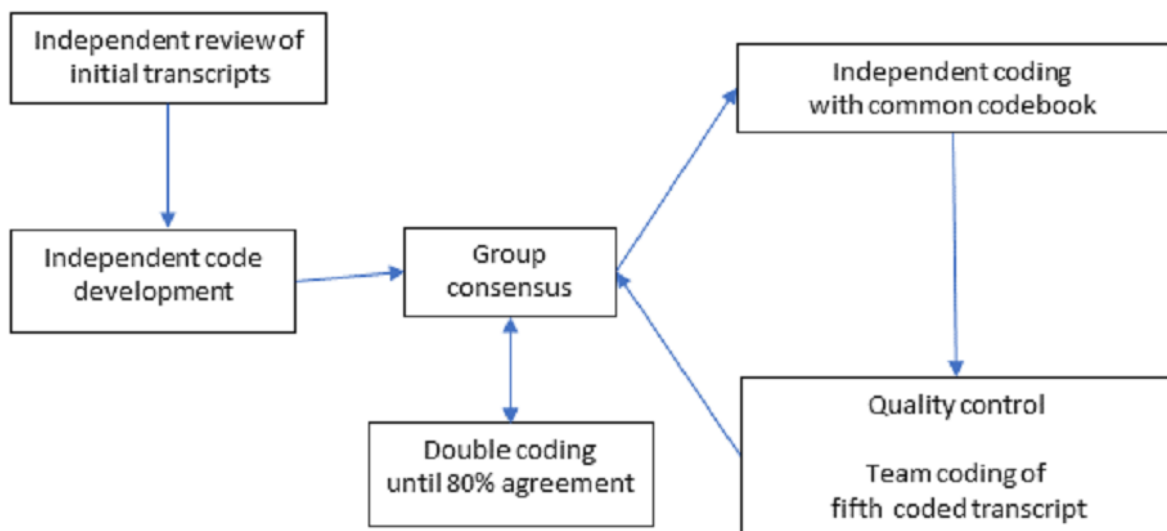
Interview transcripts are uploaded into the qualitative analysis software program ATLAS.ti v8.0 which is used to organize data and systematically develop a codebook of the interview transcripts that catalogs and defines codes and thematic

categories. The qualitative team meets regularly to analyze the interview transcripts in the following way: (1) assign first-level structured codes to units of meaning, (2) synthesize codes into complex categories, (3) compare and contrast categories to identify relationships across categories, (4) group categories into a taxonomic structure that describes the dataset, and (5) link sections of text to the coding to identify salient quotes that illustrate the codes and constructs and that support coding decisions. Memoing or analytic writing is also performed at each step of the analysis to create a written record of the process and to develop conceptual ideas relating to the data.

The qualitative team members compare and contrast perceptions of key findings following interviews. Investigators use the

following analytic strategy: (1) reviewing the first few transcripts and developing codes independently; (2) reviewing their work together and, through consensus, agreeing on codes and definitions; (3) double coding transcripts until 80% agreement is attained; and (4) after 80% agreement is attained coding transcripts independently using the common codebook. Every fifth coded transcript is randomly reviewed by the team to select portions for agreement. Investigators revise and clarify the codebook as needed by discussing points of agreement and discrepancies and making decisions jointly to determine whether new codes were needed. Data analysts meet routinely to review ongoing coding results, resolve coding issues that arise, and discuss collapsing of codes into higher-level codes and constructs (Figure 2).

Figure 2. Coding process.



Quantitative

Egocentric social network analysis examines the presence of relationships between veterans' personal (ego) social support network characteristics and successful CR as measured by the MPAI-4 [45]. Network visualization will be performed to investigate variables summarizing the number and types of ties in terms of the ego network's shape, size, and composition and their changes over time. Regression analyses will identify which of these variables at baseline and/or over time show positive or negative effects on CR.

Veterans nominate persons of influence within their lives (alters). The connectedness among alters represents network density, and number of distinct alters represents network size. Interpretation of network size is deemphasized as by design, we limited the number of alters that an ego can name; however, up to this limit, the number of positive ties may positively influence reintegration. Higher density will suggest greater social cohesion, which is desirable. Measures of network composition will include the different types of connections between an ego and each alter and their frequencies (which denote connection strength), for example, same alter can be friend, coworker, and neighbor (multidimensional connection).

The connection strength and/or type may be associated with CR. The network characteristics are collected for each ego network on each measurement occasion, which allows for observation of evolution of individual networks over time. The ego networks will be graphed, and the measures will be generated using E-NET software [46].

Using UCINET [47], CR at a given assessment (MPAI-4 scores as dependent variables) is modeled in a regression equation as a function of network-based mechanisms. Standard regression is used to analyze ego-level data (eg, density and demographics of ego). A 2-level regression model is fitted to alter-level data (eg, tie type, tie strength, and demographics of alter). Moreover, ego-level and alter-level data are tested for association with the rate of change of CR (linear slope) over time using 2-level and 3-level linear growth models, respectively.

Results

The project was funded in FY2019 and enrolment was completed FY2019. Data analysis is currently under way and the first results are expected to be submitted for publication in 2020.

Discussion

Protocol Purpose

The goal of this study protocol is to describe methods used to better understand and highlight the experiences of veterans and servicemembers with complicated mild, moderate, or severe TBI; their families; and CR workers as they transition to and sustain living in communities. This protocol illustrates an ethnographic approach to support understanding of said experiences within the context of community. To our knowledge, this protocol is unique in that it explores CR over time from multiple perspectives, within the context of community.

Strengths and Limitations

This protocol has several noteworthy strengths based on the CEnR approach. Specifically, the protocol was written to (1) provide a comprehensive understanding of veteran-perceived and contextual factors affecting CR to identify targets for interventions that can decrease barriers and strengthen facilitators for veterans with complicated mild, moderate, or severe TBI; (2) give voice to veterans and families by actively engaging them in removing barriers to CR directly for themselves and indirectly for others; and (3) provide a roadmap for designing and testing interventions to maximize CR in employment, independent living, and social relationships that are grounded in the perceptions of multiple perspectives.

Similarly, there are several limitations that are noteworthy of mention. First, the inclusion criteria originally included veterans and servicemembers who sustained a moderate or severe TBI and had recently been discharged from the local acute and transitional rehabilitation programs. However, because of decreasing military operations and changes in the patient populations being admitted to these programs, there were not sufficient numbers of eligible patients. To address this limitation, we expanded recruitment to those with complicated mild TBI and those who have received acute or transitional rehabilitation at any time. Second, the proposal originally planned to engage participants in the conduct of the study and analysis using a Web-based bulletin board for feedback and insights. This method proved ineffective, and the study team was not able to engage study participants in the Web-based bulletin board. However, the VEG provided an alternative method for engaging community-based participation in the research study. The purpose of this group is to provide a community for veterans and servicemembers and caregivers to pose questions and provide feedback on data and study issues as they arise. Finally,

the study team planned on collecting quantitative measures of CR using both the Community Reintegration for Service Members (CRIS) 147 item measure and the participation index of MPAI-4. Although comprehensive, concerns about participant burden, and the ability of participants to complete the survey led the team to remove the CRIS and rely solely on the MPAI-4 participation index as no short-form scales were available for the CRIS.

Finally, study data collection is limited to the Tampa Bay Area, which includes 1 of the 5 VHA polytrauma rehabilitation centers. The availability of community and VHA resources varies by region and county throughout the state of Florida. Greater resources are typically available in urban versus rural communities, affecting access to and use of services and supports. Access to Medicaid Waiver programs is also an important consideration. For example, the Traumatic Brain and Spinal Cord Injury Medicaid Waiver Program provides home- and community-based health care services for individuals aged 18 to 64 years with TBI or spinal cord injury in Florida. The waitlist for these services is long, and many individuals may never receive services through this program.

Conclusions

This protocol employs an ethnographic mixed method design (interviews, observations, and surveys) and a CEnR approach. The intent is to elicit definitions and perceptions of CR and a more thorough understanding of environmental and cultural factors that influence CR in veterans and servicemembers with TBI. The addition of the VEG, which includes both veterans and servicemembers with TBI and caregivers of veterans and servicemembers with TBI, in the interpretation, feedback, and direction of findings; dissemination products; and next steps, supports meaningful engagement, input, and empowerment of the population being studied. Understanding of environmental and cultural factors that influence CR may inform VHA and Department of Defense policy and programmatic changes to support veterans and servicemembers as they transition to local communities and providers. The inductive, participant-perceived, and holistic approach of ethnography highlights the practical and participatory factors involved in understanding CR. Using this protocol, a comprehensive understanding of CR can be identified and disseminated, leveraging veteran and servicemember-focused experiences that can assuage CR barriers and strengthen CR facilitators for veterans and servicemembers with TBI. Future research should target development of programs and community collaborations to address CR barriers.

Acknowledgments

This research was supported by the Award #SDR 12-302 from Health Services Research and Development Service of the Office of Research and Development, VHA, US Department of Veterans Affairs. The contents of this manuscript do not represent the views of the Department of Veterans Affairs or the US Government. This work was also supported with resources from the James A. Haley Veterans Hospital. The authors would like to acknowledge the efforts of Lynn Dirk in the preparation of this manuscript. The authors would also like to thank the participants who generously shared their time and experiences.

Conflicts of Interest

None declared.

References

1. World Health Organization. 2002. Towards a Common Language for Functioning, Disability and Health URL: <http://www.who.int/classifications/icf/training/icfbeginnersguide.pdf> [accessed 2013-03-21] [WebCite Cache ID 6FIEOc4Va]
2. World Health Organization. World Report on Disability URL: https://www.who.int/disabilities/world_report/2011/report.pdf [accessed 2013-11-19] [WebCite Cache ID 6ODG9eOmQ]
3. Field M, Jette A, Martin L. Workshop on Disability in America, A New Look: Summary and Background Papers. Washington, DC: Institute of Medicine, National Academies Press; 2006.
4. McColl MA, Carlson P, Johnston J, Minnes P, Shue K, Davies D, et al. The definition of community integration: perspectives of people with brain injuries. *Brain Inj* 1998 Jan;12(1):15-30. [Medline: 9483334]
5. Salter K, Foley N, Jutai J, Bayley M, Teasell R. Assessment of community integration following traumatic brain injury. *Brain Inj* 2008 Oct;22(11):820-835. [doi: 10.1080/02699050802425428] [Medline: 18850341]
6. Ottomanelli L, Bakken S, Dillahunt-Aspillaga C, Pastorek N, Young C. Vocational rehabilitation in the Veterans Health Administration Polytrauma system of care: current practices, unique challenges, and future directions. *J Head Trauma Rehabil* 2019;34(3):158-166. [doi: 10.1097/HTR.0000000000000493] [Medline: 31058758]
7. Elnitsky CA, Blevins C, Findlow JW, Alverio T, Wiese D. Student veterans reintegrating from the military to the university with traumatic injuries: how does service use relate to health status? *Arch Phys Med Rehabil* 2018 Feb;99(2S):S58-S64. [doi: 10.1016/j.apmr.2017.10.008] [Medline: 29097180]
8. Besterman-Dahan K, Chavez M, Njoh E. Rooted in the community: assessing the reintegration effects of agriculture on rural veterans. *Arch Phys Med Rehabil* 2018 Feb;99(2S):S72-S78. [doi: 10.1016/j.apmr.2017.06.035] [Medline: 28843773]
9. Pogoda TK, Carlson KF, Gormley KE, Resnick SG. Supported employment for veterans with traumatic brain injury: provider perspectives. *Arch Phys Med Rehabil* 2018 Feb;99(2S):S14-S22. [doi: 10.1016/j.apmr.2017.06.029] [Medline: 28784357]
10. Corrigan JD, Selassie AW, Orman JAL. The epidemiology of traumatic brain injury. *J Head Trauma Rehabil* 2010;25(2):72-80. [doi: 10.1097/HTR.0b013e3181ccc8b4] [Medline: 20234226]
11. Defense and Veterans Brain Injury Center. 2018. DoD Worldwide Numbers for TBI URL: <https://dybic.dcoe.mil/dod-worldwide-numbers-tbi> [WebCite Cache ID 6g9p4TtGH]
12. Resnik L, Bradford DW, Glynn SM, Jette AM, Hernandez C, Wills S. Issues in defining and measuring veteran community reintegration: proceedings of the Working Group on Community Reintegration, VA Rehabilitation Outcomes Conference, Miami, Florida. *J Rehabil Res Dev* 2012;49(1):87-100 [FREE Full text] [doi: 10.1682/JRRD.2010.06.0107] [Medline: 22492341]
13. Kupersmith J, Lew HL, Ommaya AK, Jaffee M, Koroshetz WJ. Traumatic brain injury research opportunities: results of Department of Veterans Affairs Consensus Conference. *J Rehabil Res Dev* 2009;46(6):vii-xvi [FREE Full text] [doi: 10.1682/JRRD.2009.06.0079] [Medline: 20104393]
14. Dillahunt-Aspillaga C, Powell-Cope G. Community reintegration, participation, and employment issues in veterans and service members with traumatic brain injury. *Arch Phys Med Rehabil* 2018 Feb;99(2S):S1-S3. [doi: 10.1016/j.apmr.2017.04.013] [Medline: 29406019]
15. Sayer NA, Carlson KF, Frazier PA. Reintegration challenges in US service members and veterans following combat deployment. *Soc Issues Policy Rev* 2014 Jan 13;8(1):33-73 [FREE Full text] [doi: 10.1111/sipr.12001]
16. Elnitsky CA, Blevins CL, Fisher MP, Magruder K. Military service member and veteran reintegration: a critical review and adapted ecological model. *Am J Orthopsychiatry* 2017;87(2):114-128. [doi: 10.1037/ort0000244] [Medline: 28206799]
17. Sander AM, Clark A, Pappadis MR. What is community integration anyway?: defining meaning following traumatic brain injury. *J Head Trauma Rehabil* 2010;25(2):121-127. [doi: 10.1097/HTR.0b013e3181cd1635] [Medline: 20134333]
18. Crocker T, Powell-Cope G, Brown LM, Besterman-Dahan K. Toward a veteran-centric view on community (re)integration. *J Rehabil Res Dev* 2014;51(3):xi-xvii [FREE Full text] [doi: 10.1682/JRRD.2014.01.00111] [Medline: 25019672]
19. Stern L. Post 9/11 veterans with service-connected disabilities and their transition to the civilian workforce. *Adv Dev Hum Resour* 2017 Feb;19(1):66-77. [doi: 10.1177/1523422316682928]
20. Smith RT, True G. Warring identities: identity conflict and the mental distress of American veterans of the wars in Iraq and Afghanistan. *Soc Ment Health* 2014;4(2):147-161. [doi: 10.1177/2156869313512212]
21. Sander AM, Maestas KL, Sherer M, Malec JF, Nakase-Richardson R. Relationship of caregiver and family functioning to participation outcomes after postacute rehabilitation for traumatic brain injury: a multicenter investigation. *Arch Phys Med Rehabil* 2012 May;93(5):842-848. [doi: 10.1016/j.apmr.2011.11.031] [Medline: 22417896]
22. Fetterman DM. *Ethnography: Step-by-Step*. Thousand Oaks, CA: Sage Publications Inc; 2009.
23. LeCompte MD, Schensul JJ. *Designing and Conducting Ethnographic Research*. Walnut Creek, CA: AltaMira Press; 1999.
24. Savage J. Ethnography and health care. *Br Med J* 2000 Dec 2;321(7273):1400-1402 [FREE Full text] [doi: 10.1136/bmj.321.7273.1400] [Medline: 11099288]

25. Spradley J. StudyBlue. 1979. Ethnography and Culture URL: <https://www.studyblue.com/notes/note/n/chapter-1-culture-and-ethnography-ethnography-and-culture-by-james-spradley/deck/11372914> [accessed 2019-09-25]
26. Michener L, Cook J, Ahmed SM, Yonas MA, Coyne-Beasley T, Aguilar-Gaxiola S. Aligning the goals of community-engaged research: why and how academic health centers can successfully engage with communities to improve health. *Acad Med* 2012 Mar;87(3):285-291 [FREE Full text] [doi: [10.1097/ACM.0b013e3182441680](https://doi.org/10.1097/ACM.0b013e3182441680)] [Medline: [22373619](https://pubmed.ncbi.nlm.nih.gov/22373619/)]
27. Oetzel JG, Villegas M, Zenone H, Hat ER, Wallerstein N, Duran B. Enhancing stewardship of community-engaged research through governance. *Am J Public Health* 2015 Jun;105(6):1161-1167. [doi: [10.2105/AJPH.2014.302457](https://doi.org/10.2105/AJPH.2014.302457)] [Medline: [25880952](https://pubmed.ncbi.nlm.nih.gov/25880952/)]
28. Creswell J, Clark V. *Designing and Conducting Mixed Methods Research*. Third Edition. Thousand Oaks, CA: SAGE Publications; 2018.
29. O' Cathain A, Murphy E, Nicholl J. Three techniques for integrating data in mixed methods studies. *Br Med J* 2010 Sep 17;341:c4587. [doi: [10.1136/bmj.c4587](https://doi.org/10.1136/bmj.c4587)] [Medline: [20851841](https://pubmed.ncbi.nlm.nih.gov/20851841/)]
30. Patton M. *Qualitative Evaluation and Research Methods*. Second Edition. Thousand Oaks, CA: SAGE Publications; 2001.
31. Bowen F, Newenham-Kahindi A, Herremans I. When suits meet roots: the antecedents and consequences of community engagement strategy. *J Bus Ethics* 2010 Jan 27;95(2):297-318. [doi: [10.1007/s10551-009-0360-1](https://doi.org/10.1007/s10551-009-0360-1)]
32. Silverman H. Protecting vulnerable research subjects in critical care trials: enhancing the informed consent process and recommendations for safeguards. *Ann Intensive Care* 2011 Apr 13;1(1):8 [FREE Full text] [doi: [10.1186/2110-5820-1-8](https://doi.org/10.1186/2110-5820-1-8)] [Medline: [21906335](https://pubmed.ncbi.nlm.nih.gov/21906335/)]
33. Roozenbeek B, Lingsma HF, Maas AI. New considerations in the design of clinical trials for traumatic brain injury. *Clin Investig (Lond)* 2012 Feb;2(2):153-162 [FREE Full text] [doi: [10.4155/cli.11.179](https://doi.org/10.4155/cli.11.179)] [Medline: [22518272](https://pubmed.ncbi.nlm.nih.gov/22518272/)]
34. Leung MW, Yen IH, Minkler M. Community based participatory research: a promising approach for increasing epidemiology's relevance in the 21st century. *Int J Epidemiol* 2004 Jun;33(3):499-506. [doi: [10.1093/ije/dyh010](https://doi.org/10.1093/ije/dyh010)] [Medline: [15155709](https://pubmed.ncbi.nlm.nih.gov/15155709/)]
35. Corbin J, Strauss A. *Basics Of Qualitative Research: Techniques And Procedures For Developing Grounded Theory*. Third Edition. Thousand Oaks, CA: Sage Publications Inc; 2008.
36. Bernard H, Wutich A, Ryan G. *Analyzing Qualitative Data: Systematic Approaches*. Second Edition. Thousand Oaks, CA: SAGE Publications; 2016.
37. Coleman RD, Rapport LJ, Ergh TC, Hanks RA, Ricker JH, Millis SR. Predictors of driving outcome after traumatic brain injury. *Arch Phys Med Rehabil* 2002 Oct;83(10):1415-1422. [doi: [10.1053/apmr.2002.35111](https://doi.org/10.1053/apmr.2002.35111)] [Medline: [12370878](https://pubmed.ncbi.nlm.nih.gov/12370878/)]
38. Wilde EA, Whiteneck GG, Bogner J, Bushnik T, Cifu DX, Dikmen S, et al. Recommendations for the use of common outcome measures in traumatic brain injury research. *Arch Phys Med Rehabil* 2010 Nov;91(11):1650-60.e17. [doi: [10.1016/j.apmr.2010.06.033](https://doi.org/10.1016/j.apmr.2010.06.033)] [Medline: [21044708](https://pubmed.ncbi.nlm.nih.gov/21044708/)]
39. Krippendorff K. *Content Analysis: An Introduction to Its Methodology*. Fourth Edition. Thousand Oaks, CA: SAGE Publications; 2018.
40. Qualtrics. 2019. Try the Top-Rated Online Survey Tool URL: <https://www.qualtrics.com/lp/survey-platform/> [accessed 2019-03-27] [WebCite Cache ID 77C00TktA]
41. Tanaka M, Atkins, David M, Zickmund S. Veterans Affairs. America's Women Veterans: Military Service History and VA Benefit Utilization Statistics URL: https://www.va.gov/vetdata/docs/specialreports/final_womens_report_3_2_12_v_7.pdf [accessed 2019-03-26] [WebCite Cache ID 77AS42J3o]
42. Health Services Research & Development - Veterans Affairs. PPO 17-053 – HSR&D Study URL: https://www.hsrd.research.va.gov/research/abstracts.cfm?Project_ID=2141706945 [accessed 2019-07-06]
43. Seidel J. Qualis Research. Appendix E: Qualitative Data Analysis URL: <http://www.qualisresearch.com/DownLoads/qda.pdf> [accessed 2019-09-19] [WebCite Cache ID 77BydS2BI]
44. Friese S. *Qualitative Data Analysis with ATLAS.ti*. Second Edition. Thousand Oaks, CA: SAGE Publications; 2014.
45. Perry B, Pescosolido B, Borgatti S. *Egocentric Network Analysis: Foundations, Methods, and Models*. United Kingdom: Cambridge University Press; 2018.
46. Borgatti S. *E-Network Software for Ego-Network Analysis*. Lexington, KY: Analytic Technologies; 2006.
47. Borgatti S, Everett M, Freeman L. *Ucinet for Windows: Software for Social Network Analysis*. Harvard, MA: Analytic Technologies; 2002.

Abbreviations

- CEnR:** community-engaged research
- CR:** community reintegration
- CRIS:** Community Reintegration for Service Members
- IC:** informed consent
- MPAI:** Mayo-Portland Adaptability Inventory-4
- NCT:** Noticing things, Collecting things, and Thinking about things
- OEF:** Operation Enduring Freedom
- OIF:** Operation Iraqi Freedom

OND: Operation New Dawn

TBI: traumatic brain injury

VHA: Veterans Health Administration

Edited by G Eysenbach; submitted 29.03.19; peer-reviewed by B Smith, A Farre, J Verbeek; comments to author 16.05.19; revised version received 10.07.19; accepted 31.08.19; published 22.11.19.

Please cite as:

Melillo C, Downs K, Dillahunt-Aspillaga C, Lind J, Besterman-Dahan K, Hahm B, Antinori N, Elnitsky C, Sander AM, Belanger HG, Toyinbo P, Powell-Cope G

Action Ethnography of Community Reintegration for Veterans and Military Service Members With Traumatic Brain Injury: Protocol for a Mixed Methods Study

JMIR Res Protoc 2019;8(11):e14170

URL: <http://www.researchprotocols.org/2019/11/e14170/>

doi: [10.2196/14170](https://doi.org/10.2196/14170)

PMID: [31755868](https://pubmed.ncbi.nlm.nih.gov/31755868/)

©Christine Melillo, Kiersten Downs, Christina Dillahunt-Aspillaga, Jason Lind, Karen Besterman-Dahan, Bridget Hahm, Nicole Antinori, Christine Elnitsky, Angelle M Sander, Heather G Belanger, Peter Toyinbo, Gail Powell-Cope. Originally published in JMIR Research Protocols (<http://www.researchprotocols.org>), 22.11.2019. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in JMIR Research Protocols, is properly cited. The complete bibliographic information, a link to the original publication on <http://www.researchprotocols.org>, as well as this copyright and license information must be included.

Original Paper

Group Sex Events Among Cisgender Men Who Have Sex With Men: Cross-Sectional and Longitudinal Survey Study to Explore Participation and Risk-Taking Behaviors

Lauren R Violette¹, MPH; Lisa A Niemann¹, MSW, MPH; Vanessa M McMahan¹, MS, PhD; David A Katz², MPH, PhD; Pollyanna R Chavez³, PhD; Hollie A Clark³, MPH; Andy Cornelius-Hudson¹, BA; Steven F Ethridge³, BS, MT(ASCP); Sarah J McDougal¹, MPH, PA; George Ure II¹; Joanne D Stekler^{1,4,5}, MPH, MD; Kevin P Delaney³, MPH, PhD

¹Department of Medicine, University of Washington, Seattle, WA, United States

²HIV/STD Program, Public Health - Seattle & King County, Seattle, WA, United States

³Division of HIV/AIDS Prevention, Centers for Disease Control and Prevention, Atlanta, GA, United States

⁴Department of Global Health, University of Washington, Seattle, WA, United States

⁵Department of Epidemiology, University of Washington, Seattle, WA, United States

Corresponding Author:

Lauren R Violette, MPH
Department of Medicine
University of Washington
325 Ninth Avenue
Box 359931
Seattle, WA, 98104
United States
Phone: 1 206 616 1054
Email: lvio@uw.edu

Abstract

Background: Group sex events (GSEs) are common among cisgender men who have sex with men (MSM), pose a unique risk profile for HIV and sexually transmitted disease (STD) transmission, and may be on the rise, in part because of Web-based networking platforms. However, collecting data on GSEs can be challenging, and many gaps exist in our knowledge about GSE participation among MSM.

Objective: The objective of this study was to develop survey questions addressing aggregate and partner-specific group sex behaviors to measure prevalence of GSEs and associated risks in persons participating in Project Diagnostic Evaluation To Expand Critical Testing Technologies (DETECT), including MSM seeking HIV and STD testing at a public clinic in Seattle, Washington.

Methods: We developed a computer self-assisted survey that included questions about participant demographics, sexual history, and risk behaviors, including group sex, as a part of Project DETECT, a Centers for Disease Control and Prevention-funded study evaluating point-of-care HIV tests. Aggregate and partner-specific questions asked about participation in all GSEs, threesomes, and four-or-more-somes including questions about number and HIV status of sex partners and condom use during the events. To evaluate question performance, we assessed the discrepancies in reporting between the aggregate and partner-specific questions, quantified question refusal rates, and calculated the additional time required to answer the GSE questions. Information about network density (number of partnerships of overlapping duration) was estimated and compared for MSM who did and did not report GSEs.

Results: Among 841 visits by 690 MSM who were asked any group sex survey question, participation in a GSE of any type in the past 3 months was reported at 293 visits (293/841, 34.8%). We found that 9.0% (76/841) of MSM in the sample reported ≥ 1 four-or-more-some in the partner-specific questions but did not report in the aggregate. The proportion of refusals on any given aggregate GSE-related question ranged from 0% (0/273) to 10.6% (15/141) (median 2.6%) and partner-specific questions ranged from 0% (0/143) to 22% (5/23) (median 3.0%), with questions about four-or-more-somes having the highest proportions of refusals. Completing the aggregate group sex questions added 1 to 2 minutes and the partner-specific questions added an additional

2 to 4 minutes per partner to the total survey length. As expected, the partner-specific GSE questions documented higher density of sexual networks that was not captured by asking about total partner counts and overlap of specific partnerships.

Conclusions: We found that the Project DETECT survey was able to obtain nuanced information about GSEs. The question skip patterns and consistency checks were effective, and survey fatigue was minimal. More research is needed on GSEs, and our survey represents a promising data collection tool to help fill gaps in knowledge about the subject.

(*JMIR Res Protoc* 2019;8(11):e15426) doi:[10.2196/15426](https://doi.org/10.2196/15426)

KEYWORDS

men who have sex with men; group sex; HIV infection; sexual networks; risk; threesomes; four-or-more-somes

Introduction

A growing body of literature indicates that group sex, a sexual interaction involving more than 2 participants, is common among cisgender men who have sex with men (MSM) [1-6]. These events can vary widely in form and context, including the number of participants, the relationships between participants, the type of sex that occurs, and the site or setting in which the event takes place [1-5]. Prevalence estimates of group sex event (GSE) participation from previous studies among cisgender MSM have ranged from approximately one-quarter of respondents reporting group sex during the last year in a venue-based sample in Washington, DC, to nearly three-quarters of respondents reporting a GSE in their lifetime in an online survey from the London metropolitan area [2,6-10]. GSE participation among cisgender MSM may be increasing, in part because of the proliferation of Web-based and mobile social networking platforms used to facilitate meeting sex partners [6,11,12].

GSEs pose a unique set of risks for transmission of HIV and other sexually transmitted diseases (STDs) because the single event enables STD transmission from 1 infected individual to multiple partners [4,13] more efficiently than a sequence of monogamous events with the same number of partners [14,15]. Some studies have also shown that GSE participation is associated with a higher prevalence of behavior associated with risk for HIV acquisition such as condomless receptive anal intercourse and using drugs or alcohol [7,8,10,12,16-18]. However, others have found that MSM who participated in GSEs were more likely to use condoms or pre-exposure prophylaxis (PrEP) than those who did not participate in GSEs [9,19,20].

Much remains to be learned about the prevalence of GSEs and the behaviors of persons who participate in them. Obtaining nuanced data on GSEs is difficult for many reasons: the sensitivity of the subject may make researchers and participants hesitant to discuss the topic, in-depth questions about GSEs can be complicated and difficult for respondents to navigate, and a history of sexual stigma against MSM might make participants hesitant to report GSE participation [5,21]. Studies on GSEs to date have largely focused on determining prevalence and associated population-level behavioral factors rather than looking at partner-level or event-level data, and the absence of partner-centric questions leaves significant gaps in our ability to understand HIV and STD transmission dynamics and characterize risk associated with GSEs [22]. Partner-specific data are important for network-based models that are

increasingly being used in the analyses of HIV and STD transmission because the density and structure of sexual networks have been shown to be important characteristics in mathematical models, especially for MSM [22]. However, the importance of collecting these details needs to be balanced against the additional time and effort required of study participants to provide information on GSE participation. Finding this balance can be particularly challenging in longer national surveys such as the Centers for Disease Control and Prevention (CDC) National HIV Behavioral Surveillance (NHBS) and the American Men's Internet Survey (AMIS). As part of an ongoing study funded by the CDC to compare the performance of point-of-care HIV tests, we developed a series of aggregate and partner-specific questions to determine the prevalence of GSEs among MSM and characterize condom use and seroadaptive behaviors of participants during GSEs. In this paper, we focus on the development of the survey questions; detailed analysis of survey results will be presented elsewhere.

Methods

Study Design and Recruitment

These questions were implemented as part of a larger behavioral survey administered via computer-assisted self-interview (CASI) to participants in Project Diagnostic Evaluation To Expand Critical Testing Technologies (DETECT) [23,24]. Participants were English-speaking individuals aged ≥ 18 years and either (1) cisgender men and transgender or gender nonconforming individuals who had sex with men seeking HIV testing at the Public Health - Seattle & King County (PHSKC) STD clinic or (2) persons with known HIV infection referred from various sources including the Madison Clinic at Harborview Medical Center (a Ryan White-funded HIV care clinic) and PHSKC HIV/STD Program staff. Participants with negative results from all study HIV tests were able to re-enroll in the study every 90 days. The study was approved by the University of Washington Human Subjects Division (study number 00001637). All participants gave either written or verbal consent (using an identical institutional review board-approved information statement) and were compensated US \$40 for study participation. Project DETECT began enrollment in September 2015, and the behavioral survey was piloted from October 30, 2015, to February 23, 2016, with the inclusion of only those participants who had discordant HIV test results (at least 1 positive and 1 negative HIV test result); 4 subjects completed the survey during this time. Beginning February 24, 2016, all study participants, regardless of their HIV test results, completed the survey.

Questionnaire

The CASI (Questionnaire Development System [QDS], version 3.0; Nova Research Company) assessed demographics, HIV testing history and interaction with the health care system, current symptoms of acute HIV infection, recent STD history, PrEP use, antiretroviral treatment (ART) use, substance use, and sexual behaviors at the aggregate and partner-specific levels. Participants were asked between 18 and 287 questions, depending on their responses. A blank piece of paper was provided to help participants with recall and track details during survey completion. Study staff were available to provide clarifications regarding questions if requested. Participants were able to refuse all questions in the survey other than the documentations for study consent and specimen storage, sex at birth, current gender, and gender of sex partners, if any, in the last year.

Analysis Sample

This analysis was limited to a subset of cisgender MSM who participated in Project DETECT. We defined MSM as reported male sex at birth, current male gender identity, and anal sex with at least 1 man in the past 3 months. These participants were first asked if they participated in any GSEs and then about threesomes and four-or-more-somes separately. Although GSEs are generally defined in the literature as a sexual interaction between ≥ 3 people, participants might consider *group sex* only to include 4 or more participants [4]. Distinguishing between threesomes and four-or-more-somes is potentially important because participation in threesomes may be associated with different partnership characteristics and behaviors than participation in four-or-more-somes [1]. For the purposes of this paper, we refer to GSEs to encompass all events that involve ≥ 3 persons including the study participant, threesomes to include events with 3 people, and four-or-more-somes to indicate GSEs that included ≥ 4 people.

Development of Group Sex Questions

As there are no pre-existing validated measures, the group sex questions were modeled on NHBS and AMIS, in which participants are asked about sexual behaviors in aggregate and then asked about behaviors with their most recent partner(s) [25,26]. When the last reported sex occurred in the context of a GSE, such questions about *most recent partner* are challenging to answer because of simultaneous partnerships. We, therefore, modified these questions for Project DETECT to account for

the possibility of GSEs in the previous 3 months by asking several questions about group sex participation with the participant's 3 most recent anal sex partners.

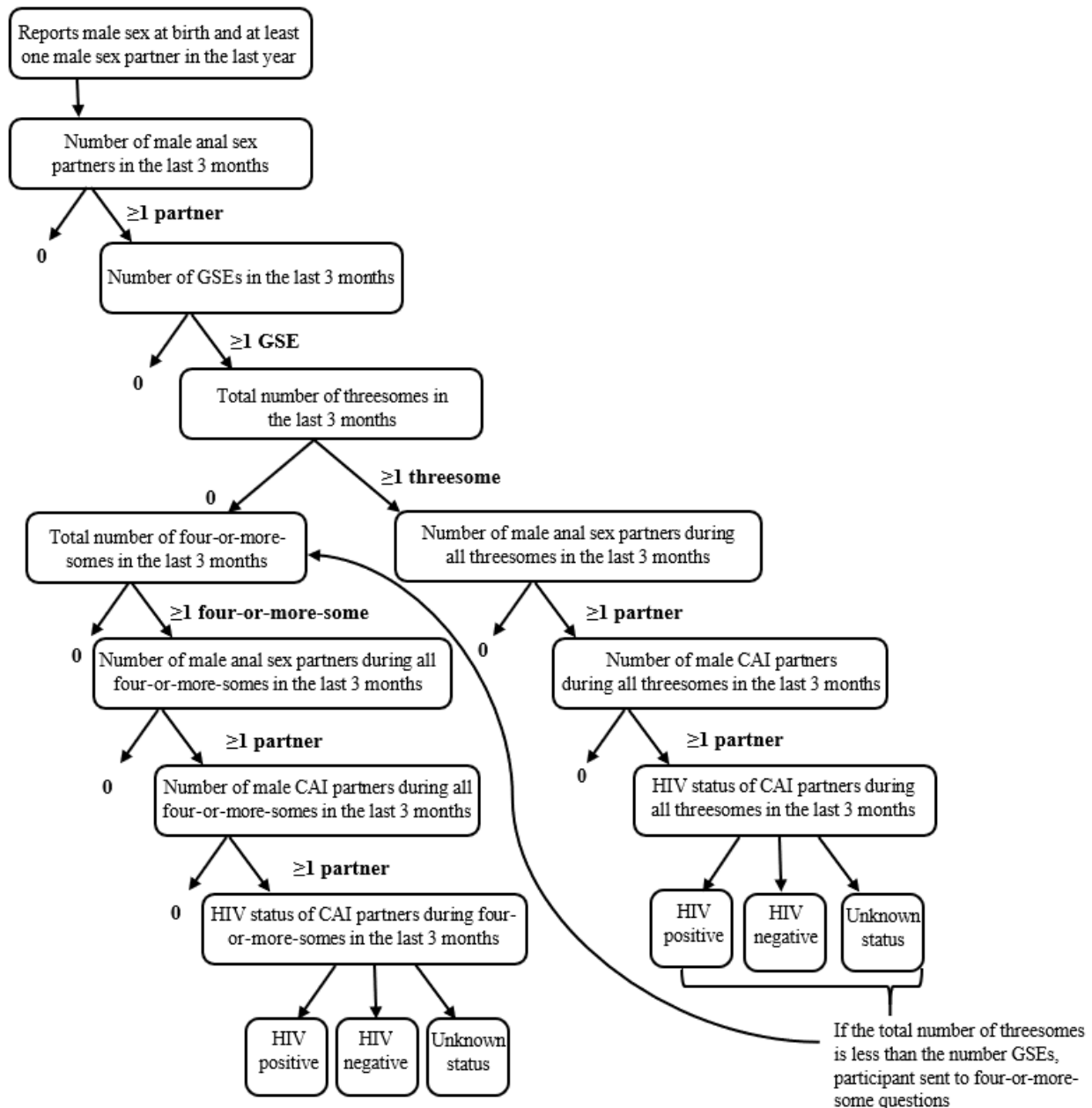
Aggregate Group Sex Questions

Depending on responses to previous questions and preprogrammed skip patterns, participants were asked between 1 and 76 questions about involvement in threesomes and four-or-more-somes in the previous 3 months (Multimedia Appendix 1).

Figure 1 illustrates the flow of the aggregate group sex questions. Participants who reported having ≥ 1 GSEs in the past 3 months were asked to report the number of threesomes during that time (Figure 1). Participants who reported at least 1 threesome were asked about the total number of anal sex partners across all threesomes; total number of partners with whom they had condomless anal intercourse (CAI) across all threesomes; and distribution of CAI partners who were HIV-positive, HIV-negative, or whose HIV status was unknown. Participants were then asked the same series of questions about four-or-more-somes if the number of reported threesomes was less than the number of total reported GSEs. If a participant refused to provide an answer to a question, they were skipped to the next appropriate question. Participants were not able to select "don't know" as an answer option to any of the aggregate GSE questions.

Consistency checks were programed within the aggregate threesome and four-or-more-some questions to ensure data accuracy. The total number of threesomes plus four-or-more-somes could not be greater than the total number of reported GSEs. Participants were not able to report more anal sex partners or CAI partners within GSEs than the total number of anal or CAI partners they had reported earlier in the survey. The number of CAI partners in threesomes plus four-or-more-somes could not exceed the number of anal sex partners reported across all GSEs. Finally, the sum of HIV-positive, HIV-negative, and unknown status CAI partners in GSEs was required to equal the total number of CAI partners reported in GSEs. From these data, the overall percentage of MSM reporting anal sex in the past 3 months who also reported participating in group sex can be estimated. Several other measures, such as the percentage of all male sex partners who were group sex partners as well as subgroups (eg, men who reported group sex but only threesomes) can also be calculated.

Figure 1. Questions and skip patterns for aggregate group sex questions. CAI: condomless anal intercourse; GSE: group sex event.



Partner-Level Group Sex Questions

Partner-level data were collected to describe up to 3 of the participants’ most recent anal sex partners (partners A-C) during the past 3 months. Participants were asked a series of questions about their relationship and sexual behaviors with partners A to C. Questions included partner demographics, when and how the participant met the partner, the self-defined nature of their relationship (eg, “is/was partner A-C someone that you feel or felt committed to?”), partner STD history, HIV status disclosure, partner HIV status and ART or PrEP use, number of sexual encounters with that partner in the past 3 months, and the dates of first and most recent anal sex encounters with the partner (Multimedia Appendix 1). We also asked about concurrency between partners A to C (ie, sexual relationships with different partners in the same period) and whether the participant knew if partners A to C had sex with each other in the same time

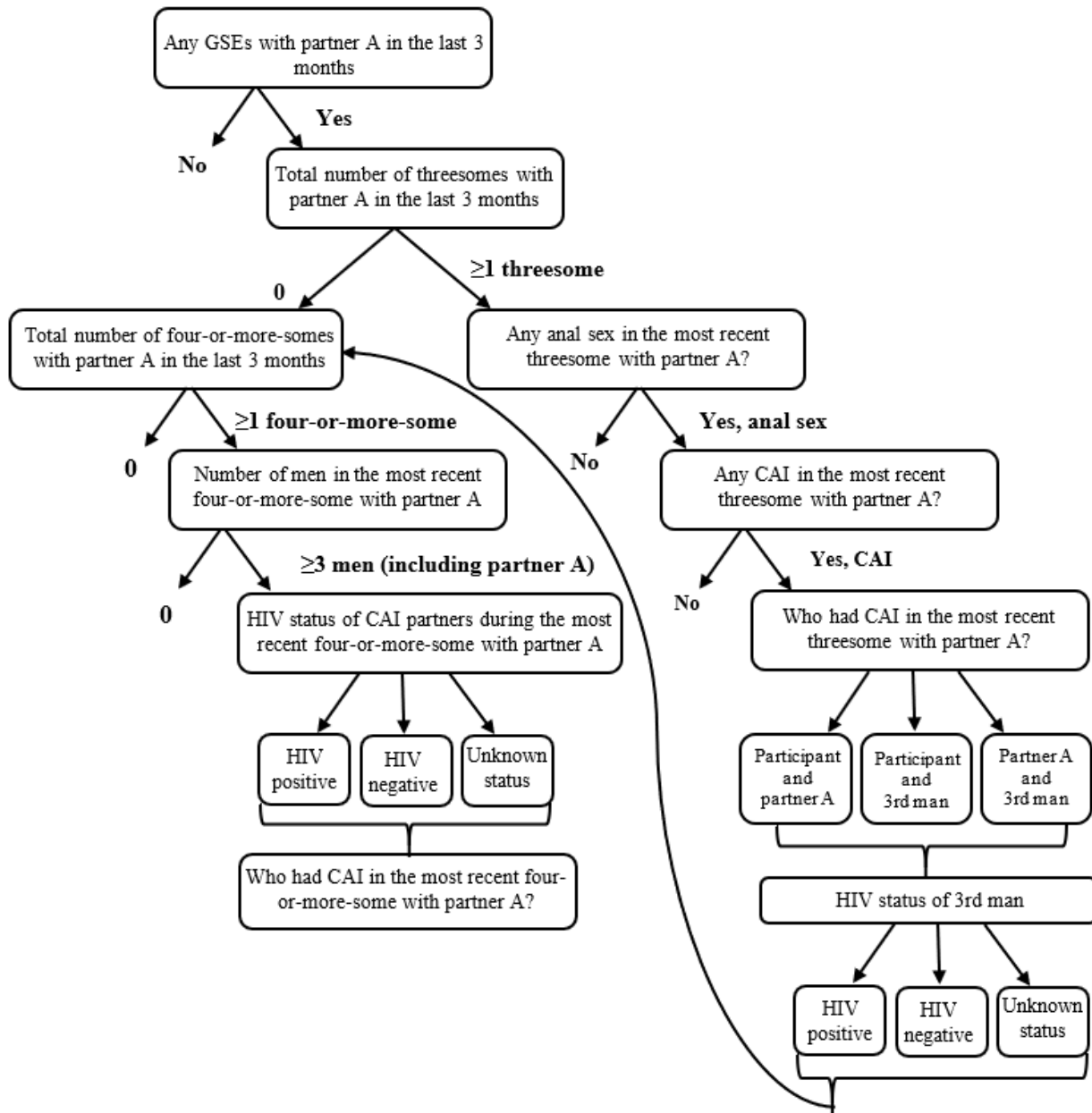
frame that they were having sex with the participant, also referred to in network modeling literature as a nondirected transitive triad or a known triangle [27]. Those who reported ≥3 anal sex partners in the past 3 months were also asked aggregate questions to describe those additional partners, including the nature of their relationship, whether they engaged in CAI in the past 3 months, and the HIV status of partners with whom they had CAI.

If the participant reported anal sex with any of partners A to C, they were asked if they had any threesomes or four-or-more-somes in the last 3 months that involved that partner. If so, they were asked to provide additional details about the most recent GSE involving that partner (Figure 2). Participants were asked about the number of threesomes that involved the partner, whether any anal sex and CAI occurred (between any participants of the threesome) in the most recent threesome involving the partner, who had CAI within the most

recent threesome, and the HIV status of the third man in the most recent threesome with the partner. Participants were then asked the number of four-or-more-somes in the past 3 months involving the partner. If participants reported at least 1

four-or-more-some with any of partners A to C, they were asked about the number of men in the most recent four-or-more-some with that partner.

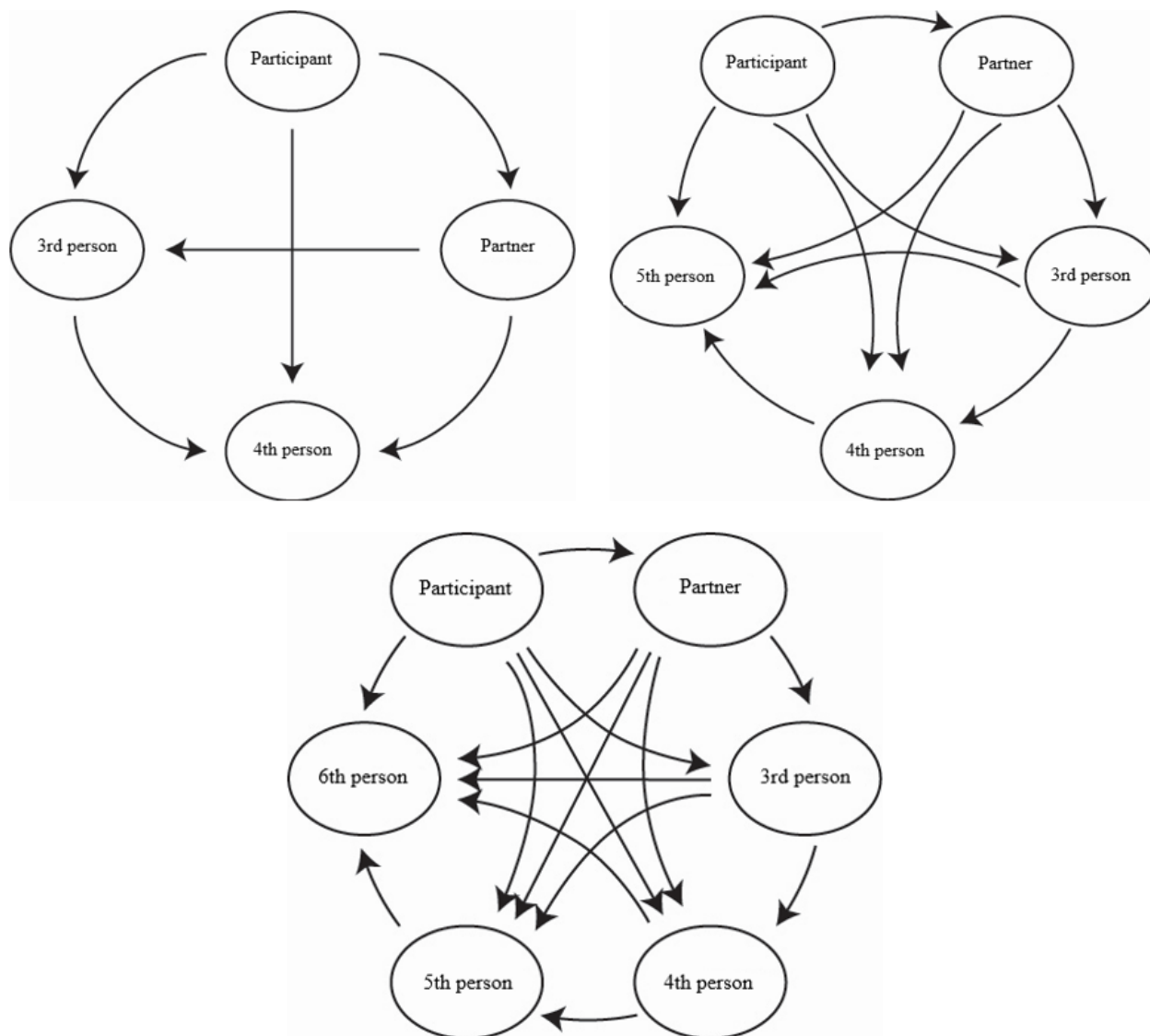
Figure 2. Questions and skip patterns for partner-specific group sex questions. CAI: condomless anal intercourse; GSE: group sex event.



Although we asked for the HIV status of all men in the participant’s most recent four-or-more-some, questions about condom use between each set of partners were limited to 4 people (partner A plus 3 additional people in the GSE) to minimize participant burden. Figure 3 demonstrates the rapidly increasing numbers of possible partner combinations with each additional partner in the GSE. For example, a threesome includes 3 potential partner-pair interactions, whereas a six-some includes 15 (Figure 3). Due to programming limitations within the survey software, we were unable to include a table or figure to simultaneously display possible partner combinations for the

participant, which might have been more intuitive for some participants to complete. Therefore, each question was programmed as an individual screen containing 1 question about condom use during the most recent event between 2 individuals (Multimedia Appendix 1). Participants were able to select “don’t know” when asked about the HIV status of partners, including the third person in their most recent threesome with partners A to C. Selecting “don’t know” was also allowed when asked about CAI between sets of partners that did not include the participant during the most recent four-or-more-some.

Figure 3. Increasing complexity of partner-partner interactions with increasing size of group sex events.



We programmed consistency checks within the partner-level GSE questions. For participants reporting sex with any named partners A to C and at least 1 other man in the same encounter, responses should have reflected at least 1 threesome or four-or-more-some with that partner; if not, the survey would return to the overall GSE question for that specific named partner to reconcile this inconsistency. The number of partners in any reported four-or-more-some was required to be 3 or more. In addition, the sum of HIV-positive, HIV-negative, and unknown status partners in the most recent four-or-more-some with any of the named partners A to C was checked to ensure that it was equal to the total number of individual participants reported in the GSE.

Data Accuracy and Consistency Between Aggregate and Partner-Level Group Sex Questions

Owing to concern for participant burden, there were no programmed consistency checks for accuracy between subtotals of GSEs reported in the aggregate and in the partner-specific sections. Participants may, therefore, report a different aggregate total of threesomes or four-or-more-somes when compared with the reported number of threesomes or four-or-more-somes

involving partners A to C. This could include reporting no GSE participation in the aggregate questions and then reporting GSE activity with any partners A to C. If we had included such consistency checks and an inconsistency occurred between the aggregate and partner-specific questions, participants would have been directed back to the aggregate questions to check their previous responses. This would have required returning to questions much earlier in the survey and reanswering multiple questions, potentially including all 3 sets of partner-specific questions. For the purpose of the descriptive analysis and comparison of participation in GSEs by visit (described below), any reported GSE activity in either the aggregate or the partner-specific question sets by a participant was identified as GSE participation. Discrepancies between the aggregate and partner-level responses were also explored during analysis.

Statistical Analysis

We first aimed to determine the acceptability and feasibility of the group sex questions by assessing participants' willingness to respond to them, survey fatigue and added burden related to these questions, and the consistency of participants' responses within and across study visits. We calculated the overall

proportion of refusals in the aggregate and partner-specific GSE question sets and compared refusal proportions for questions about partner A against questions about partner C to assess completeness of data collection and to determine if there was survey fatigue with more question exposure for participants.

We also compared the length of time required to complete the survey based on the start and end times. We compared the distribution of total time to complete the survey for those with 2 to 3 anal sex partners and those with ≥ 4 partners, as participants who reported ≥ 4 anal sex partners received up to 20 additional questions about their relationship with those partners. We then stratified by whether or not the participant reported aggregate or partner-specific group sex to assess how much time the different group sex questions added to the overall survey duration.

To assess consistency of responses within a single survey, we examined discrepancies between GSE participation reported in the aggregate and partner-specific questions of the survey and calculated frequencies of GSE reports for each question set. We also created a composite measure of group sex participation that combined any GSE report in either the aggregate or partner-specific question set and then used the composite to report the frequency of group sex participation in the sample.

To assess consistent reporting of GSEs among participants who enrolled in the study more than once, we used a person-specific medical record number to identify repeat enrollments and compared reported GSEs across all visits for each individual person.

After assessing these data quality and survey-taking measures, we summarized the additional information about network density gleaned from the group sex questions, compared with asking only aggregate or partner-specific questions about one-on-one partnerships. We calculated 4 measures of network density of partners with whom the participant reported CAI: (1) mean degree, that is, number of CAI partners in the past 3 months; (2) the percentage of participants reporting partner concurrency, that is, relationships with 2 different men in which the participant reported having CAI with both men in the same 3-month period; (3) known triangles, that is, the percentage of named partners A to C with whom the participant reported both having CAI and knowing that the 2 partners had CAI with each other; and (4) additional and otherwise hidden triangles and higher-order partner overlap, that is, the percentage of participants who did not report that named partners A to C had sex with each other in the past 3 months but did report that they had a GSE with the partner in which both the participant and that partner had CAI with at least 1 additional man.

In this last measure, we used questions about the most recent GSE to quantify occurrence of CAI with up to 3 additional partners besides the participant and the named partner A to C, which would not have been observed without the addition of the partner-specific group sex questions.

We compared these 4 measures among MSM with at least 2 total partners (meaning they could have engaged in group sex) and at least 1 anal sex partner in the previous 3 months (which was the subset of participants who were asked the GSE and partner-specific survey questions), stratified by whether or not they reported a GSE. We used Wilcoxon rank sum test to compare means and chi-square tests to compare percentages. All analyses were conducted using SAS version 9.4 (SAS Institute Inc).

Results

From September 2015 to September 2017, there were 1260 study visits in Project DETECT. Of the 833 HIV-negative study participants, 163 repeat participants (163/833, 19.6%) had a median of 2 (interquartile range [IQR] 2-3; range 2-7) study visits. Behavioral surveys were completed by 854 individual participants at 1104 visits. Behavioral surveys were missing for 154 individual participants across 156 study visits. Among study visits with a completed survey, male sex at birth was reported during 1071 (1071/1104, 97.01%) visits, and of those, 1038 (1038/1071, 96.92%) visits were among participants who identified as male gender. Of these 1038 visits, participants reported at least 1 male anal sex partner in the past 3 months (MSM) and were, therefore, asked at least 1 of the GSE questions at 841 (841/1038, 81.02%) visits with 690 individual people.

Table 1 shows GSE participation as reported through the aggregate and/or partner-specific GSE questions. In 293 (293/841, 34.8%) visits, participants reported a GSE of any type in the previous 3 months; at least 1 threesome or four-or-more-some in the past 3 months was reported in 270 (270/841, 32.1%) and 137 (137/841, 16.3%) visits, respectively (categories not mutually exclusive). For each reported GSE activity, we found that some participants did not report GSE participation in the aggregate question set but did report at least 1 GSE event with partner(s) A, B, and/or C (Table 1). Notably, 76 of 137 (55.5%) four-or-more-somes were reported by MSM in the partner-specific question set but were not reported in the aggregate. In addition to whether or not any GSEs were reported, there were also discrepancies in the number of threesomes and four-or-more-somes; for all types of GSEs, there were instances where participants reported a higher number of events in the partner-specific section when compared with their response in the aggregate (data not shown).

Table 1. Comparison of reported group sex event participation in aggregate and partner-specific group sex event questions among men who have sex with men (N=841).

| Type of GSE ^a | Reported in either aggregate or partner-specific questions or both, n (%) | Reported in both aggregate questions and partner-specific questions, n (%) | Reported in aggregate questions but not partner-specific questions, n (%) | Reported in partner-specific questions but not aggregate questions, n (%) |
|----------------------------|---|--|---|---|
| Reported GSE(s) | 293 (34.8) | 191 (22.7) | 82 (9.8) | 20 (2.4) |
| Reported threesome | 270 (32.1) | 168 (20.0) | 81 (9.6) | 21 (2.5) |
| Reported four-or-more-some | 137 (16.3) | 29 (3.4) | 32 (3.8) | 76 (9.0) |

^aGSE: group sex event.

Among the 841 visits with MSM where GSE questions were asked, 261 visits were with 110 individual people who enrolled in the study multiple times. Approximately half of the 110 repeat participants reported no GSEs at any of their study visits, whereas 20 of 110 (18.2%) reported GSEs at every visit where they were asked the questions. The remaining 37 repeat participants (37/110, 33.6%) reported GSEs at 1 or more, but not all, of their study visits.

The proportions of refusals to aggregate-level GSE questions ranged from 0% (0/273) to 10.6% (15/141), with a median of 2.6% (Table 2), and to partner-level questions stratified by partner ranged from 0% (0/143) to 22% (5/23), with a median of 3.0% (data not shown). The proportion of refusals to questions about partner C was higher when compared with that about partner A (data not shown).

Table 2. Refusal rates of aggregate group sex event questions.

| Aggregate GSE ^a question | Was asked question (n) | Refused to answer question (n) | Proportion refused (%) |
|---|------------------------|--------------------------------|------------------------|
| Number of times participant had a GSE | 841 | 9 | 1.1 |
| Number of times participant had a threesome | 273 | 0 | 0 |
| Number of men participant had anal sex with during all threesomes | 249 | 4 | 1.6 |
| Number of men participant had CAI ^b with during all threesomes | 211 | 1 | 0.5 |
| Number of CAI partners during threesomes whose HIV status was unknown | 169 | 10 | 5.9 |
| Number of CAI partners during threesomes who were HIV-positive | 169 | 13 | 7.7 |
| Number of CAI partners during threesomes who were HIV-negative | 169 | 13 | 7.7 |
| Number of times participant had a four-or-more-some | 141 | 15 | 10.6 |
| Number of men participant had anal sex with during all four-or-more-somes | 61 | 0 | 0 |
| Number of men participant had CAI with during all four-or-more-somes | 54 | 0 | 0 |
| Number of CAI partners during four-or-more-somes whose HIV status was unknown | 39 | 1 | 3 |
| Number of CAI partners during four-or-more-somes who were HIV-positive | 39 | 3 | 8 |
| Number of CAI partners during four-or-more-somes who were HIV-negative | 39 | 3 | 8 |

^aGSE: group sex event.

^bCAI: condomless anal intercourse.

The time required to complete the survey increased with both overall partner number and the number of partners with whom the participant reported group sex (Table 3). For participants reporting 2 to 3 total anal sex partners, the survey took a median of 18 minutes if they did not report group sex or only reported group sex in the aggregate questions. Participants asked the additional partner-specific group sex questions took 1 to 2 additional minutes per partner to complete the survey. Those

with ≥ 4 partners were asked an additional set of questions about the characteristics of those partners; on average, this group took an additional 3 minutes regardless of group sex participation. Those with ≥ 4 partners who reported partner-specific GSEs with all 3 of partners A to C took between 8 to 10 additional minutes to complete the version of the survey with all the additional partner-specific survey questions.





Table 3. Time required to complete the Project Diagnostic Evaluation To Expand Critical Testing Technologies (DETECT) behavioral survey, stratified by total number of anal sex partners and the number of partners with whom the participant reported participating in group sex in the previous 3 months.

| Reporting of group sex in aggregate and partner-specific questions | Reported 2-3 anal sex partners | | Reported ≥ 4 anal sex partners | |
|---|--------------------------------|----------------------|-------------------------------------|----------------------|
| | n | Median (IQR) minutes | n | Median (IQR) minutes |
| No group sex reported in the aggregate and no partner-specific group sex reported | 233 | 18 (14-22) | 122 | 21 (17-27) |
| Group sex reported in the aggregate but no partner-specific group sex reported | 20 | 18 (14-26) | 55 | 20 (17-28) |
| Group sex reported in the aggregate, partner-specific group sex with 1 partner | 46 | 20 (16-35) | 63 | 24 (20-31) |
| Group sex reported in the aggregate, partner-specific group sex with 2 partners | 22 | 21 (19-27) | 44 | 26 (20-36) |
| Group sex reported in the aggregate, partner-specific group sex with 3 partners | 4 | 21 (19-25) | 20 | 28 (23-33) |

Table 4 subsets the sample further by limiting to MSM who reported at least 2 male sex partners, the number of persons needed for a GSE to occur. Data in **Table 4** illustrates both the types of network density data collected through the partner-specific and aggregate group sex questions and how these questions impact information available about the structure of MSM sexual networks for those who do and do not report group sex. Men who reported participating in group sex reported a higher mean number of CAI partners in the past 3 months than those with at least 2 partners who did not report group sex participation (4.1 vs 2.0; $P < .001$). Although men who reported

group sex had a similar likelihood of any concurrent partnerships compared with participants who did not report GSEs (27.0% vs 23.4%; $P = .28$), they were much more likely to report that named partners also had sex with each other (a triangle) compared with participants who did not report any GSEs (26.0% vs 5.9%; $P < .001$). The aggregate questions that asked who had anal sex with whom during the most recent group sex encounter found that 14.2% of participants who did not report that partners A to C had sex with each other did report a group sex encounter where the participant and 1 of these named partners had CAI with at least 1 additional man.

Table 4. Comparison of measures of network density for persons reporting ≥ 2 sex partners and at least 1 anal sex partner by self-reported group sex event participation in the previous 3 months.

| Measures of network density | ≥ 1 group sex event reported (n=289) | No group sex event reported (n=410) | Examples |
|---|---|-------------------------------------|---|
| Mean number of condomless anal intercourse (CAI) partners | 4.1 | 2.0 |  |
| Proportion of participants reporting concurrency between anal sex partners, % | 27.0 | 23.4 |  |
| Proportion of participants who reported that ≥ 1 of named partners A-C had sex with each other (triangles), % | 26.0 | 5.9 |  |
| Proportion of participants who reported that named partners A-C did not have sex with each other but the participant, a partner, and ≥ 1 other person had CAI during the most recent GSE (triangles and higher-order CAI partner overlap), % | 14.2 | Not applicable |  |

Discussion

Principal Findings

In the context of Project DETECT, we developed and tested aggregate and partner-level questions about recent GSE participation among MSM. The questions allowed for effective analysis of nuanced information about overall and partner-specific GSEs. We found that a GSE of some type in the past 3 months was reported in 293 (34.8%) visits with MSM that we surveyed—a finding that is consistent with what has been previously reported in the literature [6,7,10,13,20,28,29].

Owing to discrepancies in reporting GSE participation between the aggregate and the partner-specific question sets, we created a composite measure of the 2 responses to form a more complete estimation of GSE participation in this population. The largest discrepancy between questions was in reporting four-or-more-somes; 9% of MSM responding to these questions reported in the aggregate questions that they did not participate in a four-or-more-some but then later reported at least 1 four-or-more-some with at least 1 of their named partners A to C in the partner-specific section. This demonstrates the importance of asking about GSEs in multiple ways, including

in the context of specific partners, to increase the likelihood of recall or question completion. Asking only aggregate GSE questions or partner-specific questions in our sample would have led to underreporting and resulted in missed opportunities for further assessing the role that simultaneous partnerships play in HIV transmission. Studies among MSM have also illustrated the importance of partner- or event-level data in addition to aggregate measures, specifically in the context of CAI [30-33] and substance use [34,35].

Overall, the majority of participants answered the GSE questions completely; the proportion of answer refusals ranged from 0% to 10.6% in the aggregate questions and from 0% to 21.7% in the partner-specific questions. Refusal rates for some of the partner-specific questions were somewhat higher than those for the aggregate questions, which could be because of survey fatigue, sensitivity of the questions asked, or that participants were not able to report specific details about their partners' behaviors in larger GSEs. Within the partner-specific questions, refusal rates for questions about partner C were higher than those about partner A. It is possible that the partner that participants labeled partner A may be the one they knew most about, were closest to, or had sex with most recently. With this bias, it is not surprising that the refusal rates for questions about partner C are higher than the refusal rates for partner A, although survey fatigue may have also contributed to this difference.

Compared with participants who reported no group sex in either the aggregate or the partner-specific questions, exposure to the aggregate GSE questions did not increase the mean time it took to complete the survey. Those who were also asked the partner-specific questions took an additional 2 to 4 minutes, on average, to complete the survey. Despite the longer survey duration, both sets of group sex questions provided novel information about the density of MSM sexual networks. This extra time spent is relatively minor compared with the overall average survey duration (19 minutes), and these questions are critical to understand the association between GSEs and HIV and STD acquisition as well as to parameterize network models that are being used to estimate the impact of different interventions on HIV epidemics [14,15,22,36].

Approximately one-fifth of the HIV-negative participants re-enrolled in our study and had multiple research visits over the course of the period that we evaluated. Of the 110 repeat participants who answered the group sex questions at multiple study visits, 36.4% reported GSEs at some, but not all, of their study visits, indicating that person-level changes did exist. This illustrates the importance of using data from all visits in future analyses, as restricting to 1 visit per person would have resulted in an underestimate of GSE participation among this sample of MSM.

The implementation of these questions allows us to identify novel information about the density of the sexual networks of MSM. Traditional behavioral surveys have described the number and percentage of all partners that are CAI partners. Only recently have surveys also tried to describe the overlap of partnerships and the duration of partnerships of different types. To our knowledge, this is the first survey that has asked about detailed partner-level interactions, enabling an understanding

of the risk-taking behaviors between partners within a GSE and increasing our knowledge of network density. We found that similar amounts of concurrency were reported by those with multiple anal sex partners who did and did not report participation in GSEs. Perhaps not surprisingly, we were also able to document that those who engaged in group sex were much more likely to report knowing that 2 of their recent named sex partners had also had sex with each other. However, our novel partner-specific questions about the most recent group sex encounter found a subset of those who engaged in group sex reported having CAI with several of the men in the encounter. This sharing of sexual partners has been shown to lead to dense subpopulations within the overall sexual network that enhance and sustain the possibility of transmission of STDs. The details of this sexual partner overlap would not have been captured without the additional partner-specific questions specifically about group sex.

Limitations

There are limitations to this study that should be considered. Results from our study participants in Seattle, Washington, may not be representative of all MSM or of other geographic areas where HIV testing, care for people living with HIV, PrEP, and other services may be less accessible or available. Owing to these differences, it is possible that our participants may be more likely to have GSEs or may have been more willing than others outside of Seattle to report on sensitive information. The majority of participants in this sample were recruited for study participation while seeking HIV testing at a local STD clinic, which means this sample may have different levels of recent HIV risk than MSM recruited from other venues. In addition, these group sex questions were not cognitively tested or validated among this population before study enrollment, which might have impacted the proportion of survey questions that were refused by participants. Anecdotally, no study participants asked clarifying questions to the study research staff, and most of the participants completed the group sex section of the survey.

Our survey asked questions about GSEs only to persons who reported being born male and who had at least 1 male anal sex partner in the past 3 months, and our analysis sample restricted further to only participants who identified as a man at the time of the survey. Participants who identify as something other than a man, MSM who report only oral sex, transgender and genderqueer individuals who do not report male sex at birth, and individuals who report nonmale partners are eligible for Project DETECT, but were not asked the group sex questions. In addition, we asked participants about *male* partners in GSEs but did not specify that partners within GSEs had to be cisgender men, which might have led to misclassification of partners included in the most recent event.

Participants also may have experienced GSEs with transgender, genderqueer, or female partners, but those events were not captured by the current version of our questions. Little research has been done on transgender and genderqueer individuals in the context of group sex, but like cisgender MSM, they are at higher risk for HIV acquisition. A 2017 meta-analysis by Baral et al [37] found an estimated pooled HIV prevalence of 21.7% in transgender women in the United States. Though prevalence

estimates in transgender men are lower, the current scope of research is limited [38]. Future surveys assessing group sex participation at the aggregate and partner-specific levels should include these groups in research, as conflating MSM with other genders may not fully address the differences in HIV risk [39].

While assessing these survey questions, we saw that participants did engage in GSEs where no anal sex was reported. In this version of the survey, we only asked about GSEs if the participant reported anal sex in the previous 3 months, thereby missing potentially important information about partner interactions and networks that might include only oral sex.

The partner-specific question set was limited to the 3 most recent male anal sex partners. Although we did collect some information on additional anal sex partners after the 3 most recent, we did not collect the same level of detail (Multimedia Appendix 1). As four-or-more-somes can include those additional partners, collecting more detailed data can add to our knowledge about network density and concurrency.

Finally, because of concern for survey length, the partner-specific questions detail only the most recent threesome and four-or-more-some. A participant's most recent GSE may not be consistent with other GSEs in the previous 3 months in which they have participated, particularly in this sample of men presenting to an STD clinic seeking an HIV test. However, research among MSM and other populations shows moderate agreement between reports of behaviors at last sex and period-level prevalence questions, indicating that last sex can serve as a valid proxy of behaviors over a period [40,41]. Although collecting detailed information about all GSE participation in the previous 3 months could be beneficial in helping to understand potential HIV and STD transmission, researchers must consider balancing this detail with participant burden and potential recall issues.

Future Research

The paper describing the analysis of the impact of group sex participation on both STD and HIV acquisition in Project DETECT will be forthcoming. This study has prompted additional related research and modifications to our original protocol. We asked 1 of the GSE questions of the venue-based sample of MSM recruited for NHBS in Seattle in 2017, as well as the 2018 AMIS survey, to field these questions in other populations than the one described here. We believe that our

findings illustrate potential for these questions to be incorporated in other national surveys and should be piloted, and ultimately validated, in different geographic regions and with different populations.

Since collecting these data, the Project DETECT behavioral survey has been updated to address some of the limitations described above. As stated above, the survey now collects aggregate GSE information from MSM who report only oral sex in the previous 3 months. This revision will enable us to collect data from MSM who may have only oral sex but be involved in GSEs where CAI is occurring between other partners.

A Spanish language version of the survey has also been created for Project DETECT to include those who can read and write in Spanish but not English (Multimedia Appendix 2). This population is important to include in HIV studies, as HIV diagnoses among Hispanic/Latino MSM increased 13% nationally between 2011 and 2015, and, in King County, where our survey was administered, Latino MSM are 39% more likely than white MSM to have an HIV diagnosis in their lifetime [42,43]. Studies that utilize surveys similar to ours could incorporate our questions to assess responses in additional sites and populations.

Using a survey software that has the ability to include tables or pictorial representations could aid in the ability to collect more accurate and detailed quantitative information about GSEs and interactions that involve multiple simultaneous partnerships. In addition, performing qualitative interviews could help us better understand STD and HIV risk in the context of GSEs, which would improve future survey instruments.

Conclusions

It is crucial to have appropriate tools to measure and understand GSEs, a sensitive but important topic for the sexual health of MSM. Our study demonstrated that although no one set of questions performed perfectly, implementing a survey with both aggregate and partner-level questions could provide a detailed picture of GSE participation and the density of sexual networks. The questions seemed to be acceptable, skip patterns and consistency checks were effective, and survey fatigue was minimal. More research is needed on this subject, and our survey represents a promising data collection tool to help fill the gaps in our knowledge.

Acknowledgments

The authors would like to thank the participants of Project DETECT; the PHSKC STD Clinic staff; Carmita Signes, Lori Saunders, and Susan Scheck from the QDS Technical Support team at Nova Research Company; Justin Smith for reviewing the GSE questions during survey development; the University of Washington/Fred Hutch Center for AIDS Research (CFAR) [National Institutes of Health P30 AI027757]; University of Washington AIDS Clinical Trials Unit; and Madison Clinic at Harborview Medical Center. Project DETECT was funded by the CDC (contract 200-2014-61285). The findings and conclusions in this protocol are those of the authors and do not necessarily represent the official position of the CDC.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Project Diagnostic Evaluation To Expand Critical Testing Technologies behavioral survey including group sex questions (English). [[PDF File \(Adobe PDF File\), 12596 KB - resprot_v8i11e15426_app1.pdf](#)]

Multimedia Appendix 2

Project Diagnostic Evaluation To Expand Critical Testing Technologies behavioral survey including group sex questions (Spanish). [[PDF File \(Adobe PDF File\), 33128 KB - resprot_v8i11e15426_app2.pdf](#)]

References

1. Grov C, Rendina HJ, Ventuneac A, Parsons JT. HIV risk in group sexual encounters: an event-level analysis from a national online survey of MSM in the U.S. *J Sex Med* 2013 Sep;10(9):2285-2294 [[FREE Full text](#)] [doi: [10.1111/jsm.12227](https://doi.org/10.1111/jsm.12227)] [Medline: [23809410](https://pubmed.ncbi.nlm.nih.gov/23809410/)]
2. Gama A, Abecasis A, Pingarilho M, Mendão L, Martins MO, Barros H, et al. Cruising venues as a context for HIV risky behavior among men who have sex with men. *Arch Sex Behav* 2017 May;46(4):1061-1068. [doi: [10.1007/s10508-016-0707-5](https://doi.org/10.1007/s10508-016-0707-5)] [Medline: [26987977](https://pubmed.ncbi.nlm.nih.gov/26987977/)]
3. Mimiaga MJ, Reisner SL, Bland SE, Driscoll MA, Cranston K, Isenberg D, et al. Sex parties among urban MSM: an emerging culture and HIV risk environment. *AIDS Behav* 2011 Feb;15(2):305-318. [doi: [10.1007/s10461-010-9809-6](https://doi.org/10.1007/s10461-010-9809-6)] [Medline: [20838870](https://pubmed.ncbi.nlm.nih.gov/20838870/)]
4. Friedman SR, Mateu-Gelabert P, Sandoval M. Group sex events amongst non-gay drug users: an understudied risk environment. *Int J Drug Policy* 2011 Jan;22(1):1-8 [[FREE Full text](#)] [doi: [10.1016/j.drugpo.2010.06.004](https://doi.org/10.1016/j.drugpo.2010.06.004)] [Medline: [20800465](https://pubmed.ncbi.nlm.nih.gov/20800465/)]
5. Meunier E. No attitude, no standing around: the organization of social and sexual interaction at a gay male private sex party in New York city. *Arch Sex Behav* 2014 May;43(4):685-695. [doi: [10.1007/s10508-013-0182-1](https://doi.org/10.1007/s10508-013-0182-1)] [Medline: [23979786](https://pubmed.ncbi.nlm.nih.gov/23979786/)]
6. Goedel WC, Duncan DT. Correlates of engagement in group sex events among men who have sex with men in London who use geosocial-networking smartphone applications. *Int J STD AIDS* 2018 Mar;29(3):244-250. [doi: [10.1177/0956462417722478](https://doi.org/10.1177/0956462417722478)] [Medline: [28764613](https://pubmed.ncbi.nlm.nih.gov/28764613/)]
7. Phillips G, Magnus M, Kuo I, Rawls A, Peterson J, West-Ojo T, et al. Correlates of group sex among a community-based sample of men who have sex with men (MSM) in Washington, DC. *AIDS Behav* 2014 Aug;18(8):1413-1419. [doi: [10.1007/s10461-013-0527-8](https://doi.org/10.1007/s10461-013-0527-8)] [Medline: [23700223](https://pubmed.ncbi.nlm.nih.gov/23700223/)]
8. Prestage G, Down I, Grulich A, Zablotska I. Sex partying among gay men in Sydney, Melbourne and Brisbane, Australia. *AIDS Behav* 2011 Feb;15(2):298-304. [doi: [10.1007/s10461-010-9824-7](https://doi.org/10.1007/s10461-010-9824-7)] [Medline: [20945156](https://pubmed.ncbi.nlm.nih.gov/20945156/)]
9. Kuhns LM, Hottom AL, Schneider J, Garofalo R, Fujimoto K. Use of Pre-exposure Prophylaxis (PrEP) in young men who have sex with men is associated with race, sexual risk behavior and peer network size. *AIDS Behav* 2017 May;21(5):1376-1382 [[FREE Full text](#)] [doi: [10.1007/s10461-017-1739-0](https://doi.org/10.1007/s10461-017-1739-0)] [Medline: [28238119](https://pubmed.ncbi.nlm.nih.gov/28238119/)]
10. Rice CE, Lynch CD, Norris AH, Davis JA, Fields KS, Ervin M, et al. Group sex and prevalent sexually transmitted infections among men who have sex with men. *Arch Sex Behav* 2016 Aug;45(6):1411-1419. [doi: [10.1007/s10508-015-0554-9](https://doi.org/10.1007/s10508-015-0554-9)] [Medline: [26392187](https://pubmed.ncbi.nlm.nih.gov/26392187/)]
11. Tang W, Tang S, Qin Y, Zhang Y, Zhang W, Liu C, et al. Will gay sex-seeking mobile phone applications facilitate group sex? A cross-sectional online survey among men who have sex with men in China. *PLoS One* 2016;11(11):e0167238 [[FREE Full text](#)] [doi: [10.1371/journal.pone.0167238](https://doi.org/10.1371/journal.pone.0167238)] [Medline: [27880823](https://pubmed.ncbi.nlm.nih.gov/27880823/)]
12. Phillips G, Magnus M, Kuo I, Rawls A, Peterson J, Jia Y, et al. Use of geosocial networking (GSN) mobile phone applications to find men for sex by men who have sex with men (MSM) in Washington, DC. *AIDS Behav* 2014 Sep;18(9):1630-1637. [doi: [10.1007/s10461-014-0760-9](https://doi.org/10.1007/s10461-014-0760-9)] [Medline: [24682866](https://pubmed.ncbi.nlm.nih.gov/24682866/)]
13. Friedman SR, Bolyard M, Khan M, Maslow C, Sandoval M, Mateu-Gelabert P, et al. Group sex events and HIV/STI risk in an urban network. *J Acquir Immune Defic Syndr* 2008 Dec 1;49(4):440-446 [[FREE Full text](#)] [doi: [10.1097/qai.0b013e3181893f31](https://doi.org/10.1097/qai.0b013e3181893f31)] [Medline: [19186355](https://pubmed.ncbi.nlm.nih.gov/19186355/)]
14. Morris M, Goodreau S, Moody J. Sexual networks, concurrency, STD/HIV. In: Holmes K, Sparling P, Stamm W, Piot P, Wasserheit J, Corey L, et al, editors. *Sexually Transmitted Diseases*. Fourth Edition. New York, NY: McGraw-Hill Medical; 2008:109-126.
15. Morris M, Kretzschmar M. Concurrent partnerships and transmission dynamics in networks. *Soc Netw* 1995 Jul;17(3-4):299-318. [doi: [10.1016/0378-8733\(95\)00268-S](https://doi.org/10.1016/0378-8733(95)00268-S)]
16. Rich AJ, Lachowsky NJ, Cui Z, Sereda P, Lal A, Moore DM, et al. Event-level analysis of anal sex roles and sex drug use among gay and bisexual men in Vancouver, British Columbia, Canada. *Arch Sex Behav* 2016 Aug;45(6):1443-1451 [[FREE Full text](#)] [doi: [10.1007/s10508-015-0607-0](https://doi.org/10.1007/s10508-015-0607-0)] [Medline: [26525571](https://pubmed.ncbi.nlm.nih.gov/26525571/)]
17. Rice CE, Maierhofer C, Fields KS, Ervin M, Lanza ST, Turner AN. Beyond anal sex: sexual practices of men who have sex with men and associations with HIV and other sexually transmitted infections. *J Sex Med* 2016 Mar;13(3):374-382 [[FREE Full text](#)] [doi: [10.1016/j.jsxm.2016.01.001](https://doi.org/10.1016/j.jsxm.2016.01.001)] [Medline: [26853044](https://pubmed.ncbi.nlm.nih.gov/26853044/)]

18. Sewell J, Miltz A, Lampe FC, Cambiano V, Speakman A, Phillips AN, Attitudes to Understanding of Risk of Acquisition of HIV (AURAH) Study Group. Poly drug use, chemsex drug use, and associations with sexual risk behaviour in HIV-negative men who have sex with men attending sexual health clinics. *Int J Drug Policy* 2017 May;43:33-43. [doi: [10.1016/j.drugpo.2017.01.001](https://doi.org/10.1016/j.drugpo.2017.01.001)] [Medline: [28189979](https://pubmed.ncbi.nlm.nih.gov/28189979/)]
19. Scheidell JD, Friedman SR, Golin C, Wohl DA, Khan MR. Group sex event participation: a link to STI risk among African-American heterosexual men incarcerated in North Carolina. *Sex Transm Infect* 2017 Mar;93(2):144 [FREE Full text] [doi: [10.1136/sextrans-2016-052980](https://doi.org/10.1136/sextrans-2016-052980)] [Medline: [28213578](https://pubmed.ncbi.nlm.nih.gov/28213578/)]
20. van den Boom W, Davidovich U, Heuker J, Lambers F, Prins M, Sandfort T, et al. Is group sex a higher-risk setting for HIV and other sexually transmitted infections compared with dyadic sex among men who have sex with men? *Sex Transm Dis* 2016 Feb;43(2):99-104 [FREE Full text] [doi: [10.1097/OLQ.0000000000000389](https://doi.org/10.1097/OLQ.0000000000000389)] [Medline: [26766526](https://pubmed.ncbi.nlm.nih.gov/26766526/)]
21. Bérubé A. The history of gay bathhouses. *J Homosex* 2003;44(3-4):33-53. [doi: [10.1300/j082v44n03_03](https://doi.org/10.1300/j082v44n03_03)]
22. Périsse AR, Langenberg P, Hungerford L, Boulay M, Charurat M, Schechter M, et al. Egocentric network data provide additional information for characterizing an individual's HIV risk profile. *AIDS* 2010 Jan 16;24(2):291-298 [FREE Full text] [doi: [10.1097/QAD.0b013e328333eb81](https://doi.org/10.1097/QAD.0b013e328333eb81)] [Medline: [19904198](https://pubmed.ncbi.nlm.nih.gov/19904198/)]
23. Delaney K. Participation in group sex and associated STD risk among MSM presenting at the Seattle/King County STD clinic. 2018 Presented at: STD Prevention Conference; August 27-30, 2018; Washington, DC.
24. Delaney K, Violette L, Ure G, Cornelius-Hudson A, Niemann L, Wesolowski L, et al. Time From HIV Infection to Earliest Detection for 4 FDA-Approved Point-of-Care Tests. In: Proceedings of the Conference on Retroviruses and Opportunistic Infections. 2018 Presented at: CROI'18; March 4-7, 2018; Boston, Massachusetts.
25. Sanchez TH, Sineath RC, Kahle EM, Tregear SJ, Sullivan PS. The annual American men's internet survey of behaviors of men who have sex with men in the United States: protocol and key indicators report 2013. *JMIR Public Health Surveill* 2015;1(1):e3 [FREE Full text] [doi: [10.2196/publichealth.4314](https://doi.org/10.2196/publichealth.4314)] [Medline: [27227126](https://pubmed.ncbi.nlm.nih.gov/27227126/)]
26. Centers for Disease Control and Prevention. HIV Infection Risk, Prevention, and Testing Behaviors among Men Who Have Sex with Men National HIV Behavioral Surveillance 20 U.S. Cities, 2014 URL: <https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-hssr-nhbs-msm-2014.pdf> [accessed 2018-11-15]
27. Exponential Random Graph Models (ERGMs) using statnet. statnet URL: <http://statnet.csde.washington.edu/index.shtml> [accessed 2019-05-03] [WebCite Cache ID 78642CcBy]
28. Hirshfield S, Schrimshaw EW, Stall RD, Margolis AD, Downing MJ, Chiasson MA. Drug use, sexual risk, and syndemic production among men who have sex with men who engage in group sexual encounters. *Am J Public Health* 2015 Sep;105(9):1849-1858. [doi: [10.2105/AJPH.2014.302346](https://doi.org/10.2105/AJPH.2014.302346)] [Medline: [25713951](https://pubmed.ncbi.nlm.nih.gov/25713951/)]
29. Phillips G, Grov C, Mustanski B. Engagement in group sex among geosocial networking mobile application-using men who have sex with men. *Sex Health* 2015 Nov;12(6):495-500 [FREE Full text] [doi: [10.1071/SH15108](https://doi.org/10.1071/SH15108)] [Medline: [26255156](https://pubmed.ncbi.nlm.nih.gov/26255156/)]
30. Card KG, Lachowsky NJ, Cui Z, Shurgold S, Armstrong HL, Rich AJ, et al. An event-level analysis of the interpersonal factors associated with condomless anal sex among gay, bisexual, and other men who have sex with men (MSM) with online-met partners. *AIDS Educ Prev* 2017 Apr;29(2):154-174 [FREE Full text] [doi: [10.1521/aeap.2017.29.2.154](https://doi.org/10.1521/aeap.2017.29.2.154)] [Medline: [28467159](https://pubmed.ncbi.nlm.nih.gov/28467159/)]
31. Pines HA, Gorbach PM, Weiss RE, Reback CJ, Landovitz RJ, Mutchler MG, et al. Individual-level, partnership-level, and sexual event-level predictors of condom use during receptive anal intercourse among HIV-negative men who have sex with men in Los Angeles. *AIDS Behav* 2016 Jun;20(6):1315-1326 [FREE Full text] [doi: [10.1007/s10461-015-1218-4](https://doi.org/10.1007/s10461-015-1218-4)] [Medline: [26471884](https://pubmed.ncbi.nlm.nih.gov/26471884/)]
32. Down I, Ellard J, Triffitt K, Zablotska I, Hurley M, Brown G, et al. High-risk sexual behaviours among gay and bisexual men: comparing event-level casual sex encounters among seroconverters and non-seroconverters. *Sex Transm Infect* 2017 Aug;93(5):327-331. [doi: [10.1136/sextrans-2016-052749](https://doi.org/10.1136/sextrans-2016-052749)] [Medline: [28325770](https://pubmed.ncbi.nlm.nih.gov/28325770/)]
33. Yang C, Latkin C, Tobin K, Seal D, Koblin B, Chander G, et al. An event-level analysis of condomless anal intercourse with a HIV-discordant or HIV status-unknown partner among black men who have sex with men from a multi-site study. *AIDS Behav* 2018 Jul;22(7):2224-2234 [FREE Full text] [doi: [10.1007/s10461-018-2161-y](https://doi.org/10.1007/s10461-018-2161-y)] [Medline: [29779160](https://pubmed.ncbi.nlm.nih.gov/29779160/)]
34. Rendina HJ, Moody RL, Ventuneac A, Grov C, Parsons JT. Aggregate and event-level associations between substance use and sexual behavior among gay and bisexual men: Comparing retrospective and prospective data. *Drug Alcohol Depend* 2015 Sep 1;154:199-207 [FREE Full text] [doi: [10.1016/j.drugalcdep.2015.06.045](https://doi.org/10.1016/j.drugalcdep.2015.06.045)] [Medline: [26190557](https://pubmed.ncbi.nlm.nih.gov/26190557/)]
35. Vosburgh HW, Mansergh G, Sullivan PS, Purcell DW. A review of the literature on event-level substance use and sexual risk behavior among men who have sex with men. *AIDS Behav* 2012 Aug;16(6):1394-1410. [doi: [10.1007/s10461-011-0131-8](https://doi.org/10.1007/s10461-011-0131-8)] [Medline: [22323004](https://pubmed.ncbi.nlm.nih.gov/22323004/)]
36. Felsher M, Koku E. Explaining HIV risk multiplexity: a social network analysis. *AIDS Behav* 2018 Nov;22(11):3500-3507. [doi: [10.1007/s10461-018-2120-7](https://doi.org/10.1007/s10461-018-2120-7)] [Medline: [29680933](https://pubmed.ncbi.nlm.nih.gov/29680933/)]
37. Baral SD, Poteat T, Strömdahl S, Wirtz AL, Guadamuz TE, Beyrer C. Worldwide burden of HIV in transgender women: a systematic review and meta-analysis. *Lancet Infect Dis* 2013 Mar;13(3):214-222. [doi: [10.1016/S1473-3099\(12\)70315-8](https://doi.org/10.1016/S1473-3099(12)70315-8)] [Medline: [23260128](https://pubmed.ncbi.nlm.nih.gov/23260128/)]

38. Becasen JS, Denard CL, Mullins MM, Higa DH, Sipe TA. Estimating the prevalence of HIV and sexual behaviors among the US transgender population: a systematic review and meta-analysis, 2006–2017. *Am J Public Health* 2019 Jan;109(1):e1-e8. [doi: [10.2105/ajph.2018.304727](https://doi.org/10.2105/ajph.2018.304727)]
39. Poteat T, German D, Flynn C. The conflation of gender and sex: gaps and opportunities in HIV data among transgender women and MSM. *Glob Public Health* 2016;11(7-8):835-848 [FREE Full text] [doi: [10.1080/17441692.2015.1134615](https://doi.org/10.1080/17441692.2015.1134615)] [Medline: [26785751](https://pubmed.ncbi.nlm.nih.gov/26785751/)]
40. Younge SN, Salazar LF, Crosby RF, DiClemente RJ, Wingood GM, Rose E. Condom use at last sex as a proxy for other measures of condom use: is it good enough? *Adolescence* 2008;43(172):927-931 [FREE Full text] [Medline: [19149154](https://pubmed.ncbi.nlm.nih.gov/19149154/)]
41. Lachowsky NJ, Card KG, Cui Z, Sereda P, Roth EA, Hogg RS, et al. Agreement between gay, bisexual and other men who have sex with men's period prevalence and event-level recall of sexual behaviour: an observational respondent-driven sampling study. *Sex Health* 2019 Feb;16(1):84-87. [doi: [10.1071/SH17223](https://doi.org/10.1071/SH17223)] [Medline: [30566851](https://pubmed.ncbi.nlm.nih.gov/30566851/)]
42. Centers for Disease Control and Prevention. 2018. HIV and Hispanics/Latinos URL: <https://www.cdc.gov/hiv/group/raciaethnic/hispaniclatinos/index.html> [accessed 2018-12-27] [WebCite Cache ID 750gCixVp]
43. King County, Washington. 2016 HIV/AIDS Epidemiology Report URL: <https://www.kingcounty.gov/~media/depts/health/communicable-diseases/documents/hivstd/2016-hiv-aids-epidemiology-annual-report.ashx> [accessed 2017-05-24]

Abbreviations

AMIS: American Men's Internet Survey
ART: antiretroviral treatment
CAI: condomless anal intercourse
CASI: computer-assisted self-interview
CDC: Centers for Disease Control and Prevention
DETECT: Diagnostic Evaluation To Expand Critical Testing Technologies
GSE: group sex event
IQR: interquartile range
MSM: men who have sex with men
NHBS: National HIV Behavioral Surveillance
PHSKC: Public Health Seattle-King County
PrEP: pre-exposure prophylaxis
QDS: questionnaire development system
STD: sexually transmitted disease

Edited by G Eysenbach; submitted 09.07.19; peer-reviewed by G Phillips, R Mpofu, S Facente; comments to author 14.08.19; revised version received 09.09.19; accepted 10.09.19; published 27.11.19.

Please cite as:

Violette LR, Niemann LA, McMahan VM, Katz DA, Chavez PR, Clark HA, Cornelius-Hudson A, Ethridge SF, McDougal SJ, Ure II G, Stekler JD, Delaney KP

Group Sex Events Among Cisgender Men Who Have Sex With Men: Cross-Sectional and Longitudinal Survey Study to Explore Participation and Risk-Taking Behaviors

JMIR Res Protoc 2019;8(11):e15426

URL: <https://www.researchprotocols.org/2019/11/e15426>

doi:[10.2196/15426](https://doi.org/10.2196/15426)

PMID:[31774403](https://pubmed.ncbi.nlm.nih.gov/31774403/)

©Lauren R Violette, Lisa A Niemann, Vanessa M McMahan, David A Katz, Pollyanna R Chavez, Hollie A Clark, Andy Cornelius-Hudson, Steven F Ethridge, Sarah J McDougal, George Ure II, Joanne D Stekler, Kevin P Delaney. Originally published in *JMIR Research Protocols* (<http://www.researchprotocols.org>), 27.11.2019. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work, first published in *JMIR Research Protocols*, is properly cited. The complete bibliographic information, a link to the original publication on <http://www.researchprotocols.org>, as well as this copyright and license information must be included.

Publisher:
JMIR Publications
130 Queens Quay East.
Toronto, ON, M5A 3Y5
Phone: (+1) 416-583-2040
Email: support@jmir.org

<https://www.jmirpublications.com/>