JMIR Research Protocols

Impact Factor (2022): 1.7
Volume 6 (2017), Issue 7 ISSN 1929-0748 Editor in Chief: Xiaomeng (Simone) Ma, PhDc, MS, BS

Contents

Protocols

An Intervention Using Gamification to Increase Human Immunodeficiency Virus and Sexually Transmitted Infection Screening Among Young Men Who Have Sex With Men in California: Rationale and Design of Stick To It (e140)
Christopher Mejia, Daniel Acland, Raluca Buzdugan, Reva Grimball, Lauren Natoli, Mark McGrath, Jeffrey Klausner, Sandra McCoy. 3

Development of a Tailored HIV Prevention Intervention for Single Young Men Who Have Sex With Men Who Meet Partners Online: Protocol for the myDEx Project (e141)
Jose Bauermeister, Ryan Tingler, Michele Demers, Gary Harper. 16

Comparing Mobile Health Strategies to Improve Medication Adherence for Veterans With Coronary Heart Disease (Mobile4Meds): Protocol for a Mixed-Methods Study (e134)
Linda Park, Eileen Collins, Janet Shim, Mary Whooley. 28

Randomized Trial Comparing the Electronic Composite Psychosocial Screener YouthCHAT With a Clinician-Interview Assessment for Young People: A Study Protocol (e135)
Hiran Thabrew, Arden Corter, Felicity Goodyear-Smith, Mary Goldfinch. 41

Effectiveness of Adaptive E-Learning Environments on Knowledge, Competence, and Behavior in Health Professionals and Students: Protocol for a Systematic Review and Meta-Analysis (e128)
Guillaume Fontaine, Sylvie Cossette, Marc-André Maheu-Cadotte, Tanya Mailhot, Marie-France Deschênes, Gabrielle Mathieu-Dupuis. 49

Sharing Annotated Audio Recordings of Clinic Visits With Patients—Development of the Open Recording Automated Logging System (ORALS): Study Protocol (e121)
Paul Barr, Michelle Dannenberg, Craig Ganoe, William Haslett, Rebecca Faill, Saeed Hassanpour, Amar Das, Roger Arend, Meredith Masel, Sheryl Piper, Haley Reicher, James Ryan, Glyn Elwyn. 59

Brazilian Samba Protocol for Individuals With Parkinson's Disease: A Clinical Non-Randomized Study (e129)
Ana Tillmann, Alexandro Andrade, Alessandra Swarowsky, Adriana Guimarães. 113

Treatment of Peritoneal Dissemination in Stomach Cancer Patients With Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy (HIPEC): Rationale and Design of the PERISCOPE Study (e136)
Rosa van der Kaaij, Hidde Braam, Henk Boot, Maartje Los, Annemieke Cats, Cecile Grootscholten, Jan Schellens, Arend Aalbers, Alwin Huitema, Catherijne Knibbe, Djamila Boerma, Marinus Wiezer, Bert van Ramshorst, Johanna van Sandick. 121

Data Preparation for West Nile Virus Agent-Based Modelling: Protocol for Processing Bird Population Estimates and Incorporating ArcMap in AnyLogic (e138)
Hamid Nasrinpour, Alexander Reimer, Marcia Friesen, Robert McLeod. . . . 130

Cross-Sectional Study of Chronic Obstructive Pulmonary Disease Prevalence Among Smokers, Ex-Smokers, and Never-Smokers in Almaty, Kazakhstan: Study Protocol (e143)
Almaz Sharman, Baurzhan Zhussupov, Dana Sharman, Assel Stambekova, Sattar Yeraliyev. . . . 148

Proposal

Natural Compounds for the Treatment of Psoriatic Arthritis: A Proposal Based on Multi-Targeted Osteoclastic Regulation and on a Preclinical Study (e132)
Shiqiang Deng, Jianwen Cheng, Jinmin Zhao, Felix Yao, Jiake Xu. . . . 73

Original Papers

Integrated Care in Prostate Cancer (ICARE-P): Nonrandomized Controlled Feasibility Study of Online Holistic Needs Assessment, Linking the Patient and the Health Care Team (e147)
Veronica Nanton, Rebecca Appleton, Jeremy Dale, Julia Roscoe, Thomas Hamborg, Sam Ahmedzai, Theodoros Arvanitis, Douglas Badger, Nicholas James, Richard Mendelsohn, Omar Khan, Deepak Parashar, Prashant Patel. . . . 82

Apps for Health-Related Education in Pharmacy Practice: Needs Assessment Survey Among Patients Within a Large Metropolitan Area (e133)
Sean Mirk, Nicole Wegrzyn. . . . 93

MotivATE: A Pretreatment Web-Based Program to Improve Attendance at UK Outpatient Services Among Adults With Eating Disorders (e146)
Sarah Muir, Ciarán Newell, Jess Griffiths, Kathy Walker, Holly Hooper, Sarah Thomas, Peter Thomas, Jon Arcelus, James Day, Katherine Appleton. . . . 102

Protocol

An Intervention Using Gamification to Increase Human Immunodeficiency Virus and Sexually Transmitted Infection Screening Among Young Men Who Have Sex With Men in California: Rationale and Design of Stick To It

Christopher M Mejia[1], MS; Daniel Acland[2], PhD; Raluca Buzdugan[3], PhD; Reva Grimball[3], MPH; Lauren Natoli[1], BA; Mark R McGrath[1], MPH; Jeffrey D Klausner[4,5], MD, MPH; Sandra I McCoy[3], PhD, MPH

[1]Public Health Division, AIDS Healthcare Foundation, Los Angeles, CA, United States
[2]Goldman School of Public Policy, University of California, Berkeley, CA, United States
[3]School of Public Health, University of California, Berkeley, CA, United States
[4]David Geffen School of Medicine, University of California, Los Angeles, CA, United States
[5]Fielding School of Public Health, University of California, Los Angeles, CA, United States

Corresponding Author:
Sandra I McCoy, PhD, MPH
School of Public Health
University of California
779 University Hall
MS #7360
Berkeley, CA, 94720-7360
United States
Phone: 1 510 642 0513
Email: smccoy@berkeley.edu

Abstract

Background: In the United States, young men who have sex with men (YMSM) remain disproportionately affected by human immunodeficiency virus (HIV) and other sexually transmitted infections (STIs). Although routine HIV/STI screening is pivotal to the timely diagnosis of HIV and STIs, initiation of appropriate treatment, and reduced onward disease transmission, repeat screening is underused. Novel interventions that incorporate elements of games, an approach known as gamification, have the potential to increase routinization of HIV/STI screening among YMSM.

Objective: The study aims to test the hypothesis that an incentive-based intervention that incorporates elements of gamification can increase routine HIV/STI screening among YMSM in California.

Methods: The study consists of a formative research phase to develop the intervention and an implementation phase where the intervention is piloted in a controlled research setting. In the formative research phase, we use an iterative development process to design the intervention, including gathering information about the feasibility, acceptability, and expected effectiveness of potential game elements (eg, points, leaderboards, rewards). These activities include staff interviews, focus group discussions with members of the target population, and team meetings to strategize and develop the intervention. The final intervention is called Stick To It and consists of 3 components: (1) online enrollment, (2) Web-based activities consisting primarily of quizzes and a countdown "timer" to facilitate screening reminders, and (3) in-person activities that occur at 2 sexual health clinics. Participants earn points through the Web-based activities that are then redeemed for chances to win various prizes during clinic visits. The pilot study is a quasi-experimental study with a minimum of 60 intervention group participants recruited at the clinics, at community-based events, and online. We will compare outcomes in the intervention group with a historical control group consisting of individuals meeting the inclusion criteria who attended study clinics in the 12 months prior to intervention implementation. Eligible participants in the pilot study (1) are 18 to 26 years old, (2) were born or identify as male, 3) report male sexual partners, and 4) have a zip code of residence within defined areas in the vicinity of 1 of the 2 implementation sites. The primary outcome is repeat HIV/STI screening within 6 months.

Results: This is an ongoing research study with initial results expected in the fourth quarter of 2017.

Conclusions: We will develop and pilot test a gamification intervention to encourage YMSM to be regularly screened for HIV/STIs. The results from this research will provide preliminary evidence about the potential effectiveness of using gamification to amplify health-related behavioral change interventions. Further, the research aims to determine the processes that are essential to developing and implementing future health-related gamification interventions.

Trial Registration: Clinicaltrials.gov NCT02946164; https://clinicaltrials.gov/ct2/show/NCT02946164 (Archived by WebCite at http://www.webcitation.org/6ri3G4HwD)

(JMIR Res Protoc 2017;6(7):e140) doi:10.2196/resprot.8064

KEYWORDS

gamification; men who have sex with men; young men who have sex with men; HIV screening; STI screening; self-determination theory; game design; game elements; incentives; intrinsic motivation; homosexuality, male; human immunodeficiency virus; sexually transmitted diseases

Introduction

New and innovative strategies for human immunodeficiency virus (HIV) infection prevention are urgently needed to increase the uptake of health services among men who have sex with men (MSM). A growing body of evidence suggests that, under the right circumstances, financial incentives can increase the demand for HIV screening, change short-term sexual behavior, enhance linkage to care after HIV diagnosis, and promote adherence to antiretroviral therapy [1-11]. Several studies have demonstrated that incorporating elements of games into incentive-based programs—an approach known as gamification—can be more effective and cost effective than simple financial incentives alone [12-14]. Ongoing and completed studies in the United States and elsewhere, including several targeting MSM, have demonstrated the feasibility and acceptability of gamification for improving engagement in HIV infection prevention and care [15-20].

We hypothesize that gamification for HIV and sexually transmitted infection (STI) prevention may work well to reengage and motivate a new generation of MSM in a cost-effective and sustainable way. A focus on young men who have sex with men (YMSM) is particularly warranted because this population remains disproportionally affected by HIV infection. Although HIV diagnoses among gay and bisexual men have stabilized in recent years, YMSM continue to experience the greatest burden of HIV compared with any other group in the United States, with young men 13 to 24 years of age accounting for 27% of new diagnoses among all gay and bisexual men [21]. Additionally, MSM are at increased risk for STIs [22]. In 2015, 59.6% of all primary and secondary syphilis diagnosis were among MSM [22]. Rectal chlamydia and gonorrhea are also common among MSM and are associated with increased HIV acquisition [23-25]. Moreover, a growing body of evidence suggests that the Internet and social media are effective ways to share sexual health information with MSM, and YMSM in particular [26-33]. To our knowledge, at least two gamification interventions for diverse YMSM in the United States are underway or have been completed, including an intervention to reduce sexual risk behaviors (healthMpowerment) [15,16] and a mobile phone-based intervention to improve antiretroviral therapy adherence (Epic Allies) [17].

To test the potential of gamification for HIV/STI prevention, our 2-year study developed and will pilot Stick To It, an HIV/STI prevention intervention for YMSM (18-26 years of age) that incorporates elements of gamification. The objective of the intervention is to increase repeat HIV/STI screening, defined as screening at least every 3 months. HIV/STI screening is critical both as the gateway to HIV/STI treatment, which can lead to reduced onward transmission, and as a critical first step to access prevention strategies such as preexposure prophylaxis [34]. This paper describes the methodology and protocol of our study.

Methods

The study consists of 2 distinct phases. The first phase is the formative research phase, in which we used focus groups, structured interviews, and rapid prototyping of intervention elements to determine the most effective and appropriate design for the intervention. The second phase consists of the implementation of the intervention in a controlled research design. First, we present the methodology of the formative phase and the insights gained from the different elements therein, leading to the final design of the intervention. Second, we present the protocol for the implementation phase.

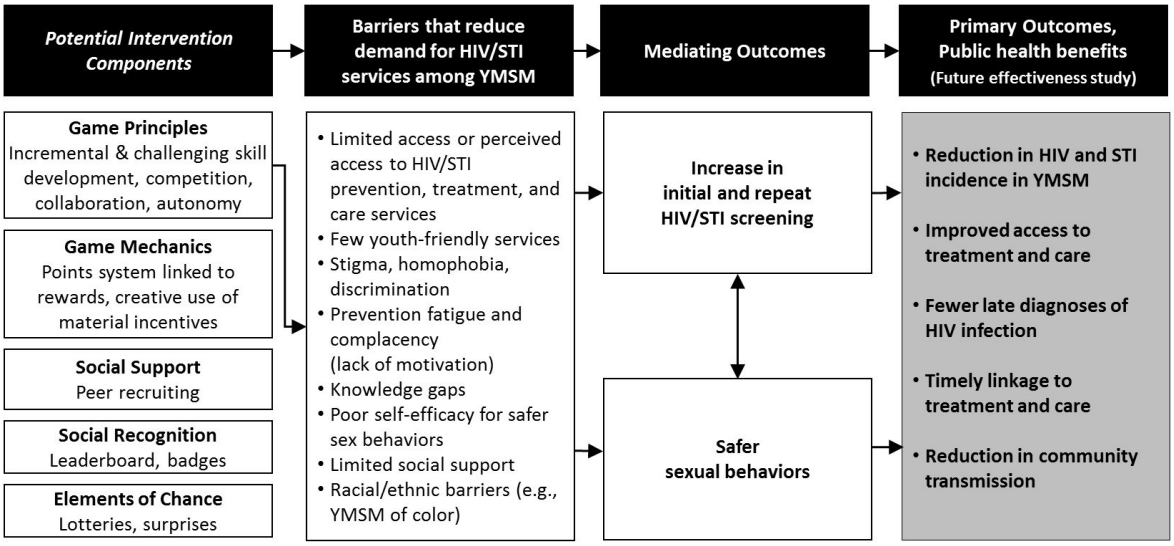
Phase 1: Formative Intervention Design

Our intervention was implemented at 2 sexual health clinics, 1 in northern California (Oakland), and 1 in southern California (Hollywood). Phase 1 formative research took place at the 2 clinics and at meeting locations on a university campus from November 2015 to July 2016. Our goal in phase 1 was to design Stick To It, an intervention incorporating gamification intended to motivate increased repeat HIV/STI screening among YMSM. Gamification, “the use of game design elements in non-game contexts,” [35] is hypothesized to amplify the motivational power of financial and nonfinancial incentives. It is informed by self-determination theory, which posits that external rewards can be internalized and generate lasting *intrinsic motivation* (defined as engaging in activities “because of the positive feelings resulting from the activities themselves”) if they are experienced in a context that satisfies three basic psychological needs: *autonomy*, *competence*, and *relatedness* [36]. Gamification scholars have argued that games and gamification can create such a context [36,37]. At the beginning of phase 1, we selected the key game elements that we intended to use in

the intervention. These included a defined theme and a number of core "game mechanics," basic mechanisms that define how the gamification intervention works. The game theme is a concept that serves to synchronize all components of the game and is critical to maximizing participant engagement [38]. Figure 1 outlines how potential gamification interventions may facilitate improved health outcomes among YMSM.

Because the formative phase of gamification design involves an iterative process of gathering information about the effectiveness of game elements and refining the intervention, we simultaneously present both the design of the formative phase of our study and the results generated by each stage of the formative research.

Figure 1. Theory of change for how a potential gamification intervention may facilitate improved health outcomes among young men who have sex with men (YMSM). HIV: human immunodeficiency virus; STI: sexually transmitted infection.



Formative Phase Methods and Results

The phase 1 research activities consisted of 4 components: (1) 10 strategy and development meetings of the entire project team, consisting of the research team, clinic staff, and a gamification consultant from the private sector; (2) 4 in-depth interviews with clinic staff about the clinic and its population; (3) 11 focus groups with 29 members of the target population (YMSM, 18-26 years of age); and (4) a series of weekly meetings of a smaller design team, consisting of 3 members of the research team and 1 of the site coordinators.

Strategy and Development Meetings

We held 10 meetings of the entire project team. Participants were the research team, including the project manager, the 2 site-specific project coordinators, the regional coordinators and research director of the implementation partner, and the gamification consultant. At the initial meetings, the emphasis was on broad game design-related issues such as the theme and aesthetics of the intervention design. Subsequent meetings consisted of extensive discussion of the game elements to be included, such as how to use points; whether to use a leaderboard; the frequency of participant interaction with the intervention; how much interaction between participants to include, if any; when or if to incorporate prizes; and how to use chance elements to determine prizes or other outcomes. Over time, these discussions were increasingly informed by the focus group findings. An important goal of these discussions was to integrate (1) extensive testing of game elements among the target population to determine the most suitable, engaging, and effective intervention design, as this is the cornerstone of gamification [38]; (2) knowledge of gamification and game design principles; (3) the research team's expertise on established public health behavior change strategies, such as reminders, incentives, and education; and (4) clinic staff's expertise on patient experience, clinic management, and overall feasibility, including the logistical realities and constrains of the participating clinics.

Staff Interviews

We conducted structured in-depth interviews with 4 staff members from both implementation sites. Interviewees were purposely selected to include testing counselors and clinic managers. The primary purpose of the interviews was to assess the kinds of game elements that would be feasible, appropriate, and best suited to increase engagement between clinic visits based on staff knowledge of the institutional setting and target population. The primary game elements discussed were theme and core game mechanics. The potential core game mechanics that we initially considered were (1) games of chance (eg, dice or spin wheels, gumball machines) and a system of points awarded for achievement of tasks and goals within the intervention, (2) prizes awarded based on accumulated points and outcomes of the chance elements, and (3) leaderboards that display the relative ranking of participants' points or accomplishments and are used to create an element of competition. We used the insights gained from the staff interviews to develop the set of potential themes, core mechanics, and game elements presented at the initial focus groups. We also asked staff members to briefly pilot the games of chance in the clinic and report their perspectives about the feasibility and acceptability of each approach.

Focus Groups

After staff interviews, we conducted an initial set of 4 focus groups with the target population in both implementation areas. These discussions followed a standard structured format designed to elicit detailed information about preferences and characteristics, with particular focus on use of smartphones and Internet technology, as well as experiences with different types of games. Special emphasis was placed on issues of concern to race and ethnic minorities and the lesbian, gay, bisexual, transgender, questioning community. In addition, we tested the themes and game mechanics that emerged from the staff interviews with focus group participants to determine those that would be most appropriate and effective.

We conducted 7 additional focus groups, which focused more narrowly on the specific game elements of the intervention and followed a progression of increasing detail and specificity of game elements as the design and content of the intervention evolved. This stage of the formative research was intended to implement the iterative game design testing process, an important component of game testing [38]. In these focus groups, we presented mock-ups of specific game elements, in the sequence in which they would be encountered by participants in the intervention, and elicited input on each of the elements and their interaction in the overall intervention design. An additional procedure was to present multiple versions of a particular game element and elicit rankings of the alternatives in terms of potential engagement and effectiveness. While we emphasized the effectiveness of game elements and their potential for participant engagement, we also prioritized issues of sensitivity and appropriateness for the target population during focus group discussions. Namely, we aimed to ensure that the proposed game mechanics and messaging were nonstigmatizing, meaningful, and relevant to the target population. Focus group facilitators used structured focus group guides but encouraged a flexible conversation based on participant input during the sessions to facilitate friendly and open communication that allowed participants to be honest about their experiences with sexual health screenings and game design. Participant input on novel designs of specific game elements or the intervention as a whole was also encouraged.

Among the 11 focus groups held, a total of 29 participants attended, with between 2 and 9 participants per group session. The mean age of participants was 24 years old. The self-identified race/ethnicity of focus group participants was as follows: American Indian/Alaskan native: 1 (3%); Asian/Pacific Islander: 3 (10%); black/African American: 4 (14%); Hispanic/Latino: 10 (34%); white: 9 (31%); mixed or other race/ethnicity: 2 (7%).

Table 1 summarizes the key results of the focus groups: the game elements that were discussed, the main insights gained with respect to each element, and the decisions that were made about each element in the iterative design process.

Table 1. Focus group results: key insights and decisions about game elements to be used in the Stick To It intervention for young men who have sex with men (YMSM) in California, 2015-2016.

Game element	Key insights from focus group discussions	Design decisions for Stick To It
Theme	Prefer contemporary to retro themes. Prefer fun, lighthearted themes to highly sexualized themes. Prefer simplicity in design.	Base theme on experiences and interests of YMSM. Use bright colors, whimsical humor, and fun content.
Reminders to screen at self-scheduled time	Reminders need to be fun and rewarding. Prefer text messages (SMS[a]) over email and social media-based reminders. Frequency matters.	Send communications via SMS. Link to a fun online activity for points. Decrease communication intervals from 3 weeks to 1 week between screenings. Incorporate a "countdown timer" to remind participants when next quarterly screening is due.
Web-based activities to accompany reminders and earn points	Prefer polls and quizzes to games. Activities should not be competitive. Interest was expressed in useful information about sexual health with a fun or whimsical approach. Time is limited, so online activities should be designed to be completed in a short period of time, such as waiting in line, commuting to work or school.	Use multiple-choice quizzes, with points for answering questions, and additional points for correct answers. Limit questions to 5 per quiz. Mix informational with fun and whimsical activities. Make questions short and to the point.
Chance element for awarding prizes for screening	Guarantee participants always win at least a small prize as a means to deflect from the anxiety and stress associated with screening encounters. Prefer a combination of high-probability small prizes and low-probability large prizes. Participants need to believe the chance mechanism isn't rigged.	Use gumball machine at the clinic as a game of chance. More points lead to more gumballs. Base prizes on color combinations of gumballs. Award small prizes for common combinations and large prizes for rare combinations.

[a]SMS: short message service.

Design Team Meetings

The smaller design team held a series of weekly meetings. The design team iteratively redesigned components of the intervention on the basis of the results of the other formative research components. Each meeting of the design team generated a revised set of game elements, which were then taken into the subsequent focus groups and strategy and development meetings for consideration.

Final Intervention Design

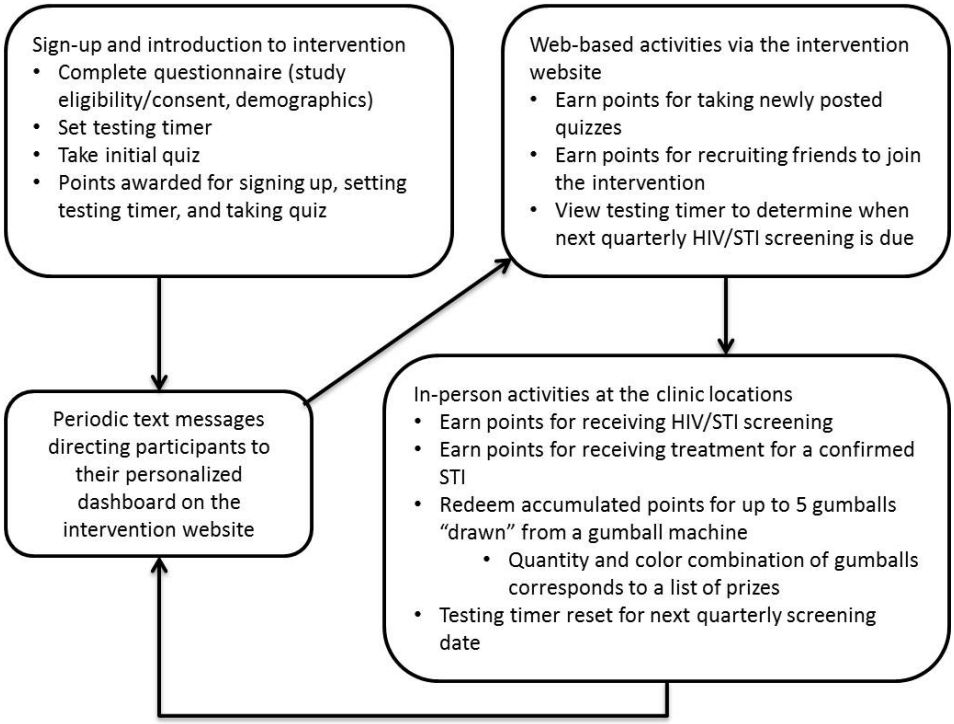
The final intervention consists of 3 components: online enrollment, Web-based activities, and in-person activities that occur at the clinic. Participants earn points through the Web-based activities, which they then redeem for a chance to win prizes during clinic visits. All content was developed prior to the implementation phase of the intervention.

In the first component, participants go through an online enrollment process and introduction to the intervention. The enrollment process consists of answering study eligibility questions, providing consent to participate in the study, and answering basic demographic questions. The introduction to the intervention consists of reading a short tutorial, inputting the date of last HIV/STI screening—used to set the countdown timer for the next recommended screening—and being invited to answer a 5-question multiple-choice quiz on a topic related to sexual health. Quizzes include questions that test knowledge of sexual health information that members of the target population may value (eg, STI symptoms, treatment, transmission risk, and prevention strategies) and questions primarily intended to be humorous or whimsical. Participants earn points for each step of this process (except for providing consent).

The second component, Web-based activities, occur on the intervention website (stick2it.org) and are intended to accomplish two primary goals. The first is to provide multiple reminders of the approaching quarterly screening date, which is accomplished through the prominent display of the countdown timer on the personalized webpage dashboard using a graphic presentation that was designed as part of the aesthetic theme of the intervention. The second is to provide participants the opportunity to accumulate points, which increases their chance of winning more valuable prizes at the clinic, thus increasing their motivation to receive quarterly HIV/STI screening. The online activities are primarily triggered by a series of short message service (SMS) text messages, inviting participants to visit the intervention website and complete various activities, such as taking the latest quiz, viewing their screening countdown timer, and inviting friends to join the intervention. Messages are sent with increasing frequency as the participant approaches their quarterly screening date, beginning with a 3-week interval, increasing to a 1-week interval. To complete each quiz, participants click a link in the SMS message directing them to their home page on the intervention website, where participants can also view their countdown timer. Points are awarded for answering the quiz questions, with additional points awarded for answering correctly. Participants are provided with an opportunity to take a new quiz every 3 weeks throughout the course of the intervention. In addition, participants earn points when they invite eligible friends who subsequently enroll in the intervention. Invited friends must meet all participant inclusion criteria.

The third component of the intervention involves the game of chance and takes place at the clinic. Participants also receive additional points for visiting the clinic for screening. Participants' accumulated points are redeemable for prizes only at the clinic (for any reason, including screening or treatment). The redemption process works as follows. Gumball machines are located at each clinic. This was both the game of chance overwhelmingly preferred by the target population through our focus group testing and the most feasible to implement at the clinics. During their clinic visit, participants can draw between 1 and 5 gumballs, depending on their accumulated points. The number of points earned corresponds with the number of gumball draws available to the participant. The color combinations of the gumballs that are drawn determine the prize received. Points redeemed for gumball draws are deducted from the participant's accumulated points at the time of redemption. The system of points and prizes was designed to result in an average prize cost of US $5 per screening visit. After screening, the countdown timer is reset for the next quarterly screening date. Multimedia Appendix 1 presents the points system and prizes used in the intervention. Multimedia Appendix 2 presents screenshots of the intervention website. Figure 2 shows a schematic of the final intervention design.

Figure 2. Schematic of final intervention design. HIV: human immunodeficiency virus; STI: sexually transmitted infection.



Phase 2 Intervention Pilot

Phase 2 will take place from October 2016 to June 2017 and will address the following aims: (1) evaluate the preliminary effectiveness of the Stick To It intervention on repeat HIV/STI screening in a pilot study, (2) evaluate the acceptability of and participant engagement with the Stick To It intervention, (3) evaluate the feasibility and cost of implementing an effectiveness evaluation on a larger scale, and (4) evaluate the cultural competence of the intervention as designed and implemented.

Study Population and Eligibility Criteria

Our study targets individuals who (1) are 18 to 26 years old, (2) were born or identify as male, (3) report male sexual partners at the time of enrollment, and (4) have a zip code of residence within defined areas in the vicinity of 1 of the 2 implementation sites. We selected YMSM aged 18 to 26 years as inclusion criteria for this pilot study given the substantial variations in the intervention design that would be required to include adolescent-aged YMSM. Additionally, a minimum inclusion age of 18 years will ensure that participants can provide independent consent to participate in the intervention.

Recruitment, Screening, and Sample Size

Participants will be recruited through three main channels. Multimedia Appendix 3 (flyers) and Multimedia Appendix 4 (video) present the recruitment tools used for the intervention.

In-Clinic Recruitment

Clinic staff will identify eligible individuals who visit the clinics for screenings, treatment, or other purposes and will inform them of the study and invite them to participate. In addition, placing flyers in the clinics and displaying the gumball machines in examination rooms will facilitate conversations about the intervention with potential participants. Those who are interested will be given a handout directing them to the intervention website, where they will be invited to complete an eligibility questionnaire and, if eligible, provide consent to participate in the study. Those with a smartphone will be invited to sign up while still at the clinic. Those who are eligible and provide consent will enter the study.

Community-Based Recruitment

We will place flyers in bars, other clinics, on mobile testing vans, and at selected community events. The advertisements and flyers include links to the intervention website, where individuals are invited to take the eligibility questionnaire and provide consent.

Online Recruitment

We will post advertisements on social networking platforms such as Facebook, Twitter, Instagram, Craigslist, and Grindr (a geolocation-based social networking app used by YMSM).

Study Design

Owing to potential spillover effects between the treatment and control groups within local peer groups, we deemed a randomized design to be impracticable. Instead, our study will use a quasi-experimental study design with a historical control group consisting of eligible participants identified within the medical records of the same clinics over the 12 months prior to the intervention phase of the study. We preregistered the study (clinicaltrials.gov NCT02946164). All eligible individuals recruited at the clinics, at community-based events, and online will be assigned to the treatment group. We will recruit a

minimum of 60 participants and a maximum of 200 participants into the treatment group and identify an identical number of individuals to serve as a historical control group. To our knowledge, this will be the first intervention using gamification to target YMSM for repeat HIV/STI screening. Accordingly, we chose a large sample size range as the upper bound, as it is not possible for us to predict what the demand will be for such an intervention among the target population.

Given the pilot nature of the study, the proposed analyses will likely be underpowered for formal testing purposes. Nevertheless, if we assume that half of the men in the comparison group will attend 1 or more repeat HIV/STI screening visits over 6 months of follow-up, with 60 men in each group, we will have 80% power to detect a minimum change of at least 27 percentage points (from 50% to 77%), which is comparable to the increase observed in an incentive-based intervention previously implemented by the community-based organization that operates the 2 clinics in our study [39].

Outcomes

For the primary outcome of repeat HIV/STI screening, we will use routinely collected client data from the clinics' electronic patient tracking and medical record system. A set of quantitative and qualitative secondary outcomes will be used to determine the acceptability and feasibility of Stick To It, and whether the intervention is suitable for a future effectiveness study on a larger scale. These implementation outcomes are as follows. First is the ability to recruit the study population: the percentage of eligible men approached who are willing to enroll and whether we can fully enroll the cohort within 6 weeks of study initiation. Second is participant engagement with the intervention: among Stick To It participants, we will determine (1) the proportion who successfully invited 1 or more other eligible individuals to the intervention, (2) the number of completed quizzes, and (3) the average number of quizzes participants completed. Third is cost: we will track the incremental cost of the program, relative to standard of care, which we will identify using the ingredients approach, in accordance with guidance from the World Health Organization [40]. Fourth is the potential for adverse events; that is, whether any adverse events occurred and the potential for adverse events in a larger effectiveness study. Fifth is the cultural competence of staff who implemented Stick To It services and activities and the cultural relevance of the intervention for members of the target population.

Data Collection

For each participant, we will collect data for a period of 6 months following their entry into the study. The primary outcome is repeat HIV/STI screening, defined as the number of screenings participants receive over the 6-month observation period, an indicator of retention in the program and its effectiveness.

In addition, we will collect qualitative information about the experiences of participants and clinic staff, described below. We will use the following methods to collect our secondary outcomes.

Postpilot Questionnaire, Administered to All Participants

A survey offered to all participants at the end of the study period will assess HIV/STI screening at other clinics (self-reported), barriers and facilitators to screening, and perceptions of the Stick To It intervention.

In-Depth Interviews

We will conduct up to 10 in-depth interviews with members of the clinic staff at the end the study period. We will gather detailed information on their perceptions of the intervention, including implementation challenges and successes, adaptability and integration with clinic operations, perceptions of effectiveness, and suggestions for future improvements.

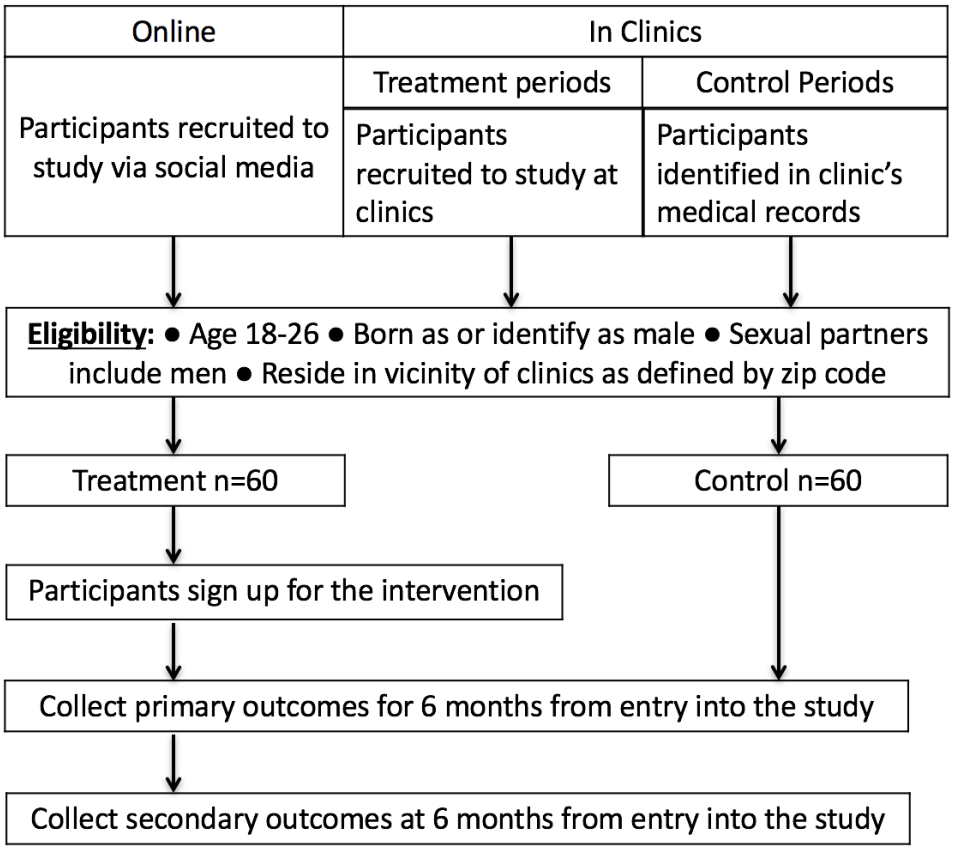
We will also conduct in-depth exit interviews with up to 40 Stick To It participants from both locations. Our goal is to gather detailed information about whether the intervention was relevant, motivating, and culturally competent. Further, we hope to assess the level of satisfaction with the process of earning and redeeming points, the rewards used, and the program's potential applicability to others. We will purposefully select a diverse group of men from different racial and ethnic groups and men who had different levels of engagement with the intervention. Topical areas will include the participant's perception of HIV/STI risk, perceptions about and experience with HIV/STI screening, willingness to discuss sexual health with others, particularly motivating elements of the game, and any unexpected challenges or adverse events.

We will examine whether Stick To It was culturally appropriate, relevant, and nonstigmatizing for YMSM, with an emphasis on African American and Latino YMSM, who are disproportionately affected by HIV [41]. Thus, at the completion of the in-depth interviews, we will administer a short interviewer-administered survey that includes the validated 20-item Public Perception of Physician's Cultural Competence Scale, which measures client perceptions of physicians' cultural competence [42]. We will adapt the scale to also refer to the clinic staff involved in Stick To It, and the design of the intervention itself. In addition, given the issues of stigma and discrimination that may adversely affect health care access among YMSM, we will include questions adapted from the validated Experiences of Discrimination [43] scale and the Discrimination in Medical Settings Scale [44] to determine whether the intervention or its implementation was stigmatizing.

In-depth interviews will be conducted in English by trained staff and will follow standard procedures [45,46]. A semistructured interview guide will cover predetermined issues (to ensure systematic data collection), but the interviewer will be free to change the sequence and wording of questions to ensure that unexpected themes can emerge [47]. Interviews will be audio recorded, with participant's consent, and later transcribed verbatim.

Figure 3 summarized our study design, screening and recruitment process, and data collection.

Figure 3. Summary of study design, screening and recruitment process, and data collection.



Data Analysis

For quantitative outcomes, we will first assess missing data, describe participant characteristics using frequency tables, and provide descriptive statistics (eg, means, standard deviations, medians, ranges, proportions) for the primary and secondary outcomes stratified by group. For the binary outcomes, we will compare the intervention and comparison groups by computing unadjusted and adjusted prevalence ratios and 95% confidence intervals using generalized linear models, such as log-binomial regression [48-50]. For the continuous and discrete outcomes, we will use ordinary least squares and zero-inflated Poisson regression (depending on the distribution of the outcomes) to determine the change in outcomes associated with participation in the intervention, before and after controlling for baseline characteristics. All regression analyses will include robust standard errors to adjust for heteroscedasticity and clustering. We will also perform a per-protocol analysis limited to participants that had a minimum level of engagement with the intervention during the study period (eg, ≥25th percentile of points earned during the game).

Qualitative data analysis will be conducted with ATLAS.ti (Scientific Software Development GmbH) following standard procedures [47,48]. In brief, we will combine inductive and deductive techniques to strengthen the validity of the coding system and our conclusions during the multistage analysis process [46-50]. Two researchers will independently review the transcripts and code according to broad, a priori, and emergent themes related to gamification theory and barriers and facilitators of regular screening. Interviewer notes capturing contextual details, quality, inconsistencies, and impressions will also be incorporated. Data reduction will be based on coding sorts of the most central themes (eg, engagement with the intervention) followed by a systematic analysis of related themes (eg, motivation, risk perception, stigma) using coding matrices to identify relationships [44,51]. To reduce threats to validity, we will solicit feedback on our hypotheses from participants (respondent validation) [52] and rigorously examine theoretical validity—whether the data are consistent or inconsistent with the underlying theoretical models [47].

Results

This is an ongoing research study with initial results expected in the fourth quarter of 2017.

Discussion

The ongoing study is intended to explore the effectiveness of incorporating gamification into an incentive-based intervention to increase repeat HIV/STI screening among YMSM. Given that this population remains disproportionally affected by HIV and STIs, novel approaches that supplement proven engagement strategies may serve an important public health function. Namely, early HIV diagnosis, as achieved through repeat HIV

screening, has been shown to facilitate timely linkage to medical care, initiation of antiretroviral therapy, and attainment of viral suppression, resulting in reduced transmission risk [53-55].

Given the success of nongamification interventions involving incentives, and considering the potential of gamification to harness and amplify intrinsic motivation for both short-term and long-term behavior change, we hypothesize that this approach may be particularly effective in increasing routine HIV/STI screening among YMSM. We emphasize that a fundamental principle of gamification is to enhance the motivational effectiveness of known behavior change mechanisms, such as reminders and incentives, and to amplify the existing motivation of individuals to accomplish desired behaviors. However, we do not expect stand-alone gamification interventions to replace or compete with existing types of interventions, but rather to enhance established strategies. Accordingly, we coupled gamification with an incentive-based structure for this very reason.

A secondary but important goal of this study is to explore the process of designing gamification interventions for health-related behavior change and to learn best practices for future intervention design. This is crucial, due to the fact that gamification interventions potentially require an extensive formative design process to determine the optimal set of game elements and intervention design required to incorporate such elements. One conjecture is that the success of any given health-related gamification intervention, and thus of health-related gamification more generally, may depend on highly context-specific and population-specific formative research. Thus, determining best practices for the formative phase is necessary to achieve the goal of being able to consistently and predictably design cost-effective interventions in a range of different circumstances. This paper, in addition to presenting the protocol of the study, is an attempt at documenting what formative research to develop a gamification-based intervention entails.

It is also important to recognize the limitations of this study. As previously discussed, we will use a historical control group for comparison. Although a randomized design has advantages, it was not practical because participants randomly assigned to the control group would have been exposed to some components of the intervention, such as recruitment materials posted in the clinic waiting and examination rooms (eg, comparison group contamination). Additionally, given the pilot state of the intervention, a cluster randomized design was neither warranted nor feasible. Although a historical comparison group will help us understand whether there is a preliminary signal of the intervention's effectiveness and whether further study is warranted, it has important limitations. Most importantly, we will be unable to make causal statements about the effect of the intervention because we will be unable to adequately control for time trends between the intervention and comparison groups and the selection bias that may result from differences between the 2 groups. Nevertheless, a historical comparison group will still provide us with baseline data on repeat testing among YMSM in the same geographic region and therefore a benchmark to which we can make preliminary comparisons about the intervention's potential effectiveness.

Acknowledgments

The authors thank the following individuals for their contributions to this work: Sagar Amin; Branden Barger; Dale Gluth, MA; Jamie Murkey, MPH; Sean Young, MS, PhD; Gabe Zichermann; and the Stick To It Community Advisory Board. Publication was made possible in part by support from the Berkeley Research Impact Initiative sponsored by the University of California, Berkeley Library. Funding for the study was provided by the National Institute of Mental Health (McCoy R34MH106359). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute of Mental Health or the National Institutes of Health.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Stick To It points system/prize decoder.

[PDF File (Adobe PDF File), 181KB - resprot_v6i7e140_app1.pdf]

Multimedia Appendix 2

Intervention website screenshots.

[PDF File (Adobe PDF File), 746KB - resprot_v6i7e140_app2.pdf]

Multimedia Appendix 3

Recruitment tools (flyers).

[PDF File (Adobe PDF File), 7MB - resprot_v6i7e140_app3.pdf]

Multimedia Appendix 4

Recruitment tools (video).

[MP4 File (MP4 Video), 10MB - resprot_v6i7e140_app4.mp4]

References

1. McCoy SI, Shiu K, Martz TE, Smith CD, Mattox L, Gluth DR, et al. Improving the efficiency of HIV testing with peer recruitment, financial incentives, and the involvement of persons living with HIV infection. J Acquir Immune Defic Syndr 2013 Jun 01;63(2):e56-e63. [doi: 10.1097/QAI.0b013e31828a7629] [Medline: 23403860]
2. Björkman-Nyqvist M, Corno L, de Walque D, Svensson J. Evaluating the impact of short term financial incentives on HIV and STI incidence among youth in Lesotho: a randomized trial. 2013 Presented at: 7th IAS Conference on HIV Pathogenesis, Treatment, and Prevention; June 30-July 3, 2013; Kuala Lumpur, Malaysia.
3. Baird SJ, Garfein RS, McIntosh CT, Ozler B. Effect of a cash transfer programme for schooling on prevalence of HIV and herpes simplex type 2 in Malawi: a cluster randomised trial. Lancet 2012 Apr 07;379(9823):1320-1329. [doi: 10.1016/S0140-6736(11)61709-1] [Medline: 22341825]
4. de Walque D, Dow WH, Nathan R, Abdul R, Abilahi F, Gong E, et al. Incentivising safe sex: a randomised trial of conditional cash transfers for HIV and sexually transmitted infection prevention in rural Tanzania. BMJ Open 2012;2:e000747 [FREE Full text] [doi: 10.1136/bmjopen-2011-000747] [Medline: 22318666]
5. Galárraga O, Genberg BL, Martin RA, Barton Laws M, Wilson IB. Conditional economic incentives to improve HIV treatment adherence: literature review and theoretical considerations. AIDS Behav 2013 Sep;17(7):2283-2292 [FREE Full text] [doi: 10.1007/s10461-013-0415-2] [Medline: 23370833]
6. Solomon SS, Srikrishnan AK, Vasudevan CK, Anand S, Kumar MS, Balakrishnan P, et al. Voucher incentives improve linkage to and retention in care among HIV-infected drug users in Chennai, India. Clin Infect Dis 2014 Aug 15;59(4):589-595 [FREE Full text] [doi: 10.1093/cid/ciu324] [Medline: 24803381]
7. Haukoos JS, Witt MD, Coil CJ, Lewis RJ. The effect of financial incentives on adherence with outpatient human immunodeficiency virus testing referrals from the emergency department. Acad Emerg Med 2005 Jul;12(7):617-621 [FREE Full text] [doi: 10.1197/j.aem.2005.02.016] [Medline: 15995093]
8. Thornton RL. The demand for, and impact of, learning HIV status. Am Econ Rev 2008 Dec 01;98(5):1829-1863 [FREE Full text] [doi: 10.1257/aer.98.5.1829] [Medline: 21687831]
9. Sibanda EL, Tumushime M, Mufuka J, Gudukeya S, Napierala Mavedzenge S, Bautista-Arredondo S, et al. Results of a cluster-randomized trial of non-financial incentives to increase uptake of couples counseling and testing among clients attending PSI mobile HIV services in rural Zimbabwe. J Int AIDS Soc 2016 Jul 22;19(Suppl 5):62. [doi: 10.7448/IAS.19.6.21264]
10. McNairy ML, Gachuhi AB, Lamb MR, Nuwagaba-Biribonwoha H, Burke S, Ehrenkranz P, et al. The Link4Health study to evaluate the effectiveness of a combination intervention strategy for linkage to and retention in HIV care in Swaziland: protocol for a cluster randomized trial. Implement Sci 2015 Jul 19;10:101 [FREE Full text] [doi: 10.1186/s13012-015-0291-4] [Medline: 26189154]
11. Björkman Nyqvist M, Corno L, de Walque D, Svensson J. Using lotteries to incentivize safer sexual behavior: evidence from a randomized controlled trial on HIV prevention. Policy research working paper. Washington, DC: World Bank; 2015 Mar. URL: https://elibrary.worldbank.org/action/doSearch?AllField=Using+Lotteries+to+Incentivize+Safer+Sexual+Behavior%3A+Evidence+from+a+Randomized+Controlled+Trial+on+HIV+Prevention [accessed 2017-04-15] [WebCite Cache ID 6rmvssExa]
12. Haisley E, Volpp KG, Pellathy T, Loewenstein G. The impact of alternative incentive schemes on completion of health risk assessments. Am J Health Promot 2012;26(3):184-188. [doi: 10.4278/ajhp.100729-ARB-257] [Medline: 22208418]
13. Ashraf N, Bandiera O, Jack K. No margin, no mission? A field experiment on incentives for pro-social tasks. 2012 Jan 24. URL: http://isites.harvard.edu/fs/docs/icb.topic964076.files/Ashraf_NoMarginNoMission.pdf [accessed 2017-04-15] [WebCite Cache ID 6rgXJeIER]
14. Mehrotra A, An R, Patel DN, Sturm R. Impact of a patient incentive program on receipt of preventive care. Am J Manag Care 2014 Jun;20(6):494-501 [FREE Full text] [Medline: 25180436]
15. Pike E. Level Up! Using gamification to spark competition, collaboration,community in online interventions. 2014 Presented at: Youth + Tech + Health Live Conference; April 6-8, 2014; San Francisco, CA.
16. Hightow-Weidman LB, Fowler B, Kibe J, McCoy R, Pike E, Calabria M, et al. HealthMpowerment.org: development of a theory-based HIV/STI website for young black MSM. AIDS Educ Prev 2011 Feb;23(1):1-12 [FREE Full text] [doi: 10.1521/aeap.2011.23.1.1] [Medline: 21341956]
17. LeGrand S, Muessig KE, McNulty T, Soni K, Knudtson K, Lemann A, et al. Epic allies: development of a gaming app to improve antiretroviral therapy adherence among young HIV-positive men who have sex with men. JMIR Serious Games 2016 May 13;4(1):e6 [FREE Full text] [doi: 10.2196/games.5687] [Medline: 27178752]
18. Enah C, Moneyham L, Vance DE, Childs G. Digital gaming for HIV prevention with young adolescents. J Assoc Nurses AIDS Care 2013;24(1):71-80. [doi: 10.1016/j.jana.2012.03.005] [Medline: 22871481]

19. Black S, Wallace M, Middelkoop K, Robbertze D, Bennie T, Wood R, et al. Improving HIV testing amongst adolescents through an integrated youth centre rewards program: insights from South Africa. Child Youth Serv Rev 2014 Oct;45:98-105. [doi: 10.1016/j.childyouth.2014.03.025]
20. Horvath KJ, Michael Oakes J, Simon Rosser B, Danilenko G, Vezina H, Rivet Amico K, et al. Feasibility, acceptability and preliminary efficacy of an online peer-to-peer social support ART adherence intervention. AIDS Behav 2013 Apr 4;17(6):2031-2044 [FREE Full text] [doi: 10.1007/s10461-013-0469-1] [Medline: 23553347]
21. Centers for Disease Control and Prevention. HIV Surveillance Report, 2014; vol. 26. Atlanta, GA: U.S. Department of Health and Human Services; 2015. URL: http://www.cdc.gov/hiv/library/reports/surveillance/ [accessed 2017-04-10] [WebCite Cache ID 6q9G2XZWr]
22. Centers for Disease Control and Prevention. Sexually Transmitted Disease Surveillance 2015. Atlanta, GA: U.S. Department of Health and Human Services; 2016. URL: https://www.cdc.gov/std/stats15/std-surveillance-2015-print.pdf [accessed 2017-04-10] [WebCite Cache ID 6q9GCNYrg]
23. Pathela P, Braunstein SL, Blank S, Schillinger JA. HIV incidence among men with and those without sexually transmitted rectal infections: estimates from matching against an HIV case registry. Clin Infect Dis 2013 Jun 25;57(8):1203-1209. [doi: 10.1093/cid/cit437] [Medline: 23800942]
24. Patton ME, Kidd S, Llata E, Stenger M, Braxton J, Asbel L, et al. Extragenital gonorrhea and chlamydia testing and infection among men who have sex with men--STD Surveillance Network, United States, 2010-2012. Clin Infect Dis 2014 Jun;58(11):1564-1570 [FREE Full text] [doi: 10.1093/cid/ciu184] [Medline: 24647015]
25. Bernstein KT, Marcus JL, Nieri G, Philip SS, Klausner JD. Rectal gonorrhea and chlamydia reinfection is associated with increased risk of HIV seroconversion. J Acquir Immune Defic Syndr 2010 Apr 01;53(4):537-543. [doi: 10.1097/QAI.0b013e3181c3ef29] [Medline: 19935075]
26. Mustanski B, Garofalo R, Monahan C, Gratzer B, Andrews R. Feasibility, acceptability, and preliminary efficacy of an online HIV prevention program for diverse young men who have sex with men: the keep it up! intervention. AIDS Behav 2013 Nov;17(9):2999-3012 [FREE Full text] [doi: 10.1007/s10461-013-0507-z] [Medline: 23673793]
27. Rosser BR, Wilkerson JM, Smolenski DJ, Oakes JM, Konstan J, Horvath KJ, et al. The future of Internet-based HIV prevention: a report on key findings from the Men's INTernet (MINTS-I, II) Sex Studies. AIDS Behav 2011 Apr;15 Suppl 1:S91-100 [FREE Full text] [doi: 10.1007/s10461-011-9910-5] [Medline: 21360127]
28. Margolis AD, Joseph H, Hirshfield S, Chiasson MA, Belcher L, Purcell DW. Anal intercourse without condoms among HIV-positive men who have sex with men recruited from a sexual networking web site, United States. Sex Transm Dis 2014 Dec;41(12):749-755. [doi: 10.1097/OLQ.0000000000000206] [Medline: 25581813]
29. Christensen JL, Miller LC, Appleby PR, Corsbie-Massay C, Godoy CG, Marsella SC, et al. Reducing shame in a game that predicts HIV risk reduction for young adult MSM: a randomized trial delivered nationally over the Web. J Int AIDS Soc 2013 Nov 13;16(3 Suppl 2):18716 [FREE Full text] [Medline: 24242264]
30. Patel V, Lounsbury D, Berrios A, Riviera S, Vega C. Developing a peer-led social media based HIV testing intervention with YMSM of color - a feasibility study. 2014 Presented at: Youth + Tech + Health Live Conference; April 6-8, 2014; San Francisco, CA.
31. Jones V, Whitlock M. What's going on online with hard to reach population? Social media use among black gay men. 2014 Presented at: Youth + Tech + Health Live Conference; April 6-8, 2014; San Francisco, CA.
32. Hirshfield S, Chiasson MA, Joseph H, Scheinmann R, Johnson WD, Remien RH, et al. An online randomized controlled trial evaluating HIV prevention digital media interventions for men who have sex with men. PLoS One 2012;7(10):e46252 [FREE Full text] [doi: 10.1371/journal.pone.0046252] [Medline: 23071551]
33. Lewis MA, Uhrig JD, Ayala G, Stryker J. Reaching men who have sex with men for HIV prevention messaging with new media: recommendations from an expert consultation. Ann Forum Collaborative HIV Res 2011 Oct 03;13(3):10-16 [FREE Full text]
34. 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]
35. Deterding S, Dixon D, Khaled R, Nacke L. From game design elements to gamefulness: defining “gamification”. 2011 Presented at: 15 International Academic MindTrek Conference: Envisioning Future Media Environments; Sept 28-30, 2011; Tampere, Finland. [doi: 10.1145/2181037.2181040]
36. Deci EL, Ryan RM. Facilitating optimal motivation and psychological well-being across life's domains. Can Psychol 2008;49(1):14-23. [doi: 10.1037/0708-5591.49.1.14]
37. Deterding S. Google Tech Talk. 2011 Jan 24. Meaningful play: getting gamification right URL: https://www.slideshare.net/dings/meaningful-play-getting-gamification-right [accessed 2017-05-14] [WebCite Cache ID 6qProeNAz]
38. Schell J. The Art of Game Design: A Book of Lenses. Burlington, MA: Morgan Kaufmann; 2008.
39. McGrath M, Anderson L, Beymer M, Cohen A, Natoli L, Javanbakht M, et al. Testing with benefits: results from a contingency management program to reduce recurrent STIs in high-risk MSM. 2015 Presented at: Annual Meeting of the American Public Health Association; Oct 31-Nov 4, 2015; Chicago, IL.

40. Tan-Torres Edejer T, Baltussen R, Adam T, Hutubessy R, Acharya A, Evans DB, et al, editors. Making Choices in Health: WHO Guide to Cost-Effectiveness Analysis. Geneva, Switzerland: World Health Organization; 2003.
41. Centers for Disease Control and Prevention. HIV Surveillance Report, 2015; vol. 27. Atlanta, GA: U.S. Department of Health and Human Services; 2016 Nov. URL: https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-2015-vol-27.pdf [accessed 2017-04-10] [WebCite Cache ID 6rgaEegPK]
42. Ahmed R, Bates BR. Development of scales to assess patients' perception of physicians' cultural competence in health care interactions. J Transcult Nurs 2012 Jul;23(3):287-296. [doi: 10.1177/1043659612441025] [Medline: 22477717]
43. Krieger N, Smith K, Naishadham D, Hartman C, Barbeau EM. Experiences of discrimination: validity and reliability of a self-report measure for population health research on racism and health. Soc Sci Med 2005 Oct;61(7):1576-1596. [doi: 10.1016/j.socscimed.2005.03.006] [Medline: 16005789]
44. Peek ME, Nunez-Smith M, Drum M, Lewis TT. Adapting the everyday discrimination scale to medical settings: reliability and validity testing in a sample of African American patients. Ethn Dis 2011;21(4):502-509 [FREE Full text] [Medline: 22428358]
45. Ulin P, Robinson E, Tolley E. Qualitative Methods in Public Health: A Field Guide for Applied Research. New York, NY: John Wiley & Sons; 2004.
46. Miles M, Huberman A. Qualitative Data Analysis: An Expanded Sourcebook. 2nd edition. Thousand Oaks, CA: Sage Publications; 1994.
47. Maxwell J. Qualitative Research Design: An Interactive Approach. 2nd edition. Thousand Oaks, CA: Sage Publications; 2005.
48. Zocchetti C, Consonni D, Bertazzi PA. Relationship between prevalence rate ratios and odds ratios in cross-sectional studies. Int J Epidemiol 1997 Feb;26(1):220-223. [Medline: 9126523]
49. Greenland S. Interpretation and choice of effect measures in epidemiologic analyses. Am J Epidemiol 1987 May;125(5):761-768. [Medline: 3551588]
50. Barros AJD, Hirakata VN. Alternatives for logistic regression in cross-sectional studies: an empirical comparison of models that directly estimate the prevalence ratio. BMC Med Res Methodol 2003 Oct 20;3:21 [FREE Full text] [doi: 10.1186/1471-2288-3-21] [Medline: 14567763]
51. Ryan G, Bernard H. Data management and analysis methods. In: Denzin N, Lincoln Y, editors. Handbook of Qualitative Research. 2nd edition. Thousand Oaks, CA: Sage Publications; 2000:769-802.
52. Bryman A. Quantity and Quality in Social Science Research. London, UK: Unwin Hyman; 1998.
53. Castel AD, Greenberg AE, Befus M, Willis S, Samala R, Rocha N, et al. Temporal association between expanded HIV testing and improvements in population-based HIV/AIDS clinical outcomes, District of Columbia. AIDS Care 2014;26(6):785-789. [doi: 10.1080/09540121.2013.855296] [Medline: 24206005]
54. Weinhardt LS, Carey MP, Johnson BT, Bickham NL. Effects of HIV counseling and testing on sexual risk behavior: a meta-analytic review of published research, 1985-1997. Am J Public Health 1999 Sep;89(9):1397-1405. [Medline: 10474559]
55. Marks G, Crepaz N, Janssen RS. Estimating sexual transmission of HIV from persons aware and unaware that they are infected with the virus in the USA. AIDS 2006 Jun 26;20(10):1447-1450. [doi: 10.1097/01.aids.0000233579.79714.8d] [Medline: 16791020]

Abbreviations

HIV: human immunodeficiency virus
MSM: men who have sex with men
SMS: short message service
STI: sexually transmitted infection
YMSM: young men who have sex with men

Edited by G Eysenbach; submitted 17.05.17; peer-reviewed by L Hightow-Weidman, D Vance; comments to author 31.05.17; revised version received 21.06.17; accepted 22.06.17; published 17.07.17.

Please cite as:
Mejia CM, Acland D, Buzdugan R, Grimball R, Natoli L, McGrath MR, Klausner JD, McCoy SI
An Intervention Using Gamification to Increase Human Immunodeficiency Virus and Sexually Transmitted Infection Screening Among Young Men Who Have Sex With Men in California: Rationale and Design of Stick To It
JMIR Res Protoc 2017;6(7):e140
URL: http://www.researchprotocols.org/2017/7/e140/
doi:10.2196/resprot.8064
PMID:28716771

Protocol

Development of a Tailored HIV Prevention Intervention for Single Young Men Who Have Sex With Men Who Meet Partners Online: Protocol for the myDEx Project

Jose Arturo Bauermeister[1], MPH, PhD; Ryan C Tingler[1], MPH; Michele Demers[2], MPH; Gary W Harper[2], PhD, MPH

[1]University of Pennsylvania, Philadelphia, PA, United States

[2]University of Michigan, Ann Arbor, MI, United States

Corresponding Author:
Jose Arturo Bauermeister, MPH, PhD
University of Pennsylvania
418 Curie Blvd
Suite 222L
Philadelphia, PA, 19104
United States
Phone: 1 215 898 9993
Email: bjose@upenn.edu

Abstract

Background: New cases of human immunodeficiency virus (HIV) among young men who have sex with men (YMSM), aged 18 to 24, underscore the importance of developmentally-informed HIV programs for YMSM. We developed an online intervention focused on risk reduction strategies across different sexual partner types. Intervention activities focus on assisting YMSM reflect on their partner-seeking behaviors, develop sexual decision-making rules to reduce their HIV risks, and consider the adoption of HIV prevention behaviors.

Objective: This pilot, randomized controlled trial (RCT) aims to examine the feasibility, acceptability, and preliminary efficacy of a tailored, Web-based HIV prevention intervention for single YMSM.

Methods: We designed a prospective RCT of online-recruited cis-gender men (N=180) who reported recent unprotected anal intercourse, self-report as HIV negative or are unaware of their HIV status, and meet sexual partners through online dating apps. Individuals in the control arm receive an attention-control condition that includes HIV/sexually transmitted infection (STI) information currently available on sex education websites. Individuals in the intervention arm receive a 6-session Web-based program tailored on their demographic information, partner-seeking behaviors and relationship desires, and prior sexual attitudes and behaviors. This tailored content will match HIV prevention messages and safer sex skills with YMSM's outcome expectancies when meeting new partners and thereby help them consider how to integrate safer sex practices into different partner types. Study assessments are taken at baseline, 30-, 60-, and 90-day follow-ups. Intervention acceptability and preliminary efficacy will be explored in sexual risk behaviors and HIV/STI testing.

Results: The RCT launched in November 2016 and is ongoing. To date, 180 eligible individuals have been enrolled, consented, and randomized. Of the 120 individuals in the intervention arm, 51.7% (62/120) identify as non-Hispanic white and half of the control arm identifies as non-Hispanic white. There were no differences observed by arm for race and/or ethnicity, age, or sexual orientation.

Conclusions: Although there are in-person evidence-based interventions with proven efficacy for YMSM, few HIV/STI prevention interventions delivered online exist. Online interventions may ease access to comprehensive HIV/STI education among YMSM and allow personalized content to be delivered. The online intervention that we developed, myDEx, aims to alleviate the gaps within HIV prevention for YMSM by utilizing tailored, Web-based content with the goal of developing skills for same-sex dating and relationship building, while reducing their risks for HIV/STI.

Trial Registration: ClinicalTrials.gov NCT02842060; https://clinicaltrials.gov/ct2/show/NCT02842060 (Archived by WebCite at http://www.webcitation.org/6rcJdxF9v)

(JMIR Res Protoc 2017;6(7):e141) doi:10.2196/resprot.7965

KEYWORDS

eHealth; HIV prevention; Internet; risk reduction; sexually transmitted infections

Introduction

Scientific Background

Interventions specific to young men who have sex with men (YMSM) are needed to curtail the rise of new *human immunodeficiency virus* (HIV)/acquired immunodeficiency syndrome (AIDS) infections. In 2015, in the United States, YMSM aged 13 to 24 years had the greatest percentage increase (87%) in diagnosed HIV infections [1], with black and Latino YMSM accounting for the greatest proportion of new infections among men who have sex with men (MSM) [2]. HIV prevention tools that are culturally and developmentally adapted for this population are needed [3]. To this end, we developed an online intervention that promotes HIV prevention behaviors (eg, condom use, pre-exposure prophylaxis (PrEP) awareness and uptake, HIV/sexually transmitted infection [STI] testing) and reduction of risk behaviors (eg, number of sexual acts where HIV transmission could be possible) for single YMSM presumed to be HIV-negative who engage in unprotected (ie, condomless) anal intercourse (UAI) with sexual partners met online.

Most individuals explore and integrate aspects of their sexuality into their personal identity as they transition from adolescence into young adulthood (ie, 15 to 24 years of age). Serial dating and involvement in different types of relationships has been documented as helping youth to define their sexual identity, to narrow the characteristics sought in long-term relationships, and to practice safer sex negotiation skills [4]. However, compared to heterosexual counterparts, YMSM may not readily receive support and advice from family, peer, and school systems on how to date and seek out same-sex partners. Furthermore, YMSM do not receive instruction on how to have anal sex as part of their sex education [5-7] or guidance on how to negotiate condom use with their partners [8]. This is particularly problematic as YMSM's participation in dating behaviors during this period coincides with their mean age of initiating anal sex [5,6,8-10], and may create unique HIV vulnerabilities as they engage in partner-seeking behaviors. Recognizing the importance of relationship pursuits in this period, we developed a comprehensive sex education intervention that addresses HIV risk reduction in the context of same-sex dating and safer sex negotiation activities with sexual partners.

Objectives

HIV prevention interventions for single YMSM who meet partners online must account for different relationship typologies common in this developmental period: romantic interests, casual encounters/hook-ups, and friends with benefits [11]. Although MSM couples-based intervention projects are underway [12], these interventions may not be translatable to single YMSM who, by definition, are not in a relationship and do not have a "main partner." This pilot, randomized control trial (RCT) aims to examine the feasibility, acceptability, and preliminary efficacy of a tailored, Web-based HIV prevention intervention for single YMSM called myDEx. The pilot RCT compares our tailored intervention to an attention-control condition. Using a 2:1 block randomization, we examine our intervention's feasibility and acceptability among 180 single, HIV-negative YMSM (50% racial/ethnic minorities), and gather preliminary behavioral data to inform a future efficacy trial. Assessments are collected at baseline, 30-, 60-, and 90-day follow-up.

Methods

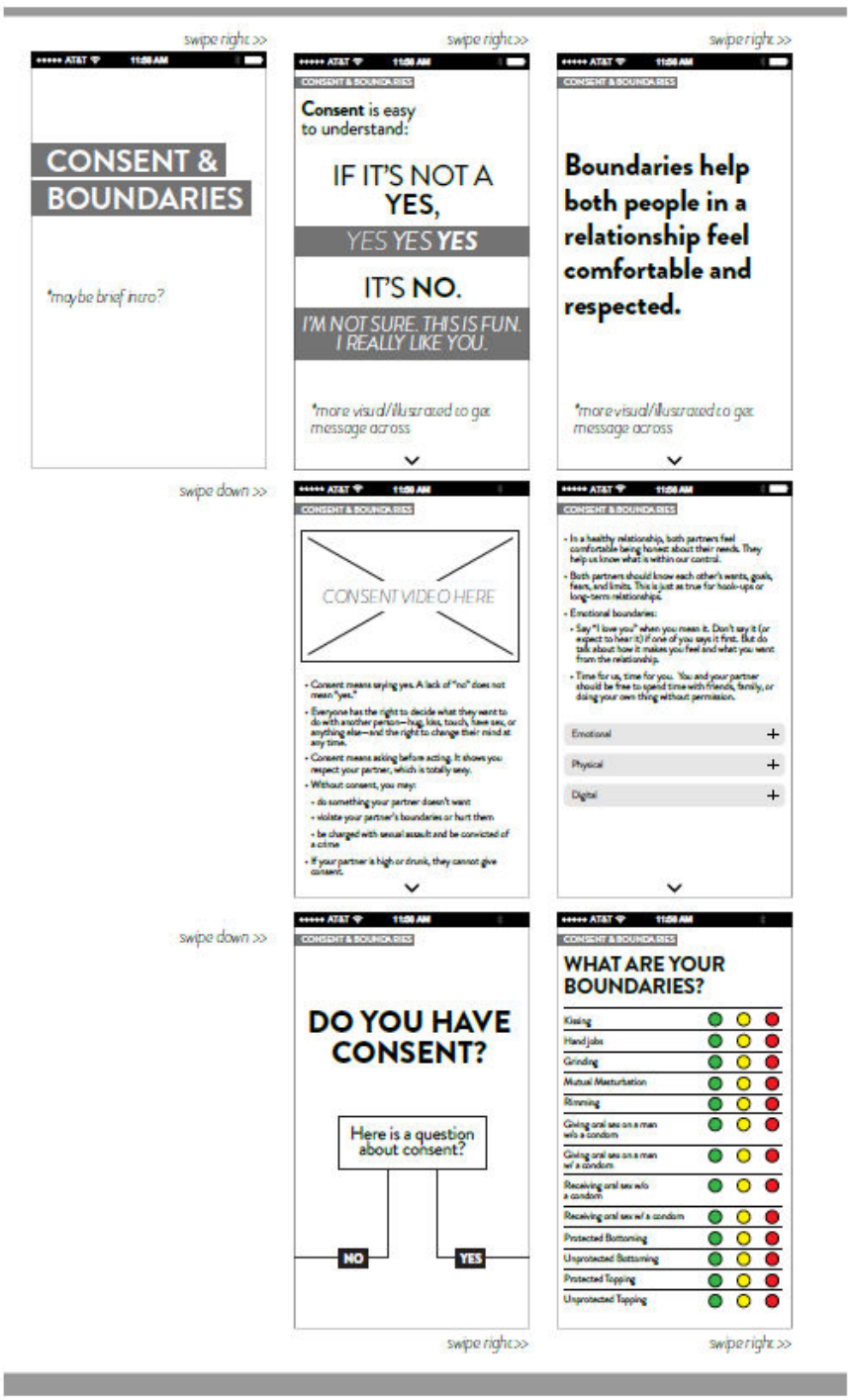
Trial Design

The research activities involve a prospective, pilot RCT of approximately 180 online-recruited cis-gendered MSM. Individuals in the experimental arm receive a 6-session, Web-based program with interactive content using story-telling, case scenarios, risk reduction strategies, and graphics and/or videos. Individuals in the control arm receive a 6-session online, non-tailored HIV prevention intervention (NTHP) using information available on the Centers for Disease Control and Prevention website. The NTHP condition will have an interface similar to myDEx aesthetics and site features to avoid confounding due to site design and navigation.

A youth advisory board (YAB) was recruited for this study. YAB members (N=3) were YMSM between the ages of 18 and 24 and diverse across race and/or ethnicity, educational attainment, socioeconomic status, faith, and urban/rural residential background. YAB members were hired as part-time research assistants. The YAB's roles and responsibilities included (1) providing input into the proposed intervention content; (2) brainstorming with the research team on how to deliver the content using active learning and youth-friendly engagement; and (3) leading or co-facilitating trainings for the WebApp developers to learn about same-sex attractions and dating behaviors and popular MSM-specific apps used for dating and hooking up. As each intervention session was developed, the YAB and research team independently brainstormed what content and activities could be included in each session. The ideas were then discussed as a team, ordered by relevance for the session and within the session, and annotated for the developers to consider while building the wireframes (Figure 1). These discussions served to inform the user navigation of our intervention, including how to organize content within sessions into 3 levels focused on a core message (level 1), in-depth discussion of topics linked to that message (level 2), and an activity component (level 3).

Our intervention will be pilot tested using a racial and/or ethnically diverse sample (50% racial/ethnic minority) of single YMSM living throughout the United States (N=120), using an attention-control comparison condition (N=60) to test our intervention's feasibility, acceptability, and preliminary efficacy. Primary outcomes of interest include increased consistent condom use across partner types and HIV/STI testing, and decreased UAI occasions and partners. Participants will complete 3 online follow-up assessments at 30, 60, and 90 days, each lasting approximately 30 minutes.

Figure 1. Wireframe example used during the development of myDEx.



Eligibility Criteria

Eligible participants are (1) male at birth and identify as male; (2) between the ages of 18 and 24 (inclusive); (3) self-report as single; (4) self-report as HIV-negative or are unaware of their HIV status; (5) speak and read English; (5) report using online dating apps; and (6) report UAI with a male partner in prior 6 months. Participants for the trial are from across the United States, with recruitment via online advertisements placed on popular social and sexual networking sites. Promotional materials describe the study and provide a link to a page containing basic study information, including a short description of study activities.

Potential participants interested in the study complete a short eligibility screener. If eligible, participants complete an online consent form. Individuals who do not meet eligibility criteria or do not consent into the study (if eligible) are thanked for their time and are exited from the study site. Once consent is obtained, participants complete a 30-minute baseline questionnaire online. As part of the baseline questionnaire, participants provide

information that may help us contact them for follow-up assessments and verify that they are not fraudulent or duplicate entries [13,14]. We use best practices [15,16] to retain participants (eg, comprehensive locator information that includes participants' cell phone number, email, Facebook username, etc). When the baseline survey is complete, participants are randomized into the 2 study arms.

Incentives

Individual participants each receive US $30, $15, $20, and $25 for completing the baseline assessment and the 30-, 60-, and 90-day follow-ups, respectively. The incentives are back loaded to encourage completion of all 3 data collection time points and reduce participant attrition over time.

Sample Size

The goal is to enroll and maintain a sample of 180 single YMSM over a 3-month study period, with an expected retention rate of 80%. As a pilot, we recognize that we may not have sufficient power to detect small effect sizes; however, this design will inform our subsequent large-scale RCT, allowing us to identify and address implementation and retention challenges that could arise in the larger trial. Specifically, the primary purposes of this pilot trial are (1) to demonstrate the feasibility of the methods proposed for a subsequent trial; (2) to stabilize procedures that are replicable; and (3) to determine important parameters with sufficient accuracy to reliably estimate sample size and power for a future RCT. As a result, we are not powered to estimate small effect sizes or carry out sophisticated statistical analyses; rather, we seek to estimate key study parameters with sample means and proportions together with 2-sided 95% CIs, and test the primary null hypotheses at the traditional 2-sided level alpha of .05.

We will have 80% power to detect a medium intervention effect (Cohen d less than .35) at alpha of .05 in a continuous measure using a repeated measures group design (N=180) with 4 observations (baseline and 3 follow-up assessments) when the standard deviation (SD) is 1 and the correlation between observations on the same subject (rho) is .6. For dichotomous outcomes, we estimate 80% power at an alpha of .05 to detect an odds ratio (OR) of 2.11 or greater assuming that the proportion for the intervention condition is .58 and the attention-control condition is .40, with rho also being .60. We note that there is some controversy regarding the use of “pilot data” to estimate actual effect size, as specified by Kraemer et al [17]. We agree with their view that clinically meaningful effect sizes should be decided based on extrinsic, clinical judgment grounds, and not based on the pilot data which are too few, typically, to obtain reliable conclusions. However, we can use these data to rule out unusually large or small effects through standard 95% CI procedures. Thus, we will confirm that extrinsic effect sizes are contained within our CIs. Even with 20% attrition, we will have preliminary effects with adequate error margins to inform the subsequent trial.

Randomization

Individuals are randomized to either the intervention arm (myDEx) or the attention-control arm (NTHP) using a stratified 2:1 block randomization design. Block randomization is stratified by race (eg, white versus non-white), with equal allocation in each group. Treatment assignments are generated with the use of a pseudo-random-number generator with permutated blocks that are used to ensure balance across participants’ assigned condition.

Theoretical Framework

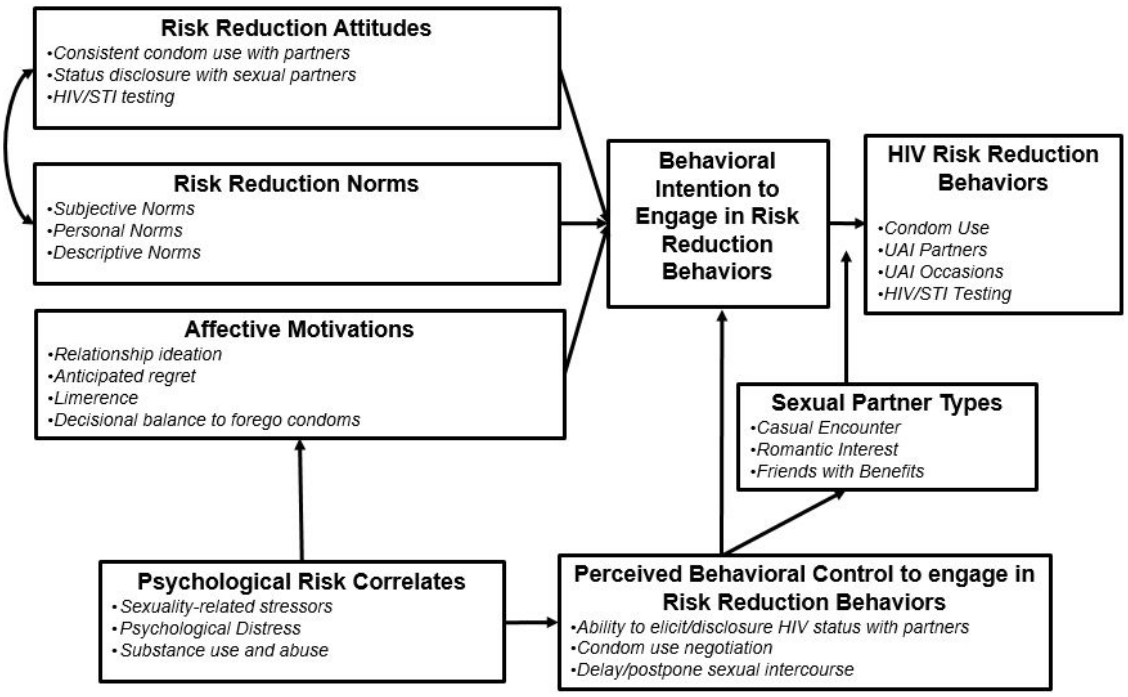
A dual processing, cognitive-emotional decision making framework [18] informs our intervention framework. Decision-making researchers have noted that affective motivations may be processed more rapidly than cognitive motivations and may result in decision-making that is affectively motivated rather than analytically motivated [19].

To increase participants’ cognitive motivations, our intervention is informed by the Integrated Behavior Model (IBM), one of the leading behavior change theories in HIV/STI research given its adaptability across populations and its application in health communication research [20]. Content geared to increasing cognitive motivations will focus on risk reduction attitudes, norms, and perceived behavioral control. Positive attitudes include assurance of avoiding STIs, increased control, responsible decision-making, and prolonged and enjoyable sexual encounters. Negative attitudes include discomfort, decreased sensitivity and ineffectiveness in preventing STIs, interrupting the mood, and assuming sickness or irresponsible and/or immoral behavior. We will also address both descriptive norms (ie, perceived prevalence of behaviors in YMSM’s social network) and personal norms (ie, anticipated regret), as YMSM’s norms may be highly influential on individual attitudes during this developmental period. Finally, we also address YMSM’s perceived behavioral control, recognizing that their ability to engage in risk reduction behaviors may vary across partner types (eg, romantic interest, casual partner, friends with benefits).

Although IBM has invaluable strengths, individuals with conflicting affective and cognitive motivations report less correspondence between their intentions and behavior [21-23]. Consequently, intervention also acknowledges that YMSM’s affective motivations may be health promotive (eg, relationship ideation) or risk enabling (eg, limerence). Building on our prior work, we hypothesize that YMSM reporting greater relationship ideation [24] will report fewer HIV/AIDS risk behaviors (ie, health promotive affective motivations). In addition, we include anticipated regret [25,26] (ie, anticipation of an emotional reaction following an unintended behavior) as a health promotive construct, as it has been associated with fewer risk-taking behaviors among MSM [27]. However, we also hypothesize that YMSM who experience greater limerence [28] and who believe that foregoing condoms with their partners will create intimacy, love, and trust (decisional balance) [28,29] may place stronger value on being in a relationship and, in turn, fuel HIV/AIDS risk behaviors (eg, more UAI partners and occasions). Therefore, in our intervention sessions, we address how affective motivations may influence YMSM’s decision-making regarding consistent condom use, UAI partnerships, and HIV/STI testing behavior. Finally, the model acknowledges that YMSM’s cognitive and affective motivations may be influenced by YMSM’s sexuality-related stressors (eg,

internalized homophobia), psychological distress (eg, depression, anxiety, loneliness, low self-esteem), and substance use and abuse [10]. These risk correlates may influence YMSM's ability to regulate their affective motivations and to engage in risk reduction behaviors due to limited behavioral control (eg, impairment due to being drunk or high). In sum, as shown in Figure 2, this cognitive-affective decision-making model offers a strong, theoretically-driven foundation to inform our intervention.

Figure 2. Conceptual model informing the myDEx intervention.



Intervention Arm

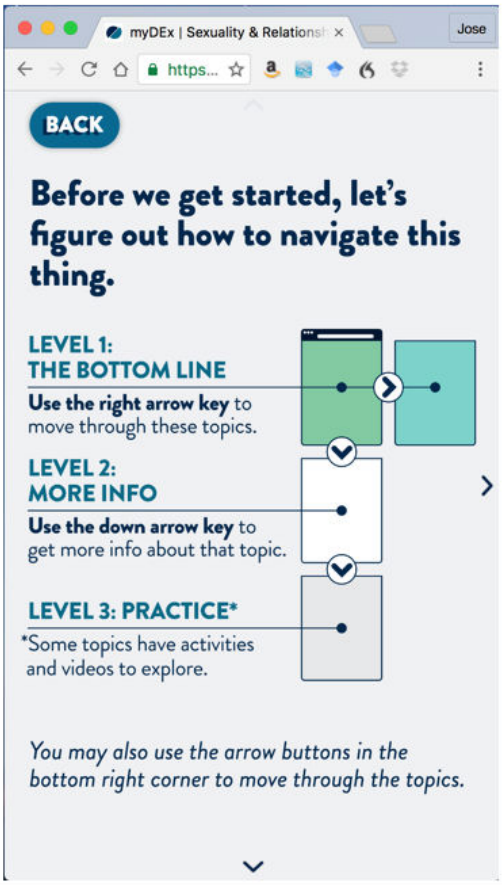
The proposed intervention consists of a 6-session, Web-based program (myDEx). Each session's modular content is delivered through interactive, tailored story-telling, case scenarios, motivational interviewing strategies, and graphics and videos. Cognizant of challenges maintaining users' attention in a Web app and to facilitate delivery through a mobile phone with app capabilities, we designed each session to keep users engaged for 10 minutes. Tailored content maximizes content persuasiveness and relevance and facilitates behavior change by enhancing message processing and message impact through personalization, content matching, and feedback. Personalization increases a user's attention to the message by raising awareness to customization of content (eg, "Based on your answers…") and making it more meaningful (eg, refer to the participants' behaviors, match photographs to age group and race/ethnicity). Content matching is a way to target factors known to influence behavior change by providing users with relevant information designed to support positive behaviors. Feedback about participants' answers increases attention and impact through self-referential thinking, comparative feedback (eg, "Compared to others...") to validate positive beliefs and adjust errors in normative beliefs, and provides evaluative opportunities linked to individuals' underlying values and motivations.

Within each session, participants have access to brief activities designed to build their HIV risk reduction skills and promote self-reflection about YMSM's sexual health and partner-seeking behaviors. Interactive activities include (1) role-play scenarios regarding condom use negotiation; (2) a diary to log their dating experiences throughout the study; (3) quizzes regarding their ideal relationships, including short-term and long-term relationships; and (4) opportunities for users to develop dating strategies. Online modules and activities can be repeated so that YMSM may compare whether their answers are consistent with the tailored suggestions and revisit content and/or revise their answers to reinforce the material.

Participants must complete the first session before they can access the other 5 sessions and interactive features. Session 1 ("Sexuality & Relationships") serves as an introduction and focuses on the importance of feeling comfortable talking about sexuality, relationship desires, and health. This session focuses on acknowledging and normalizing YMSM's affective motivations and foreshadowing where participants can learn more about different topics of interest within the remaining 5 sessions of the intervention. Session 2 ("Desires & Behaviors") transitions into a discussion regarding different relationship types (eg, romantic relationships, friends with benefits, hookups) and sexual decision-making. It highlights the importance of knowing what kind of relationship one desires, in both the short-term and long-term, and the role of sex in exploring these

relationships with different types of partners. Session 3 ("What makes good sex") provides a comprehensive sex education review focused on same-sex behaviors, including the importance of sex positivity, varying sexual practices, and sexual consent. Session 4 ("Sexual well-being") reinforces how to reduce HIV and STI risks when engaging in anal sex, including clarification on what lubricants and condoms are best suited for anal intercourse, facts about HIV and STI transmission, and the importance of status disclosure prior to sex. Session 5 ("Getting the sex you want") provides opportunities for YMSM to learn strategies to improve their sexual communication with partners before, during, and after sex. This session includes how to discuss HIV testing history and status awareness with prospective partners online, how to ensure their physical safety when meeting a new partner, and the value of discussing condoms and PrEP with partners. Session 6 ("Your body, your health") summarizes key messages from prior modules and offer HIV/STI testing resources and PrEP locations in their area. The main menu and final navigation instructions for the intervention is shown in Figure 3.

Figure 3. myDEx home screen and navigation instructions.



Control Arm

We created a 6-session, Web-based attention-control comparison to match myDEx in time and attention yet containing have non-tailored and non-interactive content (NTHP). Session 1 ("What is HIV?") focuses on an introduction to HIV, including how it is transmitted and what can increase a person's risk of acquiring it. Session 2 ("HIV and the LGBTQ community") focuses on raising awareness of the HIV prevalence and incidence among YMSM in the United States. Session 3 ("HIV Risk") focuses on behavioral strategies that can be used to reduce HIV risk. Session 4 ("Sex & HIV") describes the HIV risks associated with oral and anal sex. Session 5 ("What about condoms & lube?") focuses on the importance of condoms and lubricant. Session 6 ("What about HIV medications?") presents an overview of PrEP.

Our attention-control condition allows us to avoid confounding due to content (ie, comparing myDEx to a non-HIV "health promotion" intervention) and ensures that all YMSM receive some HIV prevention content given their high vulnerability to HIV (Figure 4). Further, this comparison will help us critically examine the extent to which tailoring increases YMSM's acceptability to the program, beyond having a non-tailored, non-interactive intervention. We acknowledge that the comparison condition will make it harder to detect an intervention effect in our outcome assessments; however, our pilot trial's primary goal is to test the intervention's feasibility and acceptability, and subsequently estimate critical parameters that may be required for adequate power estimation in a subsequent large-scale RCT trial.

Figure 4. Home screen of the control condition.

Feasibility and Acceptability Outcomes

The study assesses feasibility by examining (1) time to recruit 180 YMSM to the intervention; and (2) retention of rate across study arms. Intervention acceptability data are collected at the 30-day follow-up assessment. We use the following different assessments: (1) self-intervention evaluation form (SEF) [30]; and (2) Client Satisfaction Questionnaire (CSQ-8) [31]. The SEF is a brief, 13-item questionnaire that elicits information about the participant's experience with the intervention (ie, was the intervention interesting, was it relevant to their life, did they learn from the intervention). The CSQ-8 is used at the completion of the intervention and at the 30-day and 90-day follow-up surveys to assess YMSM's satisfaction with the intervention, including the content, site layout and design, and general satisfaction. These domains are assessed on a 4-point response scale with individually-specified anchors. The CSQ-8 has demonstrated high internal consistency across a large number of studies [32]. The SEF and CSQ-8 take approximately 10 minutes to complete.

We also track users' actions in the intervention as process evaluation data. These data include the number of times they visit the site, their geographic location and the website from which they linked to our site, time spent in each session, number of times a user returns to a session, and which interactive features were "clicked on" during sessions. In addition, we ascertain participants' acceptability and satisfaction of each session after it is viewed using the SEF.

Behavioral Outcomes

We measure the change in number of risky sexual partnerships and change in HIV testing behavior as our primary outcome measures via the baseline, 30-, 60-, and 90-day online surveys.

Sexual Behaviors

We use the Sexual Practices Assessment Schedule (SPAS) [33] to quantify the number of occasions of different sexual acts (oral, anal, receptive, and insertive) with different partner types. SPAS allows us to estimate the number of unprotected anal intercourse partners and occasions across partner types, as well as the proportion of instances when condoms were not used [28,34,35]. SPAS also ascertains YMSM's use of condoms during the past 30 days, whether they knew whether their partners were on PrEP, and whether they knew their partners' HIV status prior to sex.

HIV/STI Testing Behaviors

We ask YMSM to indicate the date of their most recent HIV and STI tests. Subsequently, we ask participants to note if they have received a medical diagnosis as having one or more STIs in their lifetime and the date of their most recent STI test if available. In each follow-up survey, we ask participants whether they have gone to get tested for HIV and/or STIs in the prior 30 days. If tested, participants are asked to indicate what tests they received and whether they had been medically diagnosed as having HIV or a STI. At follow-up, we ask YMSM whether they have had any changes in their HIV status. Newly diagnosed cases are asked if they were linked to care.

Secondary measures are also being measured in our study.

Motivations to Engage in HIV Prevention Behaviors

We measure YMSM's attitudes, subjective norms, and self-efficacy using previously tested scales with MSM. We use existing items measuring condom use intentions with different partner types and self-efficacy to negotiate condoms with different partner types [36-39]. We also measure PrEP awareness, uptake, and adherence during the study.

Substance Use Prior To or During Sex

We assess alcohol, tobacco, and other drugs (ATOD) use over the past 30 days. We then assess the use of alcohol and/or illicit drug use prior or during sex.

Psychological Well-Being

We measure depression and anxiety symptoms as markers of psychological distress. Depression (6 items) and anxiety (6 items) symptoms in the past week are measured using the Brief Symptom Inventory [40].

Statistical Analysis

Prior to conducting multivariable analyses, we examine study variables using descriptive statistics and test for differences across demographic characteristics (eg, race and/or ethnicity, age, education) using *t* tests, analysis of variance (ANOVA), and chi-square analysis, as appropriate. Systematic baseline differences are not expected due to randomization; however, in the event that some parameters differ across conditions at baseline, they will be included as covariates in subsequent analyses. We calculate descriptive summary statistics corresponding to the study variables at each visit to understand any temporal patterns, as well as compare the 2 treatment groups in terms of average change from baseline to post-intervention.

Trial Registration, Ethics, Consent, and Institutional Board Approval

The research and ethics presented in this study have been reviewed and approved by the University of Michigan Institutional Review Board (HUM00091627). The University of Pennsylvania ceded regulatory oversight to the University of Michigan. The study is also registered on ClinicalTrials.gov (NCT02842060).

Results

myDEx was launched in November 2016 and is ongoing. Initially, 23,365 individuals visited the study site and 1230 were screened for eligibility. Of the 392 eligible participants, some did not start the baseline survey (3.8%, 15/392) or did not finish the baseline survey (7.9%, 31/392). Of the 263 participants who completed the baseline survey, 31.6% (83/263) were disqualified due to having duplicate accounts or having falsified their identity (eg, cis-gender women).

We enrolled and randomized 180 YMSM into the trial (Figure 5). The majority of the participants are white (66.7%, 120/180), followed by multiracial (16.1%, 30/180), black (10.0%, 18/180), Asian (5.6%, 10/180), and Middle Eastern (0.6%, 1/120) or Native American (0.6%, 1/120). In addition, 30.0% (54/180) of the sample reported being Hispanic/Latino. Of the 120 individuals in the intervention arm, 51.7% (62/120) identify as non-Hispanic white; 50.0% (30/60) of the control arm identify as Non-Hispanic white. No differences are observed by arm for race and/or ethnicity (χ^2_4 = 0.53; *P*=.97). The mean age of participants is 21.67 (SD 1.81), with no differences observed by arm ($t_{(179)}$ = 1.05; *P*=.30). The majority of participants identify as gay (88.3%, 159/180) followed by bisexual (7.8%, 14/180) and queer (3.9%, 7/180). There are no differences between treatment arms (χ^2_2= 1.40; *P*=.50).

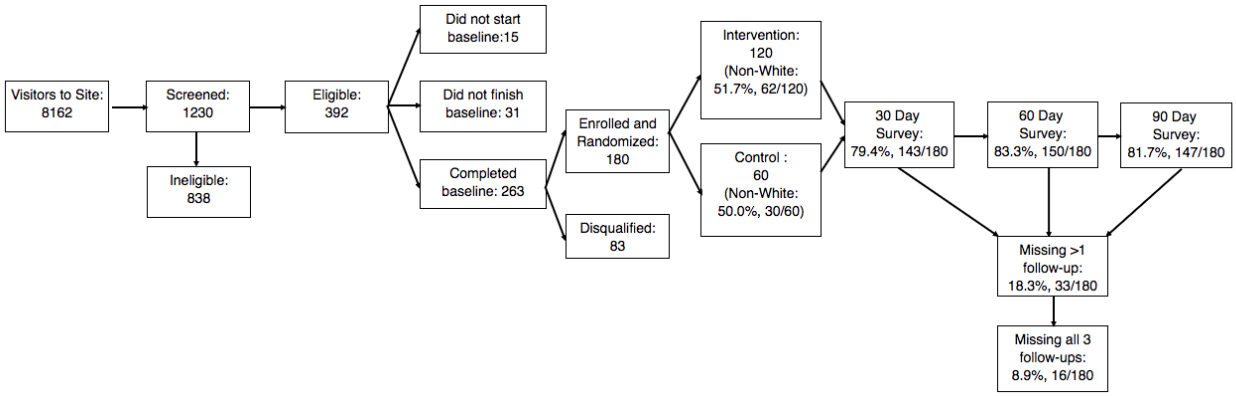
The follow-up assessments maintained high retention rates. The 30-day follow-up had a response rate of 79.4% (143/180). The 60-day follow-up had a response rate of 83.3% (150/180). The current 90-day response rate is 81.7% (147/180). Overall, we have at least 1 follow-up assessment for all study participants (ie, 9% of sample has not completed any follow-up assessment). Retention rates do not vary between treatment arms.

As we compared trial paradata to participants' self-reported behavioral surveys, we discovered that 25 (41%, 25/60) of the

control participants inadvertently accessed the intervention content through a programming error in the automated reminder emails meant to encourage continued engagement with the site. Given the cross-arm contamination, we excluded these control cases from future trial analyses between arms (N=35 control; N=120 intervention). The 25 excluded cases do not affect our randomization; we observe no sociodemographic differences between the revised control arm and intervention arm across age (t_{153} = –.80; *P*=.43), racial/ethnic minority status (χ^2_1= .10; *P*=.75; N=155), educational attainment (t_{153}= –1.24; *P*=.22), or sexual orientation (χ^2_2 = 3.23; *P*=.20; N=155). Retention rates also do not vary.

Participant recruitment for myDEx is complete. Trial data are currently being analyzed and will be completed in mid-2018.

Figure 5. Recruitment and retention of myDEx participants.



Discussion

Principal Findings

Given YMSM's self-reported desire to access comprehensive sexual education through the Internet [41,42], often ranking the Web as their top resource to explore their sexuality, learn about MSM behavior, and refine their interests [41-44], designing and testing online HIV prevention interventions may present a number of advantages to reach and address the needs of YMSM. Online interventions can deliver tailored content to each user's HIV risk behaviors and context, be accessed conveniently by a participant, presented across various platforms (eg., mobile phones, tablets, laptops), and reduce reach and accessibility issues due to geography and/or socioeconomic barriers. Furthermore, online delivered content can be standardized, ensuring higher intervention fidelity, and be presented through interactive features. This protocol may serve to address YMSM's needs and offer insights on how to reduce their risk for HIV infection when seeking partners online.

Limitations

We did not include biological confirmation of HIV/STI status through serologic tests. At this early stage of intervention development and testing, the added cost of biological testing is not warranted. HIV testing will be included in a full-scale efficacy trial. We will not be able to use the 25 excluded control cases due to contamination. This is less of a concern to this pilot trial as our protocol aims do not seek to detect differences in this trial. Moving forward, we urge scholars to examine paradata files alongside their survey data to reduce the potential of unintentionally contamination due to unforeseen programming errors.

Conclusion

myDEx provides an opportunity to develop a culturally relevant evidence-based intervention for YMSM. Although there are in-person evidence-based interventions with proven efficacy, few HIV/STI prevention interventions delivered online exist for YMSM. Online interventions may ease access to comprehensive HIV/STI education among YMSM and allow personalized content to be delivered. myDEx aims to alleviate the gaps within HIV prevention for YMSM by utilizing tailored, Web-based content with the goal of developing skills for same-sex dating and relationship building, while reducing their risks for HIV/STI.

Acknowledgments

This study is supported by a R34 grant from the National Institutes of Mental Health (R34MH101997-01A1).Views expressed in this manuscript do not necessarily represent the views of the funding agency. This work would not have been possible without the programming support of the University of Michigan's Center for Health Communication Research, study participants, and our YAB. We thank Gage Gillard, John Shaver, and Tanaka Chavanduka for their assistance during the development of this project.

Conflicts of Interest

None declared.

References

1. Centers for Disease Control and Prevention. HIV Surveillance Report. 2016. Diagnoses of HIV infection in the United States and dependent areas, 2015 URL: https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-2015-vol-27.pdf [accessed 2017-07-01] [WebCite Cache ID 6rdD4ItOX]
2. Centers for Disease Control and Prevention. CDC Fact Sheet. Trends in U.S. HIV diagnoses, 2005-2014 URL: https://www.cdc.gov/nchhstp/newsroom/docs/factsheets/hiv-data-trends-fact-sheet-508.pdf [accessed 2017-07-01] [WebCite Cache ID 6rdDBdFXJ]
3. Health Services & Resources Administration. National HIV/AIDS Strategy for the United States: Updated to 2020. Washington, DC: Office of National AIDS Policy; 2015. URL: https://www.hiv.gov/sites/default/files/nhas-update.pdf [accessed 2017-07-11] [WebCite Cache ID 6rt0HfRN7]
4. Brooks-Gunn J, Paikoff R. Sexuality developmental transitions during adolescence. In: Schulenberg J, Maggs JL, Hurrelmann K, editors. Health Risks and Developmental Transitions During Adolescence. New York: Cambridge University Press; 1997:190-219.
5. Kubicek K, Carpineto J, McDavitt B, Weiss G, Iverson EF, Au C, et al. Integrating professional and folk models of HIV risk: YMSM's perceptions of high-risk sex. AIDS Educ Prev 2008 Jun;20(3):220-238 [FREE Full text] [doi: 10.1521/aeap.2008.20.3.220] [Medline: 18558819]
6. Pingel ES, Thomas L, Harmell C, Bauermeister J. Creating comprehensive, youth centered, culturally appropriate sex education: what do young gay, bisexual and questioning men want? Sex Res Social Policy 2013 Dec 01;10(4) [FREE Full text] [doi: 10.1007/s13178-013-0134-5] [Medline: 24348222]
7. Kubicek K, Carpineto J, McDavitt B, Weiss G, Kipke MD. Use and perceptions of the internet for sexual information and partners: a study of young men who have sex with men. Arch Sex Behav 2011 Aug;40(4):803-816 [FREE Full text] [doi: 10.1007/s10508-010-9666-4] [Medline: 20809373]
8. Eisenberg A, Bauermeister J, Johns MM, Pingel E, Santana ML. Achieving safety: safer sex, communication, and desire among young gay men. J Adolesc Res 2011 Sep 01;26(5):645-669 [FREE Full text] [doi: 10.1177/0743558411402342] [Medline: 21894239]
9. Bruce D, Harper GW, Fernández MI, Jamil OB, Adolescent Medicine Trials Network for HIV/AIDS Interventions. Age-concordant and age-discordant sexual behavior among gay and bisexual male adolescents. Arch Sex Behav 2012 Apr;41(2):441-448 [FREE Full text] [doi: 10.1007/s10508-011-9730-8] [Medline: 21290255]
10. Mustanski BS, Newcomb ME, Du Bois SN, Garcia SC, Grov C. HIV in young men who have sex with men: a review of epidemiology, risk and protective factors, and interventions. J Sex Res 2011 Mar;48(2-3):218-253 [FREE Full text] [doi: 10.1080/00224499.2011.558645] [Medline: 21409715]
11. Bauermeister JA. Sexual partner typologies among single young men who have sex with men. AIDS Behav 2015 Jun;19(6):1116-1128 [FREE Full text] [doi: 10.1007/s10461-014-0932-7] [Medline: 25358726]
12. Bazzi AR, Fergus KB, Stephenson R, Finneran CA, Coffey-Esquivel J, Hidalgo MA, et al. A dyadic behavioral intervention to optimize same sex male couples' engagement across the HIV care continuum: development of and protocol for an innovative couples-based approach (Partner Steps). JMIR Res Protoc 2016 Aug 25;5(3):e168 [FREE Full text] [doi: 10.2196/resprot.6271] [Medline: 27562905]
13. Bowen AM, Daniel CM, Williams ML, Baird GL. Identifying multiple submissions in Internet research: preserving data integrity. AIDS Behav 2008 Nov;12(6):964-973 [FREE Full text] [doi: 10.1007/s10461-007-9352-2] [Medline: 18240015]
14. Bauermeister J, Pingel E, Zimmerman M, Couper M, Carballo-Diéguez A, Strecher VJ. Data quality in web-based HIV/AIDS research: handling invalid and suspicious data. Field methods 2012 Aug 01;24(3):272-291 [FREE Full text] [doi: 10.1177/1525822X12443097] [Medline: 23180978]
15. Allison S, Bauermeister JA, Bull S, Lightfoot M, Mustanski B, Shegog R, et al. The intersection of youth, technology, and new media with sexual health: moving the research agenda forward. J Adolesc Health 2012 Sep;51(3):207-212 [FREE Full text] [doi: 10.1016/j.jadohealth.2012.06.012] [Medline: 22921129]
16. Bull SS, Vallejos D, Levine D, Ortiz C. Improving recruitment and retention for an online randomized controlled trial: experience from the Youthnet study. AIDS Care 2008 Sep;20(8):887-893. [doi: 10.1080/09540120701771697] [Medline: 18777217]
17. 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] [Medline: 16651505]
18. Power TE, Swartzman LC, Robinson JW. Cognitive-emotional decision making (CEDM): a framework of patient medical decision making. Patient Educ Couns 2011 May;83(2):163-169. [doi: 10.1016/j.pec.2010.05.021] [Medline: 20573468]
19. Slovic P, Peters E, Finucane ML, Macgregor DG. Affect, risk, and decision making. Health Psychol 2005 Jul;24(4S):S35-S40. [doi: 10.1037/0278-6133.24.4.S35] [Medline: 16045417]
20. Kalichman S. The theory of reasoned action and advances in HIV/AIDS prevention. In: Ajzen I, Albarracín D, Hornik R, editors. Predicting Change in a Health Behavior: Applying a Reasoned Action Approach. New Jersey: Lawrence Erlbaum Associates; 2007:265-272.

21. Kobbeltvedt T, Wolff K. The risk-as-feelings hypothesis in a theory-of-planned-behaviour perspective. Judgm Decis Mak 2009;4(7):567-586.
22. Loewenstein GF, Weber EU, Hsee CK, Welch N. Risk as feelings. Psychol Bull 2001;127(2):267-286. [doi: 10.1037//0033-2909.127.2.267]
23. Richard R, van der Pligt J, de Vries N. Anticipated affect and behavioral choice. Basic Appl Soc Psych 1996 Jun;18(2):111-129. [doi: 10.1207/s15324834basp1802_1]
24. Bauermeister JA. Romantic ideation, partner-seeking, and HIV risk among young gay and bisexual men. Arch Sex Behav 2012 Apr;41(2):431-440 [FREE Full text] [doi: 10.1007/s10508-011-9747-z] [Medline: 21394660]
25. Abraham C, Sheeran P. Acting on intentions: the role of anticipated regret. Br J Soc Psychol 2003 Dec;42(Pt 4):495-511. [doi: 10.1348/014466603322595248] [Medline: 14715114]
26. Kaiser F. A moral extension of the theory of planned behavior: norms and anticipated feelings of regret in conservationism. Pers Individ Dif 2006 Jul;41(1):71-81. [doi: 10.1016/j.paid.2005.11.028]
27. Franssens D, Hospers HJ, Kok G. Social-cognitive determinants of condom use in a cohort of young gay and bisexual men. AIDS Care 2009 Nov;21(11):1471-1479. [doi: 10.1080/09540120902883127] [Medline: 20024726]
28. Bauermeister JA, Ventuneac A, Pingel E, Parsons JT. Spectrums of love: examining the relationship between romantic motivations and sexual risk among young gay and bisexual men. AIDS Behav 2012 Aug;16(6):1549-1559 [FREE Full text] [doi: 10.1007/s10461-011-0123-8] [Medline: 22223300]
29. Bauermeister JA, Carballo-Diéguez A, Ventuneac A, Dolezal C. Assessing motivations to engage in intentional condomless anal intercourse in HIV risk contexts ("Bareback Sex") among men who have sex with men. AIDS Educ Prev 2009 Apr;21(2):156-168 [FREE Full text] [doi: 10.1521/aeap.2009.21.2.156] [Medline: 19397437]
30. Harper G, Contreras R, Bangi A, Pedraza A. Collaborative process evaluation. J Prev Interv Community 2003 Nov 10;26(2):53-69. [doi: 10.1300/J005v26n02_05]
31. Larsen DL, Attkisson CC, Hargreaves WA, Nguyen TD. Assessment of client/patient satisfaction: development of a general scale. Eval Program Plann 1979;2(3):197-207. [Medline: 10245370]
32. Attkisson C, Greenfield T. The Client Satisfaction Questionnaire-8. In: Maruish ME, editor. The Use of Psychological Testing for Treatment Planning and Outcomes Assessment. Second Edition. New Jersey: Lawrence Erlbaum Associates; 1999:1333-1346.
33. Carballo-Diéguez A, Dolezal C, Ventuneac A. Sexual Practices Assessment Schedule. New York: HIV Center for Clinical and Behavioral Studies, Columbia University and New York State Psychiatric Institute; 2002.
34. Bauermeister JA, Leslie-Santana M, Johns MM, Pingel E, Eisenberg A. Mr. Right and Mr. Right Now: romantic and casual partner-seeking online among young men who have sex with men. AIDS Behav 2011 Feb;15(2):261-272 [FREE Full text] [doi: 10.1007/s10461-010-9834-5] [Medline: 20953689]
35. Bauermeister JA, Yeagley E, Meanley S, Pingel ES. Sexting among young men who have sex with men: results from a national survey. J Adolesc Health 2014 May;54(5):606-611 [FREE Full text] [doi: 10.1016/j.jadohealth.2013.10.013] [Medline: 24361235]
36. Lightfoot M, Song J, Rotheram-Borus MJ, Newman P. The influence of partner type and risk status on the sexual behavior of young men who have sex with men living with HIV/AIDS. J Acquir Immune Defic Syndr 2005 Jan 01;38(1):61-68. [Medline: 15608527]
37. van EP, Kok G, Jansen MW, Hoebe CJ. The additional value of anticipated regret and psychopathology in explaining intended condom use among drug users. AIDS Care 2001 Jun;13(3):309-318. [doi: 10.1080/09540120120043964] [Medline: 11397333]
38. van Kesteren NM, Hospers HJ, van Empelen P, van Breukelen G, Kok G. Sexual decision-making in HIV-positive men who have sex with men: how moral concerns and sexual motives guide intended condom use with steady and casual sex partners. Arch Sex Behav 2007 Jun;36(3):437-449 [FREE Full text] [doi: 10.1007/s10508-006-9125-4] [Medline: 17333328]
39. Misovich SJ, Fisher JD, Fisher WA. Close relationships and elevated HIV risk behavior: evidence and possible underlying psychological processes. Rev Gen Psychol 1997;1(1):72-107. [doi: 10.1037/1089-2680.1.1.72]
40. Derogatis LR, Melisaratos N. The Brief Symptom Inventory: an introductory report. Psychol Med 1983 Aug;13(3):595-605. [Medline: 6622612]
41. Grov C, Breslow AS, Newcomb ME, Rosenberger JG, Bauermeister JA. Gay and bisexual men's use of the Internet: research from the 1990s through 2013. J Sex Res 2014;51(4):390-409 [FREE Full text] [doi: 10.1080/00224499.2013.871626] [Medline: 24754360]
42. Harper G, Bruce D, Serrano P, Jamil O. The role of the internet in the sexual identity development of gaybisexual male adolescents. In: Hammack PL, Cohler BJ, editors. The Story of Sexual Identity: Narrative Perspectives on Gay and Lesbian Life Course. New York: Oxford University Press; 2009:297-326.
43. Garofalo R, Herrick A, Mustanski BS, Donenberg GR. Tip of the iceberg: young men who have sex with men, the Internet, and HIV risk. Am J Public Health 2007 Jun;97(6):1113-1117. [doi: 10.2105/AJPH.2005.075630] [Medline: 17463378]
44. Mustanski B, Lyons T, Garcia SC. Internet use and sexual health of young men who have sex with men: a mixed-methods study. Arch Sex Behav 2011 Apr;40(2):289-300 [FREE Full text] [doi: 10.1007/s10508-009-9596-1] [Medline: 20182787]

Abbreviations

AIDS: acquired immunodeficiency syndrome
CSQ: Client Satisfaction Questionnaire
HIV: human immunodeficiency virus
IBM: Integrated Behavior Model
LGBTQ: lesbian, gay, bisexual, trans, and queer
MSM: men who have sex with men
NTHP: non-tailored HIV prevention
PrEP: pre-exposure prophylaxis
RCT: randomized controlled trial
SEF: self-intervention evaluation forms
SPAS: Sexual Practices Assessment Schedule
UAI: unprotected anal intercourse
YAB: youth advisory board
YMSM: young men who have sex with men

Edited by G Eysenbach; submitted 02.05.17; peer-reviewed by L Hightow-Weidman, L Lavorgna, D Levine; comments to author 31.05.17; accepted 05.06.17; published 19.07.17.

Please cite as:
Bauermeister JA, Tingler RC, Demers M, Harper GW
Development of a Tailored HIV Prevention Intervention for Single Young Men Who Have Sex With Men Who Meet Partners Online: Protocol for the myDEx Project
JMIR Res Protoc 2017;6(7):e141
URL: http://www.researchprotocols.org/2017/7/e141/
doi:10.2196/resprot.7965
PMID:28724513

Protocol

Comparing Mobile Health Strategies to Improve Medication Adherence for Veterans With Coronary Heart Disease (Mobile4Meds): Protocol for a Mixed-Methods Study

Linda G Park[1], PhD, MSc, FNP-C; Eileen G Collins[2], PhD, RN; Janet K Shim[3], PhD, MPP; Mary A Whooley[4], MD

[1]Department of Veterans Affairs, Community Health Systems, University of California, San Francisco, San Francisco, CA, United States

[2]Edward Hines Jr., VA Hospital, Department of Biobehavioral Health Science, University of Illinois at Chicago, Chicago, IL, United States

[3]University of California, San Francisco, Social and Behavioral Sciences, San Francisco, CA, United States

[4]Department of Veterans Affairs, Department of Medicine, Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, CA, United States

Corresponding Author:
Linda G Park, PhD, MSc, FNP-C
Department of Veterans Affairs
Community Health Systems
University of California, San Francisco
2 Koret Way, Box 0608
Room 531A
San Francisco, CA, 94143
United States
Phone: 1 415 502 6616
Fax: 1 415 476 6042
Email: linda.park@ucsf.edu

Abstract

Background: Adherence to antiplatelet medications is critical to prevent life threatening complications (ie, stent thrombosis) after percutaneous coronary interventions (PCIs), yet rates of nonadherence range from 21-57% by 12 months. Mobile interventions delivered via text messaging or mobile apps represent a practical and inexpensive strategy to promote behavior change and enhance medication adherence.

Objective: The Mobile4Meds study seeks to determine whether text messaging or a mobile app, compared with an educational website control provided to all Veterans, can improve adherence to antiplatelet therapy among patients following acute coronary syndrome (ACS) or PCI. The three aims of the study are to: (1) determine preferences for content and frequency of text messaging to promote medication adherence through focus groups; (2) identify the most patient-centered app that promotes adherence, through a content analysis of all commercially available apps for medication adherence and focus groups centered on usability; and (3) compare adherence to antiplatelet medications in Veterans after ACS/PCI via a randomized clinical trial (RCT).

Methods: We will utilize a mixed-methods design that uses focus groups to achieve the first and second aims (N=32). Patients will be followed for 12 months after being randomly assigned to one of three arms: (1) customized text messaging, (2) mobile app, or (3) website-control groups (N=225). Medication adherence will be measured with electronic monitoring devices, pharmacy records, and self-reports.

Results: Enrollment for the focus groups is currently in progress. We expect to enroll patients for the RCT in the beginning of 2018.

Conclusions: Determining the efficacy of mobile technology using a Veteran-designed protocol to promote medication adherence will have a significant impact on Veteran health and public health, particularly for individuals with chronic diseases that require strict medication adherence.

Trial Registration: ClinicalTrials.gov NCT03022669

(JMIR Res Protoc 2017;6(7):e134) doi:10.2196/resprot.7327

KEYWORDS

text messaging; mobile application; mobile health; cardiovascular disease; medication; adherence

Introduction

Coronary Heart Disease and Medication Adherence

Coronary heart disease is the leading cause of death in Veterans and affects 15.5 million people in the United States [1,2]. Although coronary heart disease claims the lives of one out of every seven Americans [2], the decline in acute coronary syndrome (ACS) and coronary heart disease-related deaths over the past four decades has been attributed to the availability of critical pharmacologic and invasive therapies (ie, percutaneous coronary intervention [PCI]) [3-6]. After PCI with drug-eluting stents, premature discontinuation of antiplatelet (thienopyridine) medications is strongly associated with in-stent thrombosis, leading to myocardial infarction (MI) and death [7,8]. Despite the critical nature of taking antiplatelet medications to prevent life-threatening complications, one in seven MI patients treated with drug-eluting stents no longer take antiplatelet medications at 30 days [8].

Medication nonadherence is a pervasive public health problem among Veterans and non-Veterans [9-12]; however, Veterans suffer from increased morbidity and mortality from chronic diseases compared to non-Veterans [13]. Medication nonadherence is the number one problem in treating illnesses, as more than half of individuals with chronic diseases do not take any or all of their medications correctly [14,15]. Medication nonadherence in patients with coronary heart disease is closely linked to adverse clinical outcomes such as rehospitalization and mortality [16-18]; therefore, effective strategies are needed to improve adherence behaviors. Moreover, medication nonadherence results in an estimated US $290 billion in health care costs in the United States and is a tremendous burden on the health care system [19]. Mobile technology may represent an effective strategy to improve medication adherence during the critical time period of one year post-ACS/PCI.

Mobile Health

In the past decade, mobile health (mHealth) has been introduced as a mechanism to enhance medication adherence and demonstrates strong potential to promote behavior change. The use of technology can facilitate adoption and integration of medication adherence by promoting behavioral strategies via health messaging, emphasizing healthy habits, tracking goals, and giving incentives for behavior change [20]. While other behavioral and educational strategies have had disappointing results in adherence and treatment outcomes over many decades [21,22], the use of technology may provide an innovative, practical, personalized, and inexpensive approach to promote medication adherence. Diverse solutions are required with tailored theory-based interventions for different populations and conditions because the reasons for medication nonadherence are complex and multifactorial [23,24]. Experts agree that a patient-centered approach is critical to increase patients' knowledge about medication management [25].

Both text messaging and mobile apps are two popular forms of mHealth that provide convenient, inexpensive, and nonintrusive engagement with individuals. The use of mobile technology can particularly benefit those who have significant barriers to taking medications, such as confusion about which medications to take, forgetfulness, and lack of social support. Text messaging is more widely used by all age groups; however, mobile apps offer many more features than text messaging, and can harness the full sensing and computational capacity of mobile devices to collect and analyze health-related data in real time to deliver health and behavioral interventions [20,26].

Text messaging is popular, fast, direct, efficient, user-friendly, traceable, and provides easy data transfer [27]. Text messaging is also nonintrusive, relatively simple, and lower in cost compared to mobile voice communication [28]. In a systematic review of medication adherence studies using text messaging, we found that most interventions (18/29) resulted in improved medication adherence [29]. This review did not examine any studies related to coronary heart disease, but gaps in the literature were discussed, such as understanding factors that are needed to maintain engagement (eg, content and frequency of text messaging). In contrast to text messaging, apps can offer interactivity, gaming, and feedback. Apps have the advantages of delivering interventions to an unlimited number of individuals in a cost-effective manner with favorable cost utility [30]. While Internet interventions can be delivered via traditional desktop and laptop computers, users have the capacity to interact with mobile interventions more frequently and in the context of the behavior of interest [31]. The trend of desktop use for research/program interventions is sharply declining in our current generation, given that most people carry and access their mobile phones throughout the day for various reasons. Using real-time sensing technologies available on mobile phones, health behavioral change interventions can be delivered based on time/location, psychological state, physiological state, social context, activity level, and patterns [32].

Preliminary Studies

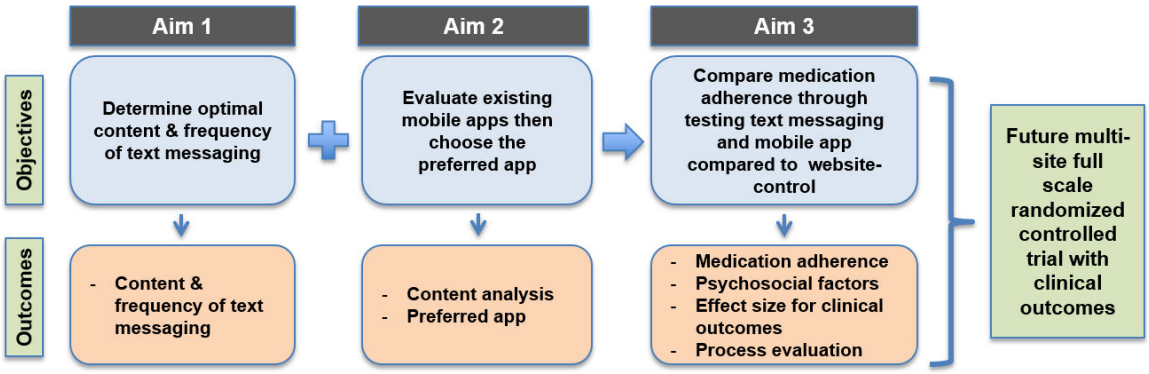
In a pilot randomized controlled trial (RCT) from 2012-2013, we compared antiplatelet and statin adherence among patients with coronary heart disease in a 30-day study who received: (1) text messaging for medication reminders and education, (2) educational text messaging only, or (3) no text messaging [33]. Among 90 patients (76% male, mean age 59.2 years), electronic devices revealed that patients who received text messaging for antiplatelets had a higher percentage of correct doses taken (P=0.02), percentage number of doses taken (P=0.01), and percentage of prescribed doses taken on schedule (P=0.01) [33]. Text messaging response rates were higher for antiplatelets than statins (P=0.005), and self-reported adherence revealed no significant differences among groups [33]. We concluded that the use of text messaging for the medication reminders/education and education text messaging only groups (compared to no text messaging for the control group) increased adherence to antiplatelet therapy by 15% to 17%, respectively. We established

feasibility and high satisfaction and concluded that mHealth interventions show promise in promoting medication adherence.

Aims

The proposed research study, Mobile4Meds, seeks to determine whether text messaging or a mobile app (compared with an educational website control provided to all Veterans) can improve adherence to antiplatelet therapy among patients post-ACS/PCI. There are three topics and aims of this proposed study. First, using *Text Messaging* we aim to determine preferences for content and frequency of text messaging to promote medication adherence. Second, using *Mobile Apps* we aim to identify the most patient-centered (user-friendly, engaging, personalized) mobile app that promotes medication adherence with stratification by low/high mobile phone use and sex. Finally, we aim to examine *Medication Adherence* by comparing adherence to antiplatelet medications upon hospital discharge from ACS/PCI via: (1) text messaging, (2) mobile app, or (3) website-control. Figure 1 illustrates the aims, objectives, and outcomes of the proposed research study. Our long-term goal is to conduct a multi-site full scale RCT to determine clinical outcomes of emergency department utilization, rehospitalization, and cardiovascular (and all-cause) morbidity and mortality.

Figure 1. Aims, objectives, and outcomes.



Methods

Theoretical Framework/Behavioral Change Model

To date, most mHealth studies have not been based on behavioral health theories [29,31]. In a systematic review of text messaging studies on medication adherence in various acute and chronic conditions, we found that only 5 of 29 studies used theory to guide research [29]. Numerous precipitating factors and barriers affect medication adherence, and this complex process can be better understood when examining theoretical relationships and process. The conceptual model that explains the relationship between variables in this study is depicted in Figure 2. No single theory can completely explain the processes that lead to medication adherence, so we will use a theory-informed approach to complete the aims for this study. We will explore the general components of theory that are closely linked with behavioral change interventions (eg, perceived norms/threats, health beliefs, self-efficacy, cues to actions).

Figure 2. Conceptual model of behavior change for medication adherence.

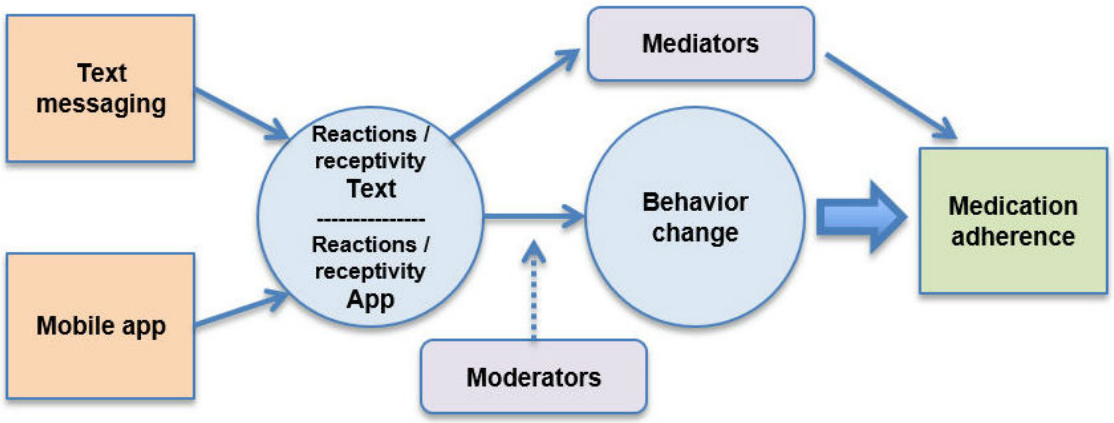
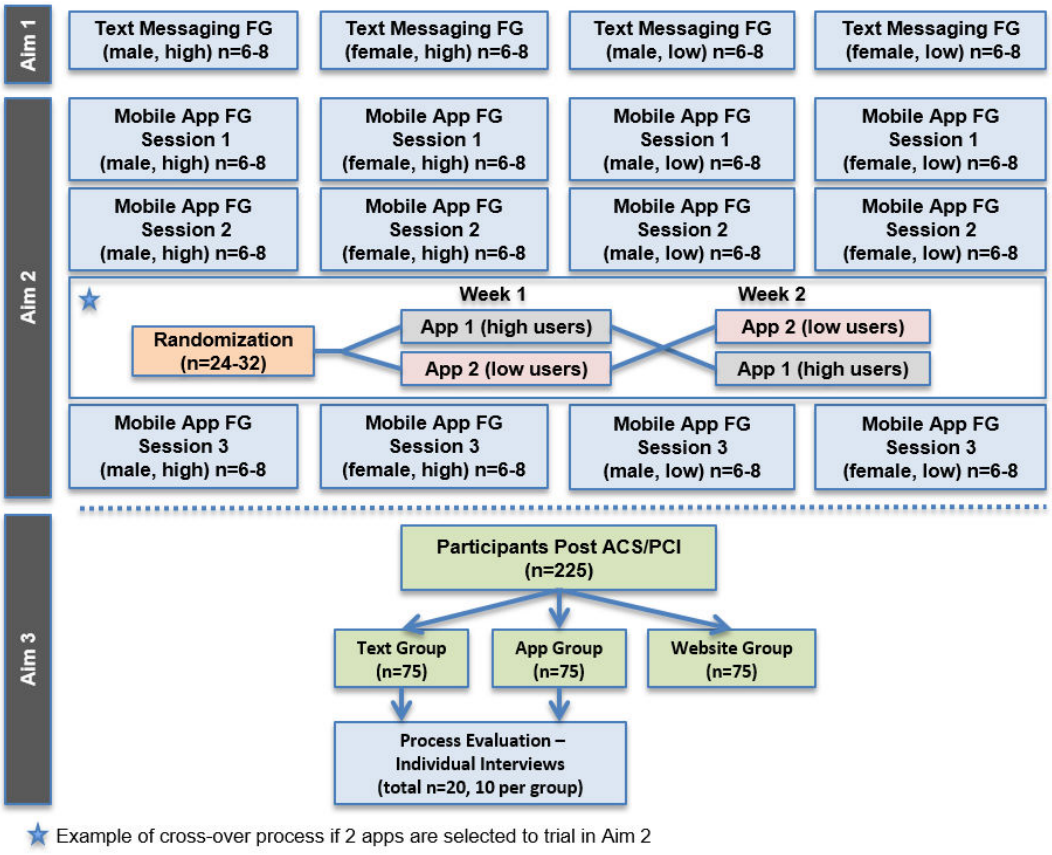


Figure 3. Overview of study structure and sample. FG: focus group.



Research Design

Mobile4Meds is a mixed-methods study using both qualitative and quantitative research methods. Engaging patients initially through qualitative methods will provide opportunities for: (1) better translation, dissemination, and use of research results; (2) better evidence to inform guidelines; (3) targeted quality improvement; and (4) using research to address concerns of diverse patients [34]. Figure 3 provides an overview of the study structure and participants involved in each of the aims.

Aim 1: Text Messaging Focus Groups

Design, Sample, Setting

We will use focus groups to fulfill the objectives of Aim 1. Each focus group will have 6-8 participants, which is a size that allows for easy exchanges of ideas and a diversity of perspectives to be represented. We will recruit a convenience sample of 24-32 participants for four focus groups. Aims 1 and 2 will include the same participants who will attend a total of four focus group sessions (Figure 3).

The participants from San Francisco Veterans Affairs Medical Center (SFVAMC) are likely to be predominantly male; therefore, we will likely recruit one group of female Veterans from SFVAMC and one focus group of female non-Veterans from John Muir Medical Center (JMMC) in the East Bay. The four groups will account for variability in mobile phone use (low/high) and sex. Inclusion criteria for Aims 1 and 2 include: (1) >21 years of age, (2) history of ACS or PCI within one year, and (3) current/former antiplatelet (thienopyridine) prescription. Exclusion criteria are: (1) cognitive impairment, and (2) lack of English proficiency/literacy.

Methods

Preliminary Development of Text Messaging

We will explore different content for the development of a text messaging intervention to determine the ideal tailored messages for delivery in the RCT (Aim 3). After studying various behavioral change theories and frameworks, we will create a text messaging intervention with the underpinnings of common behavioral change theories. A library of 80-100 sample text messages that apply personalized content will be created to enhance medication adherence. We found that education alone increased medication adherence in prior studies, so we will deliver cardiovascular risk reduction messages along with messages regarding medications. Topics will include medications, diet, exercise, risk factors for coronary heart disease (eg, smoking, obesity), depression, stress management, and preventive care. Participants will choose the frequency and timing of text messaging. An example of an automated medication text messaging may be, “John, take your Plavix 75mg at 9am. Confirm with 1.”

Recruitment

We will distribute written materials such as flyers and brochures to advertise voluntary participation in the research study. The research team (principal investigator and research assistant [RA]) will consult with the cardiac rehabilitation staff at

SFVAMC and JMMC to identify individuals who are willing to participate in a research study. The research team will meet with interested individuals and provide verbal and written explanation of the study. Participants will sign a written informed consent document.

Group Assignment

Upon recruitment into the study, participants will complete a sociodemographic questionnaire and a brief survey that will determine if he/she is a *low* or *high* mobile phone user. Separating participants into groups will help facilitate identification of common ideas and goals that low/high mobile phone users and men/women may address during the focus groups. We will use maximum variation sampling to ensure variability in age, gender, ethnicity, and low/high mobile phone use.

Focus Groups

In Aim 1, the focus group sessions will address ideal content and frequency of text messaging. First, we will give an introduction of the study aims and purpose of the focus group. Second, we will discuss the needs, preferences, perceived facilitators, and perceived barriers of using text messaging for medication adherence. Third, we will review sample text messaging, and we will ask participants which content and frequency of text messaging are the most effective and least intrusive. Finally, all participants will be able to suggest text messaging to create the most personalized messages.

Data Collection

All focus groups will be audiotaped, and the RA will take field notes on individual and group reactions that are not captured by the recording. We will complete field notes at the conclusion of each session, and all sessions will be transcribed verbatim.

Analysis

Thematic analysis will include reading and coding the completed field notes and interview transcripts. We will create an initial set of codes that account for the study aims and other topics that emerge from the data. Some codes will be generated deductively, while others will be generated inductively based on themes and issues that emerge from ongoing coding. We will compare coding, resolve differences, and revise the coding scheme. We will assess intercoder reliability by having 10% of the data cross-coded. The key outcomes will be content and frequency of text messaging, particularly focusing on how preferences vary across groups. We will use ATLAS.ti (Thousand Oaks, CA) for all qualitative analyses to determine the preferred app for Aim 3.

Aim 2: Mobile Apps: Focus Groups

Design, Sample, and Setting

Aim 2 consists of Aim 2a (*content analysis*) and Aim 2b (*usability testing*). The usability study will include the same individuals from the focus groups in Aim 1 who are stratified by low/high mobile phone use and sex, to accommodate easy exchanges of ideas and a diversity of perspectives. In contrast to Aim 1, there will be three focus group sessions to fulfill Aim 2. Recruitment, group assignment, and data collection will be the same for Aim 2a and Aim 2b.

Aim 2a – Content Analysis

Methods

We will conduct a content analysis approximately three months prior to the focus groups. The first phase will involve a comparative, descriptive assessment of smartphone apps in the categories of health and medications. To ensure a comprehensive search, the research team will search for medication adherence-oriented apps, provider websites, and app sources that are available in Apple iTunes, Android Marketplace, and Blackberry App World Store.

We will provide a comparative, descriptive assessment of the top 10 smartphone apps related to medication adherence. The content analysis will examine whether each app applies constructs from behavioral change theory. We will assess each of the selected apps using a validated behavioral theory content survey by Doshi et al [35]. The survey assesses the presence of essential constructs of four major theories of behavior change: Health Belief Model, Transtheoretical Model, Theory of Reasoned Action/Planned Behavior, and Social Cognitive/Social Learning Theory [35]. After content analysis is completed, we will rank the top 10 medication adherence apps and record usability, application of theory, user reviews, star ratings, and the total number of downloads.

Analyses

We will analyze the content analysis by following the scoring instructions of the Behavioral Theory Content Survey for the top 10 mobile apps [35]. The Behavioral Theory Content Survey will include 20 items from the following domains listed in Table 1. Mean survey score and standard deviation (SD) will be computed across the top 10 apps based on a total of 20 items from the 5 domains, each accounting for 1 point (yes=1, no=2) [35]. We will then provide a descriptive evaluation of the apps based primarily on survey scores (mean, SD) and subsequent rankings [36]. Interacting with the mobile app will include a dynamic process of iterative adjustments in response to user input, key features, and functionality that may not be apparent upon initial use and subsequent input [36].

Table 1. Behavioral strategies included in the Behavioral Theory Content Survey [35,36].

Domain	Example
1. Knowledge	General information
2. Cognitive strategies	Perceived benefits/barriers/risks, self-efficacy
3. Behavioral strategies	Self-monitoring, time management, social support
4. Emotion-focused strategies	Stress management
5. Therapeutic interventions	Motivational readiness

Aim 2b - Usability Testing: Methods

Mobile App Focus Groups – Session 1 (Formative Stage)

After the research team identifies the top 10 medication reminder apps through content analyses, the focus group for Session 1 will help to determine the top 2-4 apps the participants will use for one week at a time. Four different groups will be stratified by low/high mobile phone use and sex (Figure 3). We will briefly demonstrate the apps for participants on a large screen and ask participants to engage with the preloaded apps on our research smartphones. We will assess participants' impressions of the apps and ask them to score the apps (range 1-5) so we can determine the ideal number of apps to trial from the distribution of rankings. Participants' comments and overall scores will help determine the preferred apps.

Session 2 (Exploratory Stage)

During the focus group for Session 2, the majority of time will be spent on group assessment of overall experience with mobile apps in general. After the group assessment, we will include introduction of the preselected apps from Session 1. The selected apps from Session 1 will be downloaded to the patients' mobile phones devices. Patients will spend approximately 10-15 minutes experimenting with and evaluating the selected apps. We will conduct observations of patients as they interact with the mobile apps. Participants will be randomly assigned to use the first app in Session 2 and use that app for one week, then switch to the other app(s) in subsequent weeks. Figure 3 displays a scenario in which participants will be randomly assigned to use two mobile apps for two weeks; however, participants may trial between 2-4 mobile apps for one week each, depending on the results of the Mobile App Session 1 focus groups.

Participants will record impressions in a diary while using the apps. We will contact the participants by text/email/phone-call/visit within two days after using each mobile app to troubleshoot any difficulties. At the start of each week, we will contact participants to remind them to switch over to the next mobile app.

Session 3 (Usability Stage)

After the trial period with mobile apps, the focus group for Session 3 (which assesses usability) will include: (1) follow-up on patients' experience and preferences with using the selected mobile apps, and (2) completion of a 10-item System Usability Scale to provide a quantitative evaluation of the mobile apps to supplement the focus groups and interviews [37]. A winning app will be selected for the RCT.

Usability Testing: Analysis

The three focus group sessions for Aim 2 will be transcribed, coded, and analyzed in the same manner as in Aim 1. The System Usability Scale used in the Mobile App Session 3 focus group will yield a single number from 0 to 100 representing a composite measure of the overall usability of mobile apps being tested [37]. The scale will be scored as directed by the original authors.

Aim 3: Medication Adherence Randomized Controlled Trial

Design

The research design for Aim 3 is an RCT that lasts 12 months. In contrast to Aims 1 and 2 that included participants who were post-ACS/PCI within one year and recruited from a cardiac rehabilitation program, participants for Aim 3 will be recruited from the hospital after ACS/PCI.

Sample Size Estimation

We plan to enroll 225 total participants (75 participants per group). Allowing for a 15% attrition rate over the 12-month study, we conservatively estimate that this recruitment target will result in a total sample size of n=192, which will give 86% power to detect a medium effect size (half-SD difference) between at least one treatment group and the control group using Dunnett's method to adjust for multiple comparisons. This sample size would give more than 95% power to detect an effect size of d=0.69, as found in our previous clinical trial [33]. Analysis of the longitudinal data points with mixed-effects models will confer additional power.

Sample

The convenience sample will consist of 159 male and female Veterans from SFVAMC and 66 female participants (29% of sample) from JMMC. A sample size of 225 is considered to be feasible considering the number of post-ACS/PCI patients who are treated at both institutions. We have incorporated a 29% oversample of women to ensure a sufficient sample size to examine subgroup differences in intervention effects, given the low enrollment of female Veterans in Veterans Health Administration (6%) [38]. Inclusion criteria include: (1) >21 years of age, (2) recent ACS or PCI within one week, and (3) new antiplatelet (thienopyridine) prescription. Exclusion criteria are: (1) cognitive impairment, and (2) lack of English proficiency/literacy. For the process evaluation, we will recruit a subset of 10 participants from each experimental group (text messaging and mobile app; total n=20) for in-depth individual interviews.

Settings and Recruitment

We will recruit from SFVAMC and JMMC inpatient units using two recruitment strategies. First, we will inform the cardiologists and nurses in the cardiac units at the hospital sites about the study so they can identify patients who meet eligibility criteria. A patient-friendly handout will be made available for the health care team to give to interested participants. Second, we will obtain a daily list of patients who had PCI and their electronic medical records will be screened for eligibility in the study using a checklist to examine the inclusion and exclusion criteria. Participants who agree to participate will provide written informed consent.

Randomization

Group assignment will be generated by random allocation sequence using random blocks stratified within recruitment site (SFVAMC or JMMC) of either three or six, which will be prepared by the study biostatistician. The research team will assign patients to their groups by distributing presealed envelopes in consecutive, numbered order. Due to the nature of the study design, the research team and participants cannot be blinded to the intervention once group assignment is determined.

Baseline Data Collection

After written consent is obtained, we will collect clinical data by reviewing electronic medical records. Participants will complete the following baseline questionnaires: (1) sociodemographic information and medical history, (2) mobile phone use, and (3) Mini-Cog Test [39]. All instruments and frequency of administration are described in Table 2.

Table 2. Measurement of medication adherence with intervals.

Measure	Description	Rationale	Months					
			0	1	3	6	9	12
Key Primary Endpoint								
Medication Event Monitoring System (MEMS) [40]	Electronic pill caps time stamp when the bottle is opened, correlating with intake of medication. Primary outcome is percentage (0-100%) of prescribed doses taken	Most objective, noninvasive method and considered the "gold standard"		x		x		x
Secondary Patient-Reported Endpoints								
MEMS [40]	Percentages (0-100%) of (1) days correct doses are taken, and (2) doses taken on schedule	Most objective, noninvasive method and considered the "gold standard"		x		x		x
Morisky Scale [41,42]	Eight-item Morisky Medication Adherence Scale (MMAS-8) self-reported questionnaire on adherence behavior for a range of scores 0-8, with higher scores indicating poor adherence (Cronbach alpha=0.83).	Most popular scale and well-validated instrument with high reliability	x	x		x		x
7-Day Recall	One item asking how many days in the past week patient remembered to take medications. Final outcome is a percentage (0-100%).	Most commonly used method in the clinical setting	x	x		x		x
Secondary Objective Endpoints								
Veterans Affairs Corporate Data Warehouse (Veterans)	Veterans Affairs software program that provides detailed information on inpatient and outpatient medications. Final outcome is a percentage (0-100%) of days covered during 90-day period.	Assesses adherence via 90-day refill patterns (does not require active participation)		x	x	x	x	x
Peoplechart Meds Incontext (non-Veterans)	Private software program that uses refill data directly from retail pharmacies and Personal Benefits Manager. Final outcome is a percentage (0-100%) of days covered during 90-day period.	Assesses adherence via monthly refill patterns (does not require active participation)		x	x	x	x	x

Intervention

We will conduct an RCT with random assignment to one of three groups: (1) text messaging, (2) mobile app, or (3) website-control, for a total of 12 months. Both intervention groups will also be offered the patient education website that the control group will be given. The *text messaging group* will receive text messages with content and frequency informed by Aim 1. We will use the Veterans Affairs (VA) *Annie* text messaging program. For non-Veteran females, we will use a text messaging program from CareSpeak Communications. The *app group* will use the preferred app that is selected in Aim 2. The major purpose of the app is to remind participants to take medications; however, the app will likely include other features such as providing educational messages. The *website group* will be offered the American Heart Association patient education website (My Life Check - 7 Steps To Healthy Living) and will serve as an active control group [43]. The website will be offered to participants in all three groups. The *7 small steps to big changes* are to manage blood pressure, control cholesterol, reduce blood sugar, get active, eat better, lose weight, and stop smoking.

Follow-Up Visits

Subsequent in-person follow-up visits at 1, 6, and 12 months will take place in participants' homes or other mutual meeting

places as requested. Follow-up visits will be scheduled at times that are convenient for participants to meet.

Primary Outcome/Other Variables and Instruments

Primary Outcome: Medication Adherence

Medication adherence will be assessed with five different measures at various intervals to validate patterns of adherence, including: Medication Event Monitoring System (MEMS; key primary endpoint being percentage of prescribed doses taken), Morisky Medication Adherence Scale (MMAS-8), 7-day recall, VA Corporate Data Warehouse (Veterans), and Peoplechart Meds Incontext (non-Veterans; Table 2). In-person follow-up visits will occur at 1, 6, and 12 months, while monitoring of adherence through refill data from computer software will be done monthly to reduce participant burden.

MEMS technology uses integrated microcircuits with bottle caps that record the date and time that an individual opens a pill bottle. Participants will be given one bottle to store their antiplatelet medication, and will be directed to store their other medications as they normally would. For those who use 7-day pill boxes, we will emphasize the need to use the MEMS bottle for the antiplatelet medication. Data will be wirelessly transferred to a MEMSCap reader, which is a small device that connects to a computer software program.

Refill data from computer software will also allow us to monitor prescription adherence passively, without requiring patient participation. We will use administrative data from the national VA repository (VA Corporate Data Warehouse) to provide adherence to antiplatelet medication for Veterans. For non-Veteran females from JMMC, we will use an equivalent data source through Peoplechart Meds Incontext, which is a software program that tracks adherence through sanctioned prescription data sourced directly from retail pharmacies and Prescription Benefits Managers (ie, mail-order companies).

Other Variables and Instruments

We will examine other variables (health-related quality of life, social support, self-efficacy, depression, anxiety, and post-traumatic stress disorder) and their relationship to medication adherence. Patients will complete the instruments at baseline, 1, 6, and 12 months (Table 3).

Table 3. Instruments used to assess additional variables.

Measure	Description	Months					
		0	1	3	6	9	12
Health-related quality of life	The 12-Item Short Form Health Survey (SF-12) is the shorter version of SF-36, which measures functional health and well-being (relative validity median 0.67 and 0.97 for the physical and mental components, respectively) [44].	x	x		x		x
Social support	The 20-item Medical Outcomes Study Social Support Survey Instrument uses multi-trait scaling analyses of 4 functional support scales and provides an overall functional social support index (Cronbach alpha=0.91) [45].	x	x		x		x
Medication self-efficacy	The 13-item Self-Efficacy for Appropriate Medication Use Scale measures how confident individuals are in taking their medications correctly in certain situations (Cronbach alpha=0.89) [46].	x	x		x		x
Depression	The 9-item Patient Health Questionnaire is used to diagnose and measure the severity of depression as well as monitor response to treatment (Cronbach alpha=0.89) [47].	x	x		x		x
Anxiety	The 7-item Generalized Anxiety Disorder Assessment is used to screen and measure severity of generalized anxiety disorder (Cronbach alpha=0.92) [48].	x	x		x		x
Post-traumatic stress disorder	The 17-item Post-Traumatic Stress Disorder Checklist: Civilian is a popular self-report rating scale for post-traumatic stress disorder. The civilian version will be used instead of the military version because the majority of participants will not have been on recent active duty, >35% of Veterans with post-traumatic stress disorder had a nonmilitary trauma, and non-Veteran women will be included (29%; Cronbach alpha=0.87) [49].	x	x		x		x

Process Evaluation

Upon completion of the intervention study, we will conduct a process evaluation so that improvements can be made for a multi-site full scale study. The objectives of the process evaluation are to assess participants' perspectives on feasibility, acceptability, usability, challenges, strengths, and weaknesses of the intervention. In addition, we will ascertain reasons for nonadherence to antiplatelet medications since understanding the reasons for nonadherence is crucial to avoid negative patient outcomes. We will adopt a qualitative research approach using in-depth individual interviews from a diverse sample of participants (total n=20).

Analysis

Descriptive statistics, means, and SDs for quantitative variables, and frequencies and percentages for categorical variables, will be provided for all demographic and study variables. Random assignment of the patients to the text messaging, mobile app, and website groups should ensure that there are no preexisting differences between the three groups in personal factors (eg, sociodemographic, clinical, and psychosocial characteristics).

Medication Adherence

The primary outcome will be the percentage of prescribed doses taken based on MEMS data (aggregated over 12 months). Secondary outcomes will include: (1) percentages of days correct number of doses were taken, (2) doses taken on schedule, (3) MMAS-8, (4) 7-day recall, (5) VA Corporate Data

Warehouse (Veterans), and (6) Peoplechart Meds Incontext (non-Veterans). The MMAS-8 will be analyzed as a range of 0-8. We will synthesize adherence measures with the key primary endpoint of MEMS data compared with secondary measures of adherence to assess for concurrent and predictive validity. We will also calculate associations between all of the adherence measures but expect that they will track well together. Prior to fitting the mixed-effects linear model, we will examine univariate and bivariate relationships between the outcomes and both demographic and coded qualitative responses.

Primary Statistical Analysis

Our primary analysis will use a mixed-effects linear model. The predictors will be a categorical predictor of group (with control as reference), time, and the group-by-time interactions, as well as the recruitment site (SFVAMC vs JMMC), as randomization is stratified by site. The parameters in the group-by-time interaction are the primary parameters of interest, describing whether adherence changes differentially over baseline in each of the treatment groups compared to the control group. We will also investigate whether other models for change over time are more appropriate, including arbitrary means or nonlinear time functions through comparison of Akaike information criterion/Bayesian information criterion. Secondary analyses will adjust for select covariates that are strongly associated with adherence.

Predictors of Medication Adherence

To determine the factors related to medication adherence, we will examine sociodemographic, clinical, and psychosocial variables. The variables that show at least a moderate correlation and have a significant relationship to medication adherence (P<0.10) will be included in a multiple regression analysis in which medication adherence is the dependent variable. The multiple regression analysis will provide the optimum combination of these variables to explain the total percent of variance in medication adherence, and indicate the unique contribution of each variable to the regression model.

Process Evaluation

The in-depth individual interviews for process evaluation will be transcribed, coded, and analyzed in the same manner as in Aims 1 and 2. We will explore reasons for attrition over the 12-month period. We will complete field notes after the conclusion of each interview, and all interviews will be transcribed verbatim. Thematic analysis will include reading the completed field notes and interview transcripts. The key outcomes will be related to patient satisfaction and process evaluation, particularly focusing on how views vary across groups.

Results

We began enrollment for the Mobile4Meds focus groups in January 2017. The focus group data will inform the development of the RCT, which is scheduled to begin in early 2018. We anticipate this four-year research study will be completed in late 2020.

We believe that participants will provide valuable contributions on the content and frequency of text messaging in Aim 1. We expect that focus groups that are stratified by low/high mobile phone use and sex will have differing opinions on frequency of text messaging delivery; however, we also predict that the perceived usefulness of text messaging content will be similar across groups. Based on participants' responses, we will refine our text messaging content and frequency in preparation for Aim 3.

By conducting Aim 2, we will complete a content analysis of the top 10 commercially available mobile apps that will provide an evidence-based guide for health researchers and clinicians. We expect that using the top 2-4 selected mobile apps over 2-4 weeks on participants' personal smartphones will provide clear insight into which mobile app should be used for the RCT.

This study is powered to prove the efficacy of using different mobile strategies to promote adherence to antiplatelet medications. By conducting Aim 3, we will compare two mHealth strategies (with a website-control condition) among Veterans using multiple methods to assess adherence. We will also examine the relationship between medication adherence and important variables (ie, health-related quality of life, social support, self-efficacy, depression, anxiety, and post-traumatic stress disorder). The study duration of 12 months, which is the recommended duration of antiplatelet use for most MI/PCI patients, will provide valuable information about patterns of medication adherence.

Discussion

Evaluating the clinical application of mHealth strategies through rigorous scientific design and methodology is an important step in establishing whether there is potential for long-term benefit among Veterans who live with chronic disease [50]. The best way to ensure strict medication adherence in patients has continued to elude health care providers. Worldwide development and adoption of mobile technology has successfully spurred dramatic growth of mHealth as a platform to deliver intervention strategies for various health conditions in the past several years [51].

Researchers suggest that patient knowledge, self-monitoring, counseling, accountability, and a personalized program can contribute to improvement in medication adherence [52]. Experts and multiple stakeholders in medication adherence agree that a patient-centered approach is necessary, and increasing patient knowledge is critically important [25]. Technological solutions have been suggested to alleviate medication nonadherence, such as mHealth technology, electronic monitors, pill-monitoring technology, online resources, and social media [52]. The best manner to engage with Veterans via text messaging and mobile apps has yet to be determined among those of different ages, sexes, chronic diseases, mobile phone usage patterns, and ethnic populations. There are many opportunities to explore these unanswered questions in future studies.

Limitations

There are potential limitations associated with this study. In Aims 1 and 2, if we do not reach saturation of ideas or if we find distinct differences between groups, we may add a mixed-group to tease out differences. We may also add an additional focus group of mixed and unstratified participants to identify differences. Alternatively, we will conduct structured one-on-one interviews to acquire richer information as a supplement to the focus groups.

In Aim 3, a limitation may be attrition due to Veteran disinterest in receiving text messages or using a mobile app for 12 months. We will address the potential barrier of disinterest during the two focus groups, as planned in Aims 1 and 2, and ask Veterans how to best engage with them after ACS/PCI over 12 months. Multiple strategies will be used to maximize participant retention and decrease missing data, since the intervention is intended to last 12 months. The dropout or missing data rates for the three groups will be examined to see that they are significantly different. Sensitivity analyses will include a complete-case analysis.

Another potential limitation may be cross-over effects for the text messaging and website (control) groups if they use a mobile app concurrently during the RCT. We will request that patients not use any other electronic medication reminders, including on their mobile phones (eg, alarm, app). At the conclusion of the study, we will ask participants in the text messaging and control groups if they used any other electronic reminders. If they have, we will conduct sensitivity analyses as described.

Conclusions

As the aims of Mobile4Meds are achieved, scientific knowledge and clinical implementation of behavioral change interventions related to mobile technology and medication adherence will be advanced. Improving medication adherence through mHealth technology may have significant effects on lowering morbidity and mortality among Veterans with coronary heart disease. Since poor adherence to long-term therapies severely compromises the effectiveness of treatment, providing innovative solutions through mHealth may provide relief for this critical issue in population health from the perspective of clinical outcomes and quality of life [53]. Moreover, since medication nonadherence is a major global problem [1], using mHealth strategies may be a powerful solution to reach large, diverse populations in a cost-effective manner. In the future, implementing a strategy to promote adherence through the vulnerable period of 12 months post-ACS/PCI may be highly acceptable and generalizable. The findings from Mobile4Meds may also be highly applicable to other patient classes who require long-term treatment and strict medication adherence.

Acknowledgments

Dr. Park is supported by the Department of Veterans Affairs Health Services Research and Development Nursing Research Initiative Award (1 IK3 HX002055-01A1). Research reported in this publication was supported by the National Center for Advancing Translational Sciences of the National Institutes of Health under Award Number KL2TR001870. The content is solely the responsibility of the authors and does not represent the official views of the National Institutes of Health. This project was also supported by the University of California, San Francisco Clinical and Translational Science Institute (UL1 TR000004).

Conflicts of Interest

None declared.

Multimedia Appendix 1

This is the peer-review summary statement for the grant proposal association with this manuscript. The recommended changes were applied to the final grant proposal that was funded.

[PDF File (Adobe PDF File), 101KB - resprot_v6i7e134_app1.pdf]

References

1. Mathers C, Boerma T, Ma Fat D. The Global Burden of Disease: 2004 Update. Geneva: World Health Organization; 2008. URL: http://www.who.int/healthinfo/global_burden_disease/GBD_report_2004update_full.pdf?ua=1 [accessed 2013-03-28] [WebCite Cache ID 9789241563710]
2. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics--2015 update: a report from the American Heart Association. Circulation 2015 Jan 27;131(4):e29-322. [doi: 10.1161/CIR.0000000000000152] [Medline: 25520374]
3. Pursnani S, Korley F, Gopaul R, Kanade P, Chandra N, Shaw RE, et al. Percutaneous coronary intervention versus optimal medical therapy in stable coronary artery disease: a systematic review and meta-analysis of randomized clinical trials. Circ Cardiovasc Interv 2012 Aug 01;5(4):476-490 [FREE Full text] [doi: 10.1161/CIRCINTERVENTIONS.112.970954] [Medline: 22872053]
4. Stergiopoulos K, Brown DL. Initial coronary stent implantation with medical therapy vs medical therapy alone for stable coronary artery disease: meta-analysis of randomized controlled trials. Arch Intern Med 2012 Feb 27;172(4):312-319. [doi: 10.1001/archinternmed.2011.1484] [Medline: 22371919]

5. Ford ES, Ajani UA, Croft JB, Critchley JA, Labarthe DR, Kottke TE, et al. Explaining the decrease in U.S. deaths from coronary disease, 1980-2000. N Engl J Med 2007 Jun 07;356(23):2388-2398. [doi: 10.1056/NEJMsa053935] [Medline: 17554120]
6. Roth GA, Morden NE, Zhou W, Malenka DJ, Skinner J. Clopidogrel use and early outcomes among older patients receiving a drug-eluting coronary artery stent. Circ Cardiovasc Qual Outcomes 2012 Jan;5(1):103-112 [FREE Full text] [doi: 10.1161/CIRCOUTCOMES.111.962704] [Medline: 22147885]
7. Rossini R, Capodanno D, Lettieri C, Musumeci G, Nijaradze T, Romano M, et al. Prevalence, predictors, and long-term prognosis of premature discontinuation of oral antiplatelet therapy after drug eluting stent implantation. Am J Cardiol 2011 Jan 15;107(2):186-194. [doi: 10.1016/j.amjcard.2010.08.067] [Medline: 21211596]
8. Spertus JA, Kettelkamp R, Vance C, Decker C, Jones PG, Rumsfeld JS, et al. Prevalence, predictors, and outcomes of premature discontinuation of thienopyridine therapy after drug-eluting stent placement: results from the PREMIER registry. Circulation 2006 Jun 20;113(24):2803-2809 [FREE Full text] [doi: 10.1161/CIRCULATIONAHA.106.618066] [Medline: 16769908]
9. Airoldi F, Colombo A, Morici N, Latib A, Cosgrave J, Buellesfeld L, et al. Incidence and predictors of drug-eluting stent thrombosis during and after discontinuation of thienopyridine treatment. Circulation 2007 Aug 14;116(7):745-754 [FREE Full text] [doi: 10.1161/CIRCULATIONAHA.106.686048] [Medline: 17664375]
10. Ko DT, Chiu M, Guo H, Austin PC, Marquis J, Tu JV. Patterns of use of thienopyridine therapy after percutaneous coronary interventions with drug-eluting stents and bare-metal stents. Am Heart J 2009 Oct;158(4):592-598.e1. [doi: 10.1016/j.ahj.2009.06.030] [Medline: 19781419]
11. Neugaard BI, Priest JL, Burch SP, Cantrell CR, Foulis PR. Quality of care for veterans with chronic diseases: performance on quality indicators, medication use and adherence, and health care utilization. Popul Health Manag 2011 Apr;14(2):99-106 [FREE Full text] [doi: 10.1089/pop.2010.0020] [Medline: 21091367]
12. Roughead EE, Vitry AI, Preiss AK, Barratt JD, Gilbert AL, Ryan P. Assessing overall duration of cardiovascular medicines in veterans with established cardiovascular disease. Eur J Cardiovasc Prev Rehabil 2010 Feb;17(1):71-76. [doi: 10.1097/HJR.0b013e32832f3b56] [Medline: 19587601]
13. Rogers WH, Kazis LE, Miller DR, Skinner KM, Clark JA, Spiro A, et al. Comparing the health status of VA and non-VA ambulatory patients: the veterans' health and medical outcomes studies. J Ambul Care Manage 2004;27(3):249-262. [Medline: 15287215]
14. Osterberg L, Blaschke T. Adherence to medication. N Engl J Med 2005 Aug 4;353(5):487-497. [doi: 10.1056/NEJMra050100] [Medline: 16079372]
15. Sabaté E. World Health Organization. Switzerland: World Health Organization; 2003. Adherence to long-term therapies: evidence for action URL: http://www.who.int/chp/knowledge/publications/adherence_report/en/ [accessed 2013-03-13] [WebCite Cache ID 9241545992]
16. Dunbar-Jacob J, Bohachick P, Mortimer MK, Sereika SM, Foley SM. Medication adherence in persons with cardiovascular disease. J Cardiovasc Nurs 2003;18(3):209-218. [Medline: 12837011]
17. Ho PM, Magid DJ, Shetterly SM, Olson KL, Maddox TM, Peterson PN, et al. Medication nonadherence is associated with a broad range of adverse outcomes in patients with coronary artery disease. Am Heart J 2008 Apr;155(4):772-779. [doi: 10.1016/j.ahj.2007.12.011] [Medline: 18371492]
18. Garner JB. Problems of nonadherence in cardiology and proposals to improve outcomes. Am J Cardiol 2010 May 15;105(10):1495-1501. [doi: 10.1016/j.amjcard.2009.12.077] [Medline: 20451702]
19. New England Health Institute. New England Healthcare Institute. New England; 2009 Aug 11. Research shows patient medication nonadherence costs health care system $290 billion annually URL: http://www.nehi.net/news/344-nehi-research-shows-patient-medication-nonadherence-costs-health-care-system-290-billion-annually/view [accessed 2009-10-30] [WebCite Cache ID 6rZFY7LsE]
20. Teyhen DS, Aldag M, Centola D, Edinborough E, Ghannadian JD, Haught A, et al. Incentives to create and sustain healthy behaviors: technology solutions and research needs. Mil Med 2014 Dec;179(12):1419-1431. [doi: 10.7205/MILMED-D-14-00111] [Medline: 25469962]
21. Haynes RB, Ackloo E, Sahota N, McDonald HP, Yao X. Interventions for enhancing medication adherence. Cochrane Database Syst Rev 2008(2):CD000011. [doi: 10.1002/14651858.CD000011.pub3] [Medline: 18425859]
22. Ho PM, Bryson CL, Rumsfeld JS. Medication adherence: its importance in cardiovascular outcomes. Circulation 2009 Jun 16;119(23):3028-3035 [FREE Full text] [doi: 10.1161/CIRCULATIONAHA.108.768986] [Medline: 19528344]
23. Bosworth HB, Granger BB, Mendys P, Brindis R, Burkholder R, Czajkowski SM, et al. Medication adherence: a call for action. Am Heart J 2011 Sep;162(3):412-424 [FREE Full text] [doi: 10.1016/j.ahj.2011.06.007] [Medline: 21884856]
24. Brown MT, Bussell JK. Medication adherence: WHO cares? Mayo Clin Proc 2011 Apr;86(4):304-314 [FREE Full text] [doi: 10.4065/mcp.2010.0575] [Medline: 21389250]
25. McMullen CK, Safford MM, Bosworth HB, Phansalkar S, Leong A, Fagan MB, Centers for Education and Research on Therapeutics Patient-Centered Medication Management Workshop Working Group, et al. Patient-centered priorities for improving medication management and adherence. Patient Educ Couns 2015 Jan;98(1):102-110. [doi: 10.1016/j.pec.2014.09.015] [Medline: 25448313]

26. Kumar S, Nilsen WJ, Abernethy A, Atienza A, Patrick K, Pavel M, et al. Mobile health technology evaluation: the mHealth evidence workshop. Am J Prev Med 2013 Aug;45(2):228-236 [FREE Full text] [doi: 10.1016/j.amepre.2013.03.017] [Medline: 23867031]
27. Franklin V, Waller A, Pagliari C, Greene S. "Sweet Talk": text messaging support for intensive insulin therapy for young people with diabetes. Diabetes Technol Ther 2003;5(6):991-996. [doi: 10.1089/152091503322641042] [Medline: 14709202]
28. Cocosila M, Archer N, Haynes RB, Yuan Y. Can wireless text messaging improve adherence to preventive activities? Results of a randomised controlled trial. Int J Med Inform 2009 Apr;78(4):230-238. [doi: 10.1016/j.ijmedinf.2008.07.011] [Medline: 18778967]
29. Park LG, Howie-Esquivel J, Dracup K. A quantitative systematic review of the efficacy of mobile phone interventions to improve medication adherence. J Adv Nurs 2014 Sep;70(9):1932-1953. [doi: 10.1111/jan.12400] [Medline: 24689978]
30. Patrick K, Griswold WG, Raab F, Intille SS. Health and the mobile phone. Am J Prev Med 2008 Aug;35(2):177-181 [FREE Full text] [doi: 10.1016/j.amepre.2008.05.001] [Medline: 18550322]
31. Riley WT, Rivera DE, Atienza AA, Nilsen W, Allison SM, Mermelstein R. Health behavior models in the age of mobile interventions: are our theories up to the task? Transl Behav Med 2011 Mar;1(1):53-71 [FREE Full text] [doi: 10.1007/s13142-011-0021-7] [Medline: 21796270]
32. Pharow P, Blobel B, Ruotsalainen P, Petersen F, Hovsto A. Portable devices, sensors and networks: wireless personalized eHealth services. Stud Health Technol Inform 2009;150:1012-1016. [Medline: 19745466]
33. Park LG, Howie-Esquivel J, Chung ML, Dracup K. A text messaging intervention to promote medication adherence for patients with coronary heart disease: a randomized controlled trial. Patient Educ Couns 2014 Feb;94(2):261-268. [doi: 10.1016/j.pec.2013.10.027] [Medline: 24321403]
34. Clancy CM, Collins Sharp BA. Women's health during health care transformation. J Gen Intern Med 2013 Jul;28 Suppl 2:S500-S503 [FREE Full text] [doi: 10.1007/s11606-013-2473-6] [Medline: 23807056]
35. Doshi A, Patrick K, Sallis JF, Calfas K. Evaluation of physical activity web sites for use of behavior change theories. Ann Behav Med 2003;25(2):105-111. [Medline: 12704012]
36. Azar KM, Lesser LI, Laing BY, Stephens J, Aurora MS, Burke LE, et al. Mobile applications for weight management: theory-based content analysis. Am J Prev Med 2013 Nov;45(5):583-589. [doi: 10.1016/j.amepre.2013.07.005] [Medline: 24139771]
37. Brooks J. Smart Phone Applications for People with Brain Injury. United Kingdom: Agency for Clinical Innovation; 1986. The project implementing and evaluating smart phone applications technology across the NSW Brain Injury Rehabilitation Program (BIRP) URL: http://www.tbistafftraining.info/smartphones/documents/b5_during_the_trial_usability_scale_v1_09aug11.pdf [accessed 2015-01-02] [WebCite Cache ID 6rZhP15dA]
38. Frayne S, Phibbs C, Friedman S, Berg E, Ananth L, Iqbal S, et al. Sourcebook: Women Veterans in the Veterans Health Administration. Volume 1. Washington DC: Women's Health Evaluation Initiative, Women Veterans Health Strategic Health Care Group, Veterans Health Administration, Department of Veterans Affairs; 2010 Dec. Sociodemographic characteristics and utilization of VHA care URL: https://www.research.va.gov/media_roundtable/Sourcebook.pdf [accessed 2017-06-28] [WebCite Cache ID 6rZGBHLjt]
39. Carolan Doerflinger DM. How to try this: the mini-cog. Am J Nurs 2007 Dec;107(12):62-71. [doi: 10.1097/01.NAJ.0000301030.81651.66] [Medline: 18049065]
40. Ailinger RL, Black PL, Lima-Garcia N. Use of electronic monitoring in clinical nursing research. Clin Nurs Res 2008 May;17(2):89-97 [FREE Full text] [doi: 10.1177/1054773808316941] [Medline: 18387881]
41. Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive validity of a medication adherence measure in an outpatient setting. J Clin Hypertens (Greenwich) 2008 May;10(5):348-354 [FREE Full text] [Medline: 18453793]
42. Shalansky SJ, Levy AR, Ignaszewski AP. Self-reported Morisky score for identifying nonadherence with cardiovascular medications. Ann Pharmacother 2004 Sep;38(9):1363-1368. [doi: 10.1345/aph.1E071] [Medline: 15238622]
43. American Heart Association. My Life Check - Life's Simple 7. Dallas, TX: American Heart Association; 2017 Jun 23. URL: http://www.heart.org/HEARTORG/Conditions/My-Life-Check---Lifes-Simple-7_UCM_471453_Article.jsp [accessed 2017-06-29] [WebCite Cache ID 6rZhhZFc5]
44. Ware J, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care 1996 Mar;34(3):220-233. [Medline: 8628042]
45. Sherbourne CD, Stewart AL. The MOS social support survey. Soc Sci Med 1991;32(6):705-714. [Medline: 2035047]
46. Risser J, Jacobson TA, Kripalani S. Development and psychometric evaluation of the Self-efficacy for Appropriate Medication Use Scale (SEAMS) in low-literacy patients with chronic disease. J Nurs Meas 2007;15(3):203-219. [Medline: 18232619]
47. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med 2001 Sep;16(9):606-613 [FREE Full text] [Medline: 11556941]
48. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med 2006 May 22;166(10):1092-1097. [doi: 10.1001/archinte.166.10.1092] [Medline: 16717171]
49. Weathers FW, Litz BT, Huska JA. US Department of Veteran Affairs. 2003 Dec. PTSD checkList – civilian version URL: https://www.mirecc.va.gov/docs/visn6/3_PTSD_CheckList_and_Scoring.pdf [accessed 2017-06-28] [WebCite Cache ID 6rZF3Q5vY]

50. Nilsen W, Kumar S, Shar A, Varoquiers C, Wiley T, Riley WT, et al. Advancing the science of mHealth. J Health Commun 2012;17 Suppl 1:5-10. [doi: 10.1080/10810730.2012.677394] [Medline: 22548593]
51. Klasnja P, Pratt W. Healthcare in the pocket: mapping the space of mobile-phone health interventions. J Biomed Inform 2012 Feb;45(1):184-198 [FREE Full text] [doi: 10.1016/j.jbi.2011.08.017] [Medline: 21925288]
52. Zullig LL, Shaw RJ, Shah BR, Peterson ED, Lindquist JH, Crowley MJ, et al. Patient-provider communication, self-reported medication adherence, and race in a postmyocardial infarction population. Patient Prefer Adherence 2015;9:311-318 [FREE Full text] [doi: 10.2147/PPA.S75393] [Medline: 25737633]
53. Okuboyejo S, Eyesan O. mHealth: using mobile technology to support healthcare. Online J Public Health Inform 2014;5(3):233 [FREE Full text] [doi: 10.5210/ojphi.v5i3.4865] [Medline: 24678384]

Abbreviations

ACS: acute coronary syndrome
JMMC: John Muir Medical Center
MEMS: Medication Event Monitoring System
mHealth: mobile health
MI: myocardial infarction
MMAS-8: Morisky Medication Adherence Scale
PCI: percutaneous coronary intervention
RA: research assistant
RCT: randomized controlled trial
SD: standard deviation
SFVAMC: San Francisco Veterans Affairs Medical Center

Edited by G Eysenbach; submitted 14.01.17; peer-reviewed by J Kayser, L Schwiebert; comments to author 02.03.17; revised version received 10.04.17; accepted 14.04.17; published 18.07.17.

Please cite as:
Park LG, Collins EG, Shim JK, Whooley MA
Comparing Mobile Health Strategies to Improve Medication Adherence for Veterans With Coronary Heart Disease (Mobile4Meds): Protocol for a Mixed-Methods Study
JMIR Res Protoc 2017;6(7):e134
URL: http://www.researchprotocols.org/2017/7/e134/
doi:10.2196/resprot.7327
PMID:28720557

Protocol

Randomized Trial Comparing the Electronic Composite Psychosocial Screener YouthCHAT With a Clinician-Interview Assessment for Young People: A Study Protocol

Hiran Thabrew[1], BM, BSc (Hons), FRACP, FRANZCP; Arden Corter[1], PhD; Felicity Goodyear-Smith[1], MBChB, MD, FRNZCGP; Mary Goldfinch[2]

[1]University of Auckland, Auckland, New Zealand

[2]Tamaki College, Auckland, New Zealand

Corresponding Author:
Hiran Thabrew, BM, BSc (Hons), FRACP, FRANZCP
University of Auckland
Department of Psychological Medicine, University of Auckland, Level 12, Support Block, Auckland Hospital, Park Road, Grafton
Auckland, 1142
New Zealand
Phone: 64 21402055
Email: h.thabrew@auckland.ac.nz

Abstract

Background: Psychosocial problems such as depression, anxiety, and substance abuse are common and burdensome in young people, particularly those with long-term physical conditions such as asthma and diabetes. In New Zealand, "screening" for such problems is undertaken routinely only with Year 9 students in low-decile schools and opportunistically in pediatric settings using a nonvalidated and time-consuming clinician-administered Home, Education/employment, Eating, Activity, Drugs, Sexuality, Suicide/depression, Safety (HEEADSSS) interview. The Youth version, Case-finding and Help Assessment Tool (YouthCHAT) is a relatively new, locally developed, eTablet-based composite screener for identifying similar psychosocial issues to HEEADSSS. Based on individually validated screening instruments, it is self-administered within minutes. Preliminary testing has revealed its acceptability to young people, but further research is required to expand its modules to cover all HEEADSSS domains, to evaluate its acceptability for young people with and without long-term physical conditions, and to compare its effectiveness against HEEADSSS.

Objective: Our aim is to (1) ascertain acceptability and utility of YouthCHAT for children with long-term physical illness and high school students, (2) validate three additional YouthCHAT domains against comparable HEEADSSS domains, and (3) compare the performance of YouthCHAT and HEEADSSS in the high school setting.

Methods: During the first phase of the study, three additional YouthCHAT domains were codesigned with high school students. During the second phase of the study, the updated version of YouthCHAT will be administered to 30 young people with long-term physical conditions, and to 150 high school students either before or after HEEADSSS in the form of a randomized trial with counter-balanced design. Primary outcomes include comparability between HEEADSSS and YouthCHAT in detecting psychosocial issues, and time to administer; acceptability of YouthCHAT as an acceptable alternative or companion to HEEADSSS assessment; and the utility of YouthCHAT in helping streamline assessment processes.

Results: Recruitment for the first phase of this project commenced in November 2016, and the phase will run from February to November 2017.

Conclusions: If YouthCHAT is found to be acceptable to study participants and as effective as a HEEADSSS assessment, it could be an innovative and more efficient means of routine screening for common psychosocial health issues in young people with and without long-term physical conditions.

Trial Registration: Australian New Zealand Clinical Trials Registry (ANZCTR) ACTRN12616001243404p; https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=371422 (Archived by WebCite at http://www.webcitation.org/6rmlEiM1L)

(JMIR Res Protoc 2017;6(7):e135) doi:10.2196/resprot.7995

KEYWORDS

mass screening; adolescents; substance-related disorders; depression; anxiety; primary health care; school health; services; chronic disease

Introduction

Psychosocial problems are a significant issue for young people in New Zealand, particularly those with long-term physical conditions. Recent figures indicate that 27% of high school students are affected by anxiety and depression [1], and at 18 years of age the prevalence of hazardous drinking exceeds 50%. New Zealand's 2011 youth suicide rate was the second highest in the Organisation for Economic Co-operation and Development (OECD) [2]. As mental health and lifestyle issues often present in adolescence, it is important to intervene early so that problems do not become entrenched, leading to costly poor health and social outcomes [3-5].

Young people with long-term physical conditions are at even greater risk of psychosocial problems [6]. Depressive symptoms have been reported in as many as 40% of children with a long-term condition and socialization problems [7]. Anxiety has also been identified in children and young people with long-term physical conditions as an area of clinical significance [8]. The likelihood of such problems developing is related to young people's internal ability to manage stress, which develops over time; family factors; and the impact of illness and treatment, particularly association with distress and pain [9].

The World Health Organization and New Zealand policies and programs all emphasize the importance of addressing youth mental health with appropriately targeted services and recognize the need for easily accessible services, including use of appropriate tools [10-12]. Young people want a greater say in how services are designed and delivered, and they expect services to be diverse, contemporary, and responsive. These requirements are echoed in many national policies including the New Zealand Mental Health Commission's Blueprint II [13,14], the New Zealand Ministry of Health's Rising to the Challenge 2012-2017 [15], Statement of Intent 2014-2018 [16], and the New Zealand Suicide Prevention Action Plan 2013-2016 [17].

Home, Education/employment, Eating, Activities, Drugs and Alcohol, Sexuality, Suicide/depression, Safety (HEEADSSS) assessment is a clinician-administered, interview-based assessment of youth that can identify mental health and substance use problems [18,19]. Currently, all Year 9 (13-14 year olds) students in low-decile schools (those with the highest proportion of students from low socioeconomic communities), and some attendees at primary care and pediatric services in New Zealand are screened for well-being via HEEADSSS assessment. While HEEADSSS assessment offers a straightforward, holistic, and gradual approach to assessing young people across many domains, it is a face-to-face assessment, not a screening tool. Drawbacks include its lack of validation for problem identification, the cost of resourcing, time required for its administration (up to 45 minutes), and variability of assessment depending on the skill and experience of the assessor. In many high schools, it takes a full school year and more than one school nurse to screen all Year 9 students (personal communication M Goldfinch). In pediatric settings around New Zealand, routine screening for psychosocial problems is not usually undertaken and HEEADSSS assessments are conducted by some medical and nursing staff in an ad hoc manner.

The Youth version of the electronic Case-Finding and Help Assessment Tool (YouthCHAT) [20,21] is a self-report screening tool that covers ten domains: smoking, drinking, recreational drug use (based on the Substances and Choices Scale [SACS]) [22], problematic gambling, depression (based on the Patient Health Questionnaire – Adolescent Version [PHQ-A]) [23], anxiety (based on the Generalized Anxiety Disorder scale, 7 item [GAD-7]) [24], sexual health, exposure to abuse, anger management, and physical activity. For each positive domain screened, there is a "help" question that asks participants if they would "like help today," "want help, but another time," or "don't want help." Responses to the "help" question support conversations between young people and their health providers about the issues they would like addressed, which facilitates shared decision making, with increased likelihood that real sustained changes will be made.

YouthCHAT provides summary reports to authorized school/health clinic staff plus a guide to stepped-care management from self-help through to secondary care. It is a rapid screening system (taking 5-15 minutes to complete) and can be conducted on any electronic device. YouthCHAT has a 14-year history of development in primary care, youth, and school clinics [20,21,25-31]. Recently, it was successfully implemented in a rural school clinic and favorably received by both young patients and clinic staff. Evidence indicates that students are more likely to disclose information about challenges they are facing through electronic means than an initial in-person assessment [32].

As a validated and rapid screening tool, YouthCHAT has the potential to overcome barriers associated with HEEADSSS assessment, while providing a similar holistic assessment of mental health and lifestyle issues. Additionally, as YouthCHAT collects and provides electronic data, the additional paperwork that HEEADSSS requires is not needed. YouthCHAT may be a more efficient screener and serve as a useful substitute or precursor to HEEADSSS assessment. YouthCHAT currently screens for all HEEADSSS domains except three: eating issues, conduct problems/bullying, and resilience/strengths. Additional screening questions to cover these domains have been added, based on those available in the existing literature, with appropriate wording advised by high school students, including those of Māori and Pacific Island descent via focus groups to ensure the updated version of YouthCHAT is appropriate for young people from all major ethnic groups in New Zealand.

The aims of this study are to (1) validate three additional YouthCHAT domains against comparable HEEADSSS domains, (2) ascertain the acceptability and utility of YouthCHAT for

children with long-term physical illness and high school students, and (3) compare the performance of YouthCHAT and HEEADSSS in the high school setting.

We hypothesize that a version of YouthCHAT matched to HEEADSSS for all domains will be an acceptable alternative to a HEEADSSS assessment to both young people and the clinical staff conducting the screen. We further hypothesize that screening using YouthCHAT, followed up by a targeted or full HEEADSSS assessment where indicated, will be a much more streamlined and efficient system to enable identification and intervention of young people at risk.

Methods

Study Design

We will use a mixed-methods participatory action research approach to development and validation of a YouthCHAT mapped to all HEEADSSS domains, and assessment of the acceptability and utility of YouthCHAT at a tertiary pediatric hospital and a low-decile high school. A randomized controlled trial (RCT) with counterbalanced design will be conducted at the high school to assess the comparability of YouthCHAT and HEEADSSS.

Participants and Recruitment

During the first phase, up to 20 senior students aged 16-18 years from Tamaki College, a low-decile high school in Auckland, New Zealand, were invited to participate in focus groups to update YouthCHAT via flyers sent to their school. These students were chosen as they were all able to give their own consent.

During the second phase, approximately 150 Year 9 students (aged 13-14 years) from the same high school will be invited to participate in the RCT and school-based acceptability evaluation via letters will be sent to their parents. Parents may use a reply-paid form to opt out of the study if they do not wish their children to participate. However, regardless of this, all students will receive mandatory HEEADSSS assessments (as is routine for all students in this class). Students who choose to participate in the study will be randomly assigned to one of the two conditions (YouthCHAT followed by HEEADSSS assessment or HEEADSSS assessment followed by YouthCHAT) via a computer-generated random numbers table, with resulting lists provided to clinic staff. Sampling will be consecutive until all enrolled students have completed assessment. All screening will take place in the student health clinic on a desktop computer. A subset of 32 students will be invited to participate in four focus groups, and four school staff (nurses and counsellors) will be invited to complete semistructured interviews on the acceptability, utility, and comparability of YouthCHAT and HEEADSSS assessment. This age group of participants was chosen as it matches the age group of students who routinely receive HEEADSSS assessments in New Zealand low-decile schools.

Also during the second phase, 30 young people aged 13-18 years with long-term physical conditions (eg, diabetes, asthma, cystic fibrosis and congenital heart disease) attending outpatient clinics at Starship Children's Hospital, a tertiary pediatric hospital will be invited to participate in the study via flyers disseminated by clinic staff. Following individual or parental consent (and personal assent), they will be asked to complete YouthCHAT and a postconsultation survey to assess its acceptability and utility. This age group of participants has been chosen as it matches the age range to which YouthCHAT is targeted. Pediatricians and specialist nurses who have conducted these consultations will be also invited to undertake a short semistructured interview to provide a clinical perspective on the use of YouthCHAT in a pediatric setting.

Outcome Variables

The main study variables are (1) comparability (eg, is YouthCHAT at least as good or better than HEEADSSS assessment at detecting mental health and lifestyle issues among Year 9 youth? Is it a faster method of screening?), (2) acceptability (eg, is YouthCHAT content/format an acceptable alternative or companion to HEEADSSS assessment?), and (3) utility (eg, is YouthCHAT useful in helping to streamline assessment processes?).

Our primary outcome measures are (1) comparable detection rates for each domain for HEADSSS and YouthCHAT as measured by mental health or lifestyle issue "present" or "absent" (Tamaki sample only), (2) time taken to complete YouthCHAT and HEEADSSS screening (Tamaki sample only), and (3) acceptability and utility of YouthCHAT as assessed via feedback from staff and students/patients (Starship and Tamaki participants). Secondary outcome measures include differences in YouthCHAT versus HEEADSSS screening outcomes by gender and ethnicity.

Measures and Data Collection

YouthCHAT

YouthCHAT covers 10 domains: smoking, drinking, recreational drug use, problematic gambling, depression, anxiety, sexual health, exposure to abuse, anger management, and physical activity. In the case of positive screens, branching logic links users to validated assessment tools including SACS for drug and alcohol use, PHQ-9 for depression, and GAD-7 for anxiety. For the purpose of this project, three new domains have been added to YouthCHAT related to diet, body image, and bullying. Questions related to these domains have been developed based on existing validated tools and have been trialled with student focus groups prior to initiation of the study comparing YouthCHAT with HEEADSSS. Interested readers are welcome to contact the authors for the complete list of YouthCHAT questions.

HEEADSSS

HEEADSSS is a clinician-administered, interview-based assessment of youth that can identify mental health and substance use problems [18,19]. It covers the domains of Home, Education/employment, Eating, Activities, Drugs and Alcohol, Sexuality, Suicide/depression, and Safety. It is currently administered by trained school health nurses to all Year 9 students in low-decile schools and some attendees at primary care and pediatric services in New Zealand.

Administrative Data

Administrative data such as staff time to complete screening/assessments, psychosocial issues identified via HEEADSSS and YouthCHAT, and referrals made based on positive screens will be collected.

Participant Survey

Following completion of YouthCHAT, participants at Starship and Tamaki College will be asked to complete a survey comprised of Likert scales, free-text options, and forced-choice questions on the acceptability and utility of YouthCHAT.

Clinician Interviews

Taped and transcribed semistructured interviews with the participating school, Starship, and hospital staff will be conducted (N=10-15). Interviews will focus on perceptions of the utility and acceptability of YouthCHAT (both settings) and comparability with HEEADSSS (Tamaki only) and will be conducted in person or by telephone as preferred by participants.

Focus Groups

Two taped and transcribed student focus groups to advise on the face validity and wording of the newly added YouthCHAT modules were conducted at Tamaki College during the first phase of the research. An additional four taped and transcribed student focus groups that address acceptability and utility of the assessments will be conducted at Tamaki College at the end of the school year during the second phase.

Procedure

During the first phase, screening questions to address the HEEADSSS domains of eating issues, conduct problems/bullying, and resilience/strengths were selected based on existing validated tools sourced through the peer-reviewed literature. These questions were adapted to the New Zealand youth context using focus groups with high school students. Students were asked to judge whether the questions make sense, explain what they think the questions are asking, identify any words or phrases they find unclear, and suggest alternative youth-friendly language. They were also asked to indicate the order in which the questions should appear and enhancements followed majority opinion. In the spirit of biculturalism, at least one focus group was undertaken with only Māori young people to identify any culturally relevant viewpoints, issues, or concerns. Focus groups were audiotaped, confidentially transcribed, and suggestions categorized and tabulated. The resulting additional modules were programmed into YouthCHAT.

During the second phase, a counterbalanced RCT of YouthCHAT and HEEADSSS will be undertaken with high school students. During this study, one group will receive YouthCHAT before HEEADSSS assessment (Condition 1), and the other HEEADSSS assessment before YouthCHAT (Condition 2) and findings from YouthCHAT and HEEADSSS assessment will be compared. In addition, the acceptability and utility of YouthCHAT will be evaluated in two settings—the high school where YouthCHAT and HEEADSSS assessments are undertaken and a tertiary pediatric hospital setting where young people aged 13-18 years with long-term physical conditions are attending pediatric outpatient appointments. Following the use of YouthCHAT by both audiences, focus groups will be undertaken to identify positive feedback, issues, and concerns regarding the electronic screener. Once again, at least one focus group will be undertaken in each setting with only Māori young people to identify any culturally relevant viewpoints, issues, or concerns. In addition to feedback from young people, feedback regarding appeal and utility will be sourced from school nurses at the high school and pediatricians and specialist nurses at the pediatric hospital.

Any focus group participants at the tertiary pediatric hospital who are distressed or develop psychosocial concerns during or following the study will be referred to the hospital-based consult liaison (mental health) service for further assessment and management, in a similar manner to what would occur as part of usual care. Within the high school setting, stepped-care resources and a clinical pathway (algorithms relating to domain and severity of identified problem) will be provided to augment usual care options. These include self-help resources (helplines, psychoeducation and information sheets, websites, and e-therapies), clinician interventions (medications and brief interventions), local community agencies, and referral to adolescent secondary care mental health and drug and alcohol services.

Data Handling

HealthLink, an electronic data management system, will provide secure storage of all YouthCHAT screening data. It will also enable encrypted secure data transmission to the clinic's MedTech32 practice management system (PMS) software by the same private network used for their electronic referrals solution. Clinical staff will access their YouthCHAT summary reports directly from the website. This allows a brief version to be cut and pasted into clinical notes, or a PDF generated to attach to the patient file. HEEADSSS data will be managed as per standard care via the school nurse and his/her team. All HEEADSSS data are entered into the PMS, with a summary report provided to the Ministry of Health. HEEADSSS data will need to be manually inputted into a Microsoft Excel spreadsheet by a research assistant. Each YouthCHAT generates a unique code for each participant. This code will be transferred by the school nurse into the PMS HEEADSSS file for data-matching. Thus, research data will be anonymized and de-identified prior to being analyzed.

Power Calculation and Data Analysis

For the RCT component of the study, an estimated 150 Year 9 students will be randomly allocated to either Condition 1 (YouthCHAT first) or Condition 2 (HEEADSSS first). A power calculation shows that given 144 participants, there will be 90% power to detect differences between the two assessments assuming a mean duration of 15 minutes for YouthCHAT (SD 30) and 45 minutes for HEEADSSS assessment (SD 90).

Quantitative data will be analyzed using Microsoft Excel and Statistical Software Package (SPSS). Analyses will include basic descriptive statistics (eg, number of youth screened, YouthCHAT summary data, HEEADSSS summary data, demographic characteristics of the sample). Parametric data

will be analyzed using *t* tests and analysis of variance (ANOVA). Nonparametric data will be analyzed using Wilcoxon signed-rank tests.

Qualitative data will be analyzed using a general inductive approach [33] with collated text analyzed to identify emerging themes, which will then be independently coded by 2 researchers with consensus reached by adjudication. Data analysis will be conducted at the end of 2017.

Ethical Approval

This trial received ethical approval from the New Zealand Health and Disability Ethics Committee (Reference: 16/CEN/137) on October 14, 2016.

Results

Participant recruitment for the first phase of this study was undertaken in November 2016. Recruitment for the second phase of the study commenced in January 2017 and will continue until November 2017, with results expected before July 2018.

Discussion

Principal Considerations

If effective, YouthCHAT could offer an inexpensive, simple, scientifically valid, and acceptable vehicle for routine psychosocial screening in all young people in New Zealand high schools (not just those in Year 9 within low-decile schools) and all young people with long-term physical conditions (eg, during routine outpatient visits/annual check-up appointments in pediatric settings). It may also be useful to screen young people in multiple settings overseas.

On an individual level, early detection and intervention of mental health and substance misuse issues can have downstream benefits including improved physical health and better compliance with medical treatments, better engagement in education and subsequent employment, reduced youth suicide, and improved social relationships. Detecting and intervening in risky sexual behaviors can lead to a reduction in unwanted pregnancies and sexually transmitted infections. Dealing with bullying, physical and sexual abuse, and assisting youth with anger control will likely have significant psychosocial benefits. Helping youth make healthy eating choices and increase their physical activity can contribute to their physical and mental health and well-being, and reduce the incidence of conditions such as obesity and related illnesses. Although one other HEEADSSS-based electronic screener for young people (TickIT) has been evaluated for acceptability with this audience [34], no composite screener of this kind has yet been shown to be as effective in identifying psychosocial problems as face-to-face HEEADSSS assessment and there is no other gold standard for psychosocial screening. Evidence of efficacy of screening instruments is as relevant as evidence of acceptability, and this study hopes to demonstrate both for YouthCHAT.

On a population level, the potential impact of such screening and early intervention is enormous. HEEADSSS assessment is currently costly and is therefore limited to a subset of the adolescent population of New Zealand. No routine psychosocial screening is currently undertaken with young people who have long-term physical conditions and are at higher risk of such problems. If the updated version of YouthCHAT is as effective as HEEADSSS assessment in detecting psychosocial issue and is as acceptable to young people, it may be routinely introduced as a first-line screener for psychosocial problems in all youth, especially those at high risk of psychosocial problems. This is likely to have cost benefits with short-term economic impacts including reductions in staff time required to conduct HEEADSSS assessments. Long term, there is the potential for cost effectiveness across many spheres, such as reductions in health care costs associated with helping youth maintain better health through lifestyle choices, reductions in benefits payouts via improving chances of education and employment, and reductions in costs associated with the youth justice system via supporting youth to make prosocial lifestyle choices.

A key advantage of YouthCHAT is its person-centered approach. Young people are asked to indicate which issues they would like help with. Clinical staff are provided with stepped-care resources to use depending on the issue and its severity, including a number of self-management options such as e-therapies. The systematic approach of annual screening and provision of algorithms for stepped-care intervention is likely to lead to early and more comprehensive intervention of youth mental health, substance misuse, and other lifestyle issues, which will have large impacts on their subsequent physical, mental, and social health and well-being, as outlined above.

Conclusion and Recommendations

If the outcomes indicate that YouthCHAT provides a comparable mental health and psychosocial assessment to HEEADDSSS, is acceptable to young people and clinical staff, and is faster to administer, we propose the following clinical changes.

- All Year 9 students in low-decile high schools should be screened using YouthCHAT, and currently routine HEEADSSS assessments should not be undertaken where there is a negative screen. Instead, a tailored (targeted) HEEADSSS assessment should be conducted for the YouthCHAT positive domains.
- Young people with long-term physical conditions who are admitted to pediatric hospitals or attending routine outpatient clinics for long-term physical conditions should undergo an annual YouthCHAT screen, with targeted HEEADSSS assessment where needed.
- All students in New Zealand high schools should be screened using YouthCHAT annually.
- The potential for YouthCHAT to be used in other countries should also be explored.

Acknowledgments

This study is being funded by the Starship Foundation, New Zealand (grant #SF1343).

Conflicts of Interest

FG-S has been the lead investigator in the development, evaluation, and validation of YouthCHAT.

References

1. Auckland District Health Board. The Integrated Child and Youth Mental Health and Addiction Direction 2013-2023.: Auckland District Health Board; 2013. URL: http://www.adhb.govt.nz/Publications/The_Integrated_Child_and_Youth_Mental_Health_and_Addiction_Direction.pdf [accessed 2017-07-07] [WebCite Cache ID 6rmaEl7Aa]
2. Ministry of Health. Understanding suicide in New Zealand. Wellington, NZ: New Zealand Ministry of Health; 2016. URL: http://www.health.govt.nz/our-work/mental-health-and-addictions/working-prevent-suicide/understanding-suicide-new-zealand [accessed 2017-06-29] [WebCite Cache ID 6rankZTGS]
3. Smith JP, Smith GC. Long-term economic costs of psychological problems during childhood. Soc Sci Med 2010 Jul;71(1):110-115 [FREE Full text] [doi: 10.1016/j.socscimed.2010.02.046] [Medline: 20427110]
4. Gibb SJ, Fergusson DM, Horwood LJ. Burden of psychiatric disorder in young adulthood and life outcomes at age 30. Br J Psychiatry 2010 Aug;197(2):122-127 [FREE Full text] [doi: 10.1192/bjp.bp.109.076570] [Medline: 20679264]
5. United States Congress. Health Care Reform Legislation. Washington, DC: United States Congress; 2010. Patient Protection Affordable Care Act 42 U.S.C 18001 et seq URL: https://www.healthcare.gov/glossary/patient-protection-and-affordable-care-act/ [accessed 2017-06-29] [WebCite Cache ID 6rao8M8Tz]
6. Marin TJ, Chen E, Munch JA, Miller GE. Double-exposure to acute stress and chronic family stress is associated with immune changes in children with asthma. Psychosom Med 2009 May;71(4):378-384 [FREE Full text] [doi: 10.1097/PSY.0b013e318199dbc3] [Medline: 19196805]
7. Denny S, de Silva M, Fleming T, Clark T, Merry S, Ameratunga S, et al. The prevalence of chronic health conditions impacting on daily functioning and the association with emotional well-being among a national sample of high school students. J Adolesc Health 2014 Apr;54(4):410-415. [doi: 10.1016/j.jadohealth.2013.09.010] [Medline: 24210897]
8. Pao M, Bosk A. Anxiety in medically ill children/adolescents. Depress Anxiety 2011 Jan;28(1):40-49 [FREE Full text] [doi: 10.1002/da.20727] [Medline: 20721908]
9. Lewis M, Vitulano LA. Biopsychosocial issues and risk factors in the family when the child has a chronic illness. Child Adolesc Psychiatr Clin N Am 2003 Jul;12(3):389-399, v. [Medline: 12910814]
10. World Health Organization. Mental Health Action Plan 2013-2020. 2013. URL: http://apps.who.int/iris/bitstream/10665/89966/1/9789241506021_eng.pdf [accessed 2017-07-07] [WebCite Cache ID 6rmb9I2V1]
11. Ministry of Health. Prime Minister's Youth Mental Health Project. New Zealand; 2012. URL: http://www.superu.govt.nz/ymh [accessed 2017-07-07] [WebCite Cache ID 6rmbJwjxT]
12. Ministry of Social Development. Te Puni Kokiri. New Zealand; 2010. Wh?nau Ora programme URL: https://www.msd.govt.nz/about-msd-and-our-work/publications-resources/corporate/regional-plans/2010-12/waikato/communities/whanau-ora.html [accessed 2017-07-07] [WebCite Cache ID 6rmc1mcTn]
13. Mental Health Commission. Blueprint II: Improving mental health and wellbeing for all New Zealanders. How things need to be. 2012. URL: http://www.hdc.org.nz/media/207642/blueprint%20ii%20how%20things%20need%20to%20be.pdf [accessed 2017-07-07] [WebCite Cache ID 6rmc9sHM4]
14. Mental Health Commission. Blueprint II: Improving mental health and wellbeing for all New Zealanders. Making change happen. 2012. URL: https://www.mentalhealth.org.nz/assets/ResourceFinder/mhc3722-making-change-happen-web-pdf.pdf [accessed 2017-07-07] [WebCite Cache ID 6rmcS3kPT]
15. Ministry of Health. Rising to the challenge: the mental health and addiction service plan development plan 2012-. Wellington, NZ: New Zealand Ministry of Health; 2017. URL: https://www.mentalhealth.org.nz/assets/ResourceFinder/rising-to-the-challenge-mental-health-addiction-service-development-plan.pdf [accessed 2017-07-07] [WebCite Cache ID 6rmcorc12]
16. Ministry of Health. New Zealanders live longer, healthier, more independent livestatement of Intent 2014 to 2018.: New Zealand Ministry of Health URL: https://www.health.govt.nz/system/files/documents/publications/statement-of-intent-2014-to-2018-ministry-of-health-oct14-v2.pdf [accessed 2017-07-07] [WebCite Cache ID 6rmcyBtUa]
17. Ministry of Health. New Zealand Suicide Prevention Action Plan 2013-2016. Wellington, NZ: New Zealand Ministry of Health; 2013. URL: http://www.health.govt.nz/publication/new-zealand-suicide-prevention-action-plan-2013-2016 [accessed 2017-06-29] [WebCite Cache ID 6raodkuJs]
18. Goldenring J, Cohen E. Getting into adolescent heads. Contemp Pediatr 1988;5(7):75-90 [FREE Full text]
19. Goldenring J, Cohen E. Getting into adolescent heads: an esential update. Contemp Pediatr 2004;21(1).
20. Goodyear-Smith F, Warren J, Bojic M, Chong A. eCHAT for lifestyle and mental health screening in primary care. Ann Fam Med 2013;11(5):460-466 [FREE Full text] [doi: 10.1370/afm.1512] [Medline: 24019278]

21. Goodyear-Smith F, Warren J, Elley CR. The eCHAT program to facilitate healthy changes in New Zealand primary care. J Am Board Fam Med 2013;26(2):177-182 [FREE Full text] [doi: 10.3122/jabfm.2013.02.120221] [Medline: 23471931]
22. Christie G, Marsh R, Sheridan J, Wheeler A, Suaalii-Sauni T, Black S, et al. The substances and choices scale (SACS)--the development and testing of a new alcohol and other drug screening and outcome measurement instrument for young people. Addiction 2007 Sep;102(9):1390-1398. [doi: 10.1111/j.1360-0443.2007.01916.x] [Medline: 17645425]
23. Johnson JG, Harris ES, Spitzer RL, Williams JBW. The patient health questionnaire for adolescents: validation of an instrument for the assessment of mental disorders among adolescent primary care patients. J Adolesc Health 2002 Mar;30(3):196-204. [Medline: 11869927]
24. Spitzer RL, Kroenke K, Williams JBW, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med 2006 May 22;166(10):1092-1097. [doi: 10.1001/archinte.166.10.1092] [Medline: 16717171]
25. Goodyear-Smith F. Evolution of the eCHAT: Case-finding to improve health and happiness. Auckland, NZ: The University of Auckland; 2011. URL: https://researchspace.auckland.ac.nz/handle/2292/10622 [accessed 2017-07-07] [WebCite Cache ID 6rmfroQPX]
26. Goodyear-Smith F, Arroll B, Coupe N. Asking for help is helpful: validation of a brief lifestyle and mood assessment tool in primary health care. Ann Fam Med 2009;7(3):239-244 [FREE Full text] [doi: 10.1370/afm.962] [Medline: 19433841]
27. Goodyear-Smith F, Arroll B, Coupe N, Buetow S. Ethnic differences in mental health and lifestyle issues: results from multi-item general practice screening. N Z Med J 2005 Apr 01;118(1212):U1374. [Medline: 15806177]
28. Goodyear-Smith F, Arroll B, Kerse N, Sullivan S, Coupe N, Tse S, et al. Primary care patients reporting concerns about their gambling frequently have other co-occurring lifestyle and mental health issues. BMC Fam Pract 2006 Apr 10;7:25 [FREE Full text] [doi: 10.1186/1471-2296-7-25] [Medline: 16606465]
29. Goodyear-Smith F, Arroll B, Sullivan S, Elley R, Docherty B, Janes R. Lifestyle screening: development of an acceptable multi-item general practice tool. N Z Med J 2004 Nov 05;117(1205):U1146. [Medline: 15570330]
30. Goodyear-Smith F, Arroll B, Tse S. Asian language school student and primary care patient responses to a screening tool detecting concerns about risky lifestyle behaviours. N Z Fam Physician 2004;31(2):84-89.
31. Goodyear-Smith F, Coupe NM, Arroll B, Elley CR, Sullivan S, McGill A. Case finding of lifestyle and mental health disorders in primary care: validation of the 'CHAT' tool. Br J Gen Pract 2008 Jan;58(546):26-31 [FREE Full text] [doi: 10.3399/bjgp08X263785] [Medline: 18186993]
32. Jiang L, Bazarova N, Hancock J. From perception to behavior: Disclosure reciprocity and the intensification of intimacy in computer-mediated communication. Comm Res 2013;40:125-143.
33. Thomas D. A general inductive approach for analyzing qualitative evaluation data. Am J Eval 2006 Jun 01;27(2):237-246. [doi: 10.1177/1098214005283748]
34. Whitehouse SR, Lam PY, Balka E, McLellan S, Deevska M, Penn D, et al. Co-Creation With TickiT: Designing and Evaluating a Clinical eHealth Platform for Youth. JMIR Res Protoc 2013 Oct 18;2(2):e42. [doi: 10.2196/resprot.2865] [Medline: 24140595]

Abbreviations

GAD-7: Generalized Anxiety Disorder scale – 7 item
HEEADSSS: Home, Education/employment, Activity, Drugs, Sexuality, Suicide/depression, Safety
MS: Practice Management System
PHQ-A: Patient Health Questionnaire – Adolescent version
RCT: randomized controlled trial
SACS: Substances and Choices Scale
YouthCHAT: Youth version Case-finding and Help Assessment Tool

Edited by G Eysenbach; submitted 07.05.17; peer-reviewed by S Merry, A Lundervold; comments to author 07.06.17; revised version received 11.06.17; accepted 12.06.17; published 31.07.17.

Please cite as:
Thabrew H, Corter A, Goodyear-Smith F, Goldfinch M
Randomized Trial Comparing the Electronic Composite Psychosocial Screener YouthCHAT With a Clinician-Interview Assessment for Young People: A Study Protocol
JMIR Res Protoc 2017;6(7):e135
URL: http://www.researchprotocols.org/2017/7/e135/
doi:10.2196/resprot.7995
PMID:28760727

Protocol

Effectiveness of Adaptive E-Learning Environments on Knowledge, Competence, and Behavior in Health Professionals and Students: Protocol for a Systematic Review and Meta-Analysis

Guillaume Fontaine[1,2], RN, MSc; Sylvie Cossette[1,2], RN, PhD; Marc-André Maheu-Cadotte[1,2], RN, BSc; Tanya Mailhot[1,2,3], RN, PhD; Marie-France Deschênes[2,4], RN, MSc; Gabrielle Mathieu-Dupuis[5], BSc

[1]Montreal Heart Institute Research Center, Montreal, QC, Canada
[2]Faculty of Nursing, Université de Montréal, Montreal, QC, Canada
[3]Faculty of Medicine, Université de Montréal, Montreal, QC, Canada
[4]Center for Innovation in Nursing Education, Université de Montréal, Montreal, QC, Canada
[5]School of Librarianship and Information Science, Université de Montréal, Montreal, QC, Canada

Corresponding Author:
Guillaume Fontaine, RN, MSc
Montreal Heart Institute Research Center
5000 Belanger Street
Room S-2490
Montreal, QC, H1T 1C8
Canada
Phone: 1 514 376 3330 ext 3069
Fax: 1 514 593 7441
Email: guillaume.fontaine@umontreal.ca

Related Article:

This is a corrected version. See correction statement: http://www.researchprotocols.org/2017/8/e131

Abstract

Background: Adaptive e-learning environments (AEEs) can provide tailored instruction by adapting content, navigation, presentation, multimedia, and tools to each user's navigation behavior, individual objectives, knowledge, and preferences. AEEs can have various levels of complexity, ranging from systems using a simple adaptive functionality to systems using artificial intelligence. While AEEs are promising, their effectiveness for the education of health professionals and health professions students remains unclear.

Objective: The purpose of this systematic review is to assess the effectiveness of AEEs in improving knowledge, competence, and behavior in health professionals and students.

Methods: We will follow the Cochrane Collaboration and the Effective Practice and Organisation of Care (EPOC) Group guidelines on systematic review methodology. A systematic search of the literature will be conducted in 6 bibliographic databases (CINAHL, EMBASE, ERIC, PsycINFO, PubMed, and Web of Science) using the concepts "adaptive e-learning environments," "health professionals/students," and "effects on knowledge/skills/behavior." We will include randomized and nonrandomized controlled trials, in addition to controlled before-after, interrupted time series, and repeated measures studies published between 2005 and 2017. The title and the abstract of each study followed by a full-text assessment of potentially eligible studies will be independently screened by 2 review authors. Using the EPOC extraction form, 1 review author will conduct data extraction and a second author will validate the data extraction. The methodological quality of included studies will be independently assessed by 2 review authors using the EPOC risk of bias criteria. Included studies will be synthesized by a descriptive analysis. Where appropriate, data will be pooled using meta-analysis by applying the RevMan software version 5.1, considering the heterogeneity of studies.

Results: The review is in progress. We plan to submit the results in the beginning of 2018.

Conclusions: Providing tailored instruction to health professionals and students is a priority in order to optimize learning and clinical outcomes. This systematic review will synthesize the best available evidence regarding the effectiveness of AEEs in improving knowledge, competence, and behavior in health professionals and students. It will provide guidance to policy makers, hospital managers, and researchers in terms of AEE development, implementation, and evaluation in health care.

Trial Registration: PROSPERO International Prospective Register of Systematic Reviews: CRD42017065585; https://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42017065585 (Archived by WebCite® at http://www.webcitation.org/6rXGdDwf4)

(JMIR Res Protoc 2017;6(7):e128) doi:10.2196/resprot.8085

KEYWORDS

adaptive learning environments; intelligent tutoring systems; interactive learning environments; medical education; nursing education; e-learning; systematic review; meta-analysis

Introduction

Background

Since the beginning of the 21st century, the complexification of care and the limitation of financial resources in health systems across the globe pose great challenges to the education of health professionals [1]. Academic and clinical leaders must find innovative and effective ways to maintain and update the curricula of their institutions in order to address systemic problems, such as the mismatch of health professionals' competencies to patient and population needs [1]. We have known since the 1980s that individual learning, through one-on-one human tutoring, is more effective than learning through group lectures [2,3]. The consideration of users' navigation behavior, individual goals, knowledge, and preferences provides opportunities for individualized instruction and optimizes learning outcomes [4]. However, while one-on-one human tutoring has its benefits, it is costly, lacks accessibility, and realistically cannot be replicated on a large scale.

E-learning, defined as instruction delivered on a digital device that is intended to support learning [5], is an ever-expanding field in health sciences education. Conventional e-learning courses use words, in the form of spoken or printed text, and multimedia (eg, illustrations, animations, videos) [5]. Content is typically presented linearly, much like reading a book. E-learning can be both asynchronous, (i.e., being designed for self-study) and synchronous (i.e., attending a Web-based class taught by an instructor in real time) [5]. Various presentations of e-learning are increasingly present in clinical settings for the continuing education of health professionals [6] and in academic settings for the education of health professions students [7]. Systematic reviews have demonstrated the effectiveness of e-learning to optimize knowledge, competence, and behavior in health professionals and students [8-13]. E-learning is generally considered to be as effective as non–e-learning educational interventions, such as traditional classroom instruction and printed text in improving learning outcomes [8,12]. Specific instructional design variations within e-learning platforms, such as interactivity, feedback, repetition, and practice exercises, result in better learning outcomes [14].

While e-learning can provide these features, it generally fails to provide individualized instruction equivalent to one-on-one human tutoring [15,16]. Indeed, e-learning is rarely designed to suit the learning goals, knowledge, and preferences of health professionals and students. Moreover, e-learning doesn't provide opportunities for case-based problem solving and simulations of complex real-world tasks while providing tailored feedback and guidance [15]. This is problematic because these instructional strategies have been shown to be effective to improve learning outcomes in face-to-face education [17-19].

Adaptive e-learning environments (AEEs) shows great promise in providing tailored instruction to health professionals and students by adapting the training to each user [20]. By continuously collecting data to build a user's profile (eg, navigation behavior, individual objectives, knowledge, preferences), interpreting these data through algorithms, and adapting in real-time content, navigation, presentation, multimedia, and tools, AEEs can provide a dynamic and evolutionary learning path for each user [21]. However, a wide variety of systems may provide adaptive functionality with various levels of complexity in different fields of study. For instance, adaptive hypermedia systems [21-23] and intelligent tutoring systems [24-26] may both provide variations of an adaptive functionality.

In recent years, AEEs with various levels of complexity, ranging from systems using an adaptive functionality, to systems using artificial intelligence, have been evaluated in some academic settings with positive results regarding learning outcomes [24-27]. However, the effectiveness of AEEs for health professionals' and students' education remains unclear. To our knowledge, no systematic review assessed the effectiveness of AEEs on knowledge, competence, and behavior in health professionals and students.

Systematic Review Objective

To systematically identify, appraise, and synthesize the best available evidence regarding the effectiveness of AEEs in improving knowledge, competence, and behavior in health professionals and health professions students.

Systematic Review Question

What is the effectiveness of AEEs in improving knowledge, competence, and behavior in health professionals and students in comparison with nonadaptive e-learning environments or non–e-learning educational interventions?

Methods

Systematic Review Protocol Development and Registration

This systematic review protocol has been developed according to the Preferred Reporting Items for Systematic review and Meta-Analysis Protocols (PRISMA-P) [28] (Multimedia Appendix A).

This protocol has also been registered prospectively on the PROSPERO database (registration number: CRD42017065585).

Inclusion Criteria

Types of Studies

We will include randomized controlled trials (RCTs), non-RCTs, controlled before-after studies, interrupted time series studies, and repeated measures studies. In order to assess the eligibility of study designs, we will use the algorithm proposed by the Effective Practice and Organisation of Care (EPOC) Cochrane Review Group [29]. If no studies employing these designs are identified, we will consider quasiexperimental study designs for inclusion, such as 1-group pretest/posttest studies and nonequivalent groups studies.

Studies published in French or English, between 2005 and 2017, and conducted in all academic and clinical settings will be considered for inclusion, regardless of the geographic location.

A meta-analysis on the effectiveness of a subtype of AEEs, intelligent tutoring systems, with college students in computer science, physics, and mathematics, found that studies published before 2005-2006 seem to have a bias toward more positive results [25]. This could be explained by the novelty of e-learning in earlier studies, which could have positively affected student motivation and learning outcomes. Thus, we will only include primary studies published from 2005 onward.

Types of Participants

We will consider primary studies conducted with licensed health professionals, students, trainees, and residents in any health care context. From now on, in the context of this review, we will call health professionals and students "users."

Types of Interventions

For the purpose of this review, we define an AEE as an e-learning platform, which continuously collects data to build each user's profile (eg, navigation behavior, individual objectives, preferences, knowledge), interprets these data through algorithms, and adapts in real-time the content (eg, showing/hiding information, providing tailored feedback), navigation (eg, specific links and paths), presentation (eg, device adaptation, page layout), multimedia presentation (eg, images, models, views, widgets, graphics items, scripts, and strategies), or tools (eg, different set of features for the different types of users) to provide a dynamic and evolutionary learning path for each user [20,21,30]. We will use the definitions of each type of adaptation proposed by Knutov and colleagues [21]. The AEE can involve variable levels of technological complexity, ranging from simple adaptive functionality to the use of artificial intelligence [20].

Types of Comparators

Eligible comparators will be nonadaptive e-learning interventions and non–e-learning educational interventions. Nonadaptive e-learning interventions can include interactive features, such as quizzes and practice exercises, and multimedia, but present the same content linearly for each user. Non–e-learning educational interventions can be, for example, traditional classroom instruction, a PowerPoint presentation, printed text, or a combination of these interventions.

Types of Outcomes Measures

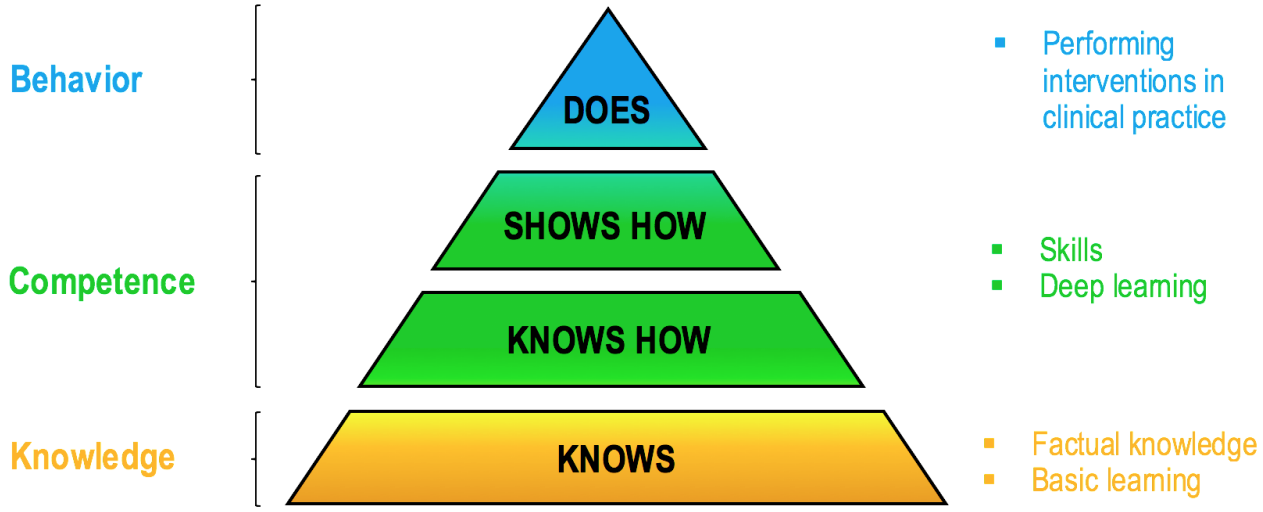
We will consider for inclusion studies reporting the following outcomes: knowledge, competence, and behavior in health professionals and students.

In order to define the outcomes of this systematic review, we adopted the modified conceptual model of Miller [31], which is a framework that identifies 4 stages of clinical practice development: knows, knows how, shows how, and does. Through cognitive and behavioral changes, health professionals and students progress from developing their knowledge about a particular health condition to performing interventions in clinical practice [31]. In the modified version of the model [32], the stages of development have been modified to better match the design and effects of educational interventions (Figure 1).

Primary Outcome Measures

Primary studies reporting an objective measure of users' knowledge (eg, multiple-choice test for assessing factual or conceptual understanding) or a subjective measure of users' knowledge (eg, self-reported knowledge) will be considered for inclusion.

Figure 1. The modified conceptual model of Miller.



Secondary Outcome Measures

Primary studies reporting an objective measure of users' competence (eg, behavior change counseling competence scores) or a subjective measure of users' competence (eg, self-reported skills) will be considered for inclusion.

Primary studies reporting an objective measure of users' behavior (eg, clinical interventions reported in patients' medical file, number of tests ordered) and a subjective measure of users' clinical behavior (eg, self-reported performance of clinical interventions) will be considered for inclusion.

Exclusion Criteria

Any study that does not correspond to the inclusion criteria in terms of study design, participants, intervention, comparator, or outcome measures will be excluded.

We will also exclude: (1) studies that do not provide a sufficient description of the AEE assessed for judging which type(s) and techniques of adaptation are applied; (2) RCTs not published in peer-reviewed journals (eg, dissertations and case reports); (3) systematic reviews, literature reviews, letters, commentaries, editorials, study protocols; and (4) secondary subgroup analyses of RCTs or RCT-generated data modeling studies.

Literature Search

Information Sources

Bibliographical Databases

Eligible primary studies will be identified through a comprehensive literature search of 6 bibliographic databases: CINAHL (EBSCO), EMBASE (OVID), ERIC (ProQuest), PsycINFO (APA PsycNET), PubMed (NCBI), and Web of Science – SCI and SSCI (ISI – Thomson Scientific).

Hand Searching

Relevant journals will be hand-searched for additional articles. Such journals include: *User Modeling and User-Adapted Interaction*, *Computers and Education*, *Journal of Computer Assisted Learning*, *Journal of Medical Internet Research*, *Educational Technology Research and Development*, and *British Journal of Educational Technology*.

Reference Searching

Reference lists of primary studies included will be hand-searched for additional relevant articles. We will also search the reference lists of systematic reviews and meta-analyses in the field of AEEs for relevant articles.

Search Strategy for Bibliographical Databases

The search strategy was developed in collaboration with a Master's student in information science. The search strategy uses a combination of keywords and MeSH terms that relate to 3 key concepts (adaptive e-learning environments; health professionals/health sciences students; effects on knowledge, skills, and behavior) (Multimedia Appendix B). We first developed the strategy for PubMed, and then translated it for other databases (Multimedia Appendix C).

Data Collection and Analysis

Selection of Studies

The titles and abstracts of studies retrieved by the search strategy will be independently screened and "eligibility criteria will be applied by 2 review authors. Disagreements will be resolved through discussion and consensus. A third author will be involved in case of a persistent disagreement. Reference management will be done using the EndNote software, version 8.0.

A full-text assessment of selected articles after the initial screening will be independently conducted by 2 review authors. Access to articles will be gained through the library system of the Université de Montréal. Reasons for the exclusion of articles will be documented and the process of study selection will be reported in a PRISMA flow diagram [33].

Data Extraction and Management

The data of included studies will be extracted using a modified version of the data collection form of the EPOC Cochrane Review Group data collection checklist by 2 review authors [34] (Textbox 1). Data will then be entered in the Review

Manager (RevMan) software, version 5.1. In the case of unclear data, authors will be contacted to obtain relevant data. Data collection forms will then be sent to the first authors of included primary studies for validation.

Assessment of Risk of Bias

The quality of included studies will be independently assessed by 2 review authors using the EPOC risk of bias criteria based upon the data extracted with the data collection checklist [34]. Discrepancies in rating will be resolved through discussion and consensus. Based on the EPOC Cochrane Review Group risk of bias criteria [34], the following 9 criteria will be considered to assess included studies for potential bias: (1) Was the allocation sequence adequately generated? (2) Was the allocation adequately concealed? (3) Were baseline outcome measurements similar? (4) Were baseline characteristics similar? (5) Were incomplete outcome data adequately addressed? (6) Was knowledge of the allocated interventions adequately prevented during the study? (7) Was the study adequately protected against contamination? (8) Was the study free from selective outcome reporting? (9) Was the study free from other risks of bias?

Each criterion will be rated as "low risk" if the bias is unlikely to have seriously affected the results, "high risk" if the bias likely weakened the reliability of the results, and "unclear risk" when there is not enough information to rate the bias as low or high [35]. Justification of each author's assessment will be noted in the risk of bias table.

Textbox 1. Information to extract from included primary studies.

Population and setting

- For descriptive purposes: study setting, inclusion criteria, and exclusion criteria.
- For statistical analyses purposes: study population and study sample.

Methods

For descriptive purposes: study aim, study design, unit of allocation, study start and end date, duration of participation.

Risk of bias assessment

For statistical analysis purposes: random sequence generation, allocation concealment, similarity of baseline outcome measurements, similarity of baseline characteristics, incomplete outcome data, blinding of participants and personnel, blinding of outcome assessments, measures against contamination, selective outcome reporting, other risk of bias.

Participants

For descriptive purposes: withdrawals and exclusions, age, sex, level of instruction, number of years of experience as a health professional, practice setting, previous experience using e-learning.

Interventions (AEE and comparator)

- For descriptive purposes: name of intervention, theoretical framework, statistical model/algorithm, subject, number of training sessions, duration of each training session, mode of delivery, presence of other educational interventions and strategies.
- For statistical analysis purposes: total duration of the training, type and degree of adaptation within the AEE (content, navigation, presentation, multimedia presentation, tools).

Outcomes

For descriptive purposes: name, time-points measured, definition, person measuring, unit of measurement, scales, validation of measurement tool.

Results

- For descriptive purposes: comparison, time-point, baseline data, statistical methods used, and key conclusions.
- For statistical analysis purposes: results according to our primary (knowledge) and secondary (competence, behavior) outcomes.

Table 1. Reasons for downgrading the quality of a body of evidence for a specific outcome.

Factor	Description	Interpretation
Limitations in the design and implementation (within-study risk of bias)	The assessments with the EPOC Cochrane Group risk of bias criteria should feed directly into this factor.	Review authors will interpret the risk of bias as follows: 'low risk of bias' would indicate 'no limitation'; 'unclear risk of bias' would indicate either 'no limitation' or 'serious limitation'; 'high risk of bias' would indicate either 'serious limitation' or 'very serious limitation'.
Indirectness of evidence	Indirect comparisons between intervention A and B; Restricted version of the main review question in terms of population, intervention, comparator, or outcomes.	Review authors will make judgments based on differences in anticipated effects in the group of primary interest.
Unexplained heterogeneity or inconsistency of results	Studies yield widely differing estimates of effect (heterogeneity or variability in results)	Review authors will downgrade the quality of evidence when there is no plausible explanation to the heterogeneity that exists and affects the interpretation of results.
Imprecision of the results	Studies include few participants and few events and have wide confidence intervals.	Review authors will lower their rating of the quality of the evidence if there is imprecision in results of included primary studies.
High probability of reporting bias	The assessments made regarding funnel plot asymmetry should feed directly into this factor.	Review authors will downgrade the quality of evidence level if there is a high probability of reporting bias based on funnel plot asymmetry.

Textbox 2. Subgroup analysis.

Change in targeted health professionals and students

- Doctors and student doctors;
- Nurses and student nurses;
- Other allied health professionals and students.
- Hypothesis: AEEs are more effective for doctors and student doctors than for nurses and student nurses or for health professionals and students.

Change in degree of AEE adaptation: we will rate the degree of adaptation of each AEE from 1-5 according to the types of adaptation (content, navigation, presentation, multimedia presentation, tools).

- ≤2 of 5 types of adaptation;
- ≥3 of 5 types of adaptation.
- Hypothesis: AEEs including ≥3 of 5 types of adaptation are more effective than those including ≤2 of 5 types of adaptation.

Change in type of AEE adaptation

- Content adaptation;
- Other types of adaptation (navigation, presentation, multimedia presentation, tools).
- Hypothesis: AEEs including content adaptation are more effective than those including other types of adaptation.

Change in AEE training program duration

- AEE training programs lasting 1 week or less;
- AEE training programs lasting more than 1 week.
- Hypothesis: AEEs training programs lasting more than 1 week are more effective than those lasting 1 week or less.

Change in publication years

- Studies published before 2010;
- Studies published after 2010.
- Hypothesis: AEEs reported in studies published after 2010 are more effective than those reported in studies published before 2010.

Dealing With Unclear Data

We will contact the investigators of included studies if there is any unclear or missing data. If unsuccessful, we will provide a narrative synthesis of the data as presented in the study.

Assessment of Heterogeneity

Heterogeneity will first be assessed by examining the characteristics of included studies, the similarities and disparities between the types of participants, the types of interventions, and the types of outcomes.

Heterogeneity will then be assessed by using the chi-square and the I^2 statistics within the RevMan software. The I^2 statistic describes the percentage of variance in effect estimates that is due to heterogeneity. As suggested by Higgins et al. [36], we will interpret the I^2 values as follows: 0%-40%: might not be important; 30%-60%: may represent moderate heterogeneity; 50%-90%: may represent substantial heterogeneity; and 75%-100%: considerable heterogeneity.

We intend to use the random-effects model where moderate to substantial heterogeneity is observed. If substantial or considerable heterogeneity is observed and study effects are discordant, we will not pool data, unless heterogeneity is explained by subgroup differences.

Assessment of Reporting Biases

Reporting biases will be assessed by using funnel plots if more than 10 studies are included in the meta-analysis, as recommended by the Cochrane Handbook. We will follow the guidelines regarding funnel plot asymmetry as described in the *Cochrane Handbook for Systematic Reviews of Interventions* 5.1.0 [35]. For analyses performed on less than 10 primary studies, we will assess reporting bias qualitatively.

Assessment of the Quality of Evidence

The quality of the evidence regarding the outcomes reported in this systematic review will be assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach, based upon the data extracted with the data collection checklist [37,38]. The GRADE approach specifies 4 levels of quality (high, moderate, low, and very low) for each individual outcome.

In order to attribute a level of quality, the GRADE approach considers 5 factors for downgrading the quality of a body of evidence for a specific outcome (Table 1). The certainty of the evidence will be independently assessed by 2 review authors. Any disagreement will be resolved through discussion.

Data Synthesis

Characteristics of included primary studies, such as population studied and study design, will be presented in a table format.

Data will then be synthesized by a descriptive analysis. We will describe the characteristics of AEEs including, when possible: intervention name, theoretical framework, statistical model or algorithm, subject, number of training sessions, duration of each training session, total duration of the training, mode of delivery, and presence of other educational interventions and strategies.

We will undertake a meta-analysis that will compare changes between intervention and control participants in primary and secondary outcomes, for which data from at least 2 studies are available. Knowledge, competence, and behavior will be addressed and analyzed separately. Statistical analysis will be conducted upon consideration of dichotomous outcome variables (eg, content adaptation, yes/no) and continuous outcome variables (eg, change in behavior change counseling competence scores).

Sensitivity Analysis

We will perform sensitivity analyses in order to exclude high risk of bias studies (as assessed with the EPOC risk of bias criteria) and small sample size studies (n≤20). Sensitivity analyses will allow us to determine if our conclusions are robust or if the key findings disappear with the exclusion of high risk of bias and small sample size studies.

Subgroup Analysis

Contextual heterogeneity will be considered by conducting the analyses in subgroups, according to potential effect modifiers. If sufficient data is available, we plan to perform 5 subgroup analyses (Textbox 2).

Results

The review is in progress. We plan to submit the manuscript in the beginning of 2018. The anticipated findings of this systematic review will have implications for policy, practice, and research. First, it will provide evidence for policy makers and hospital managers of whether or not AEEs can increase the learning effectiveness and efficiency for health professionals and students, potentially lowering training costs and optimizing clinical practice. Second, this systematic review will identify specific considerations regarding AEE design, implementation, and evaluation in health care, indicating what would need to be taken into account for future studies.

Discussion

Providing tailored instruction to health professionals and students is a priority in order to optimize learning and clinical outcomes. This systematic review will provide a summary of the best available evidence regarding the effectiveness of AEEs in improving the knowledge, competence, and behavior of health professionals and students.

Acknowledgments

We wish to thank Quebec's Healthcare Research Fund, Quebec's Ministry of Higher Education, the Montreal Heart Institute Foundation, and the Faculty of Nursing at the Université de Montréal for the financial support they provided to GF.

We also wish to thank Kate Johnson for her careful manuscript editing.

Authors' Contributions

GF and GMD developed and tested the search strategy. GF wrote the initial protocol. All authors contributed to protocol writing. All authors read and approved the final version of the manuscript.
GF and MAMC will be responsible for title and abstract screening, full-text assessment of studies, data extraction, and risk of bias assessment. GF and SC will perform statistical analysis, which will be validated by an experienced biostatistician.

Conflicts of Interest

None declared.

Multimedia Appendix 1

PRISMA-P Checklist.

[PDF File (Adobe PDF File), 69KB - resprot_v6i7e128_app1.pdf]

Multimedia Appendix 2

Concept plan used to build the search strategy.

[PNG File, 496KB - resprot_v6i7e128_app2.png]

Multimedia Appendix 3

Search strategy for PubMed.

[PNG File, 304KB - resprot_v6i7e128_app3.png]

References

1. Frenk J, Chen L, Bhutta ZA, Cohen J, Crisp N, Evans T, et al. Health professionals for a new century: transforming education to strengthen health systems in an interdependent world. Lancet 2010;376:1923-1958. [doi: 10.1016/S0140-6736(10)61854-5] [Medline: 21112623]
2. Bloom BS. The 2 sigma problem: the search for methods of group instruction as effective as one-to-one tutoring. Educ Res 1984;13:4-16. [doi: 10.3102/0013189X013006004]
3. Cohen P, Kulik JA, Kulik CLC. Educational outcomes of tutoring: a meta-analysis of findings. Am Educ Res J 1982;19:237-248. [doi: 10.3102/00028312019002237]
4. Evens M, Michael J. One-on-One Tutoring by Humans and Computers. Mahwah, New Jersey: Lawrence Erlbaum Associates, Inc; 2006.
5. Clark R, Mayer R. E-Learning and the Science of Instruction: Proven Guidelines for Consumers and Designers of Multimedia Learning. Hoboken, New Jersey: John Wiley & Sons; 2016.
6. Cheng B, Wang M, Mørch A, Chen NS, Kinshuk K, Spector JM. Research on e-learning in the workplace 2000–2012: a bibliometric analysis of the literature. Educ Res Rev 2014;11:56-72. [doi: 10.1016/j.edurev.2014.01.001]
7. George P, Papachristou N, Belisario JM, Wang W, Wark PA, Cotic Z, et al. Online eLearning for undergraduates in health professions: a systematic review of the impact on knowledge, skills, attitudes and satisfaction. J Glob Health 2014;4:010406 [FREE Full text] [doi: 10.7189/jogh.04.010406] [Medline: 24976965]
8. Cook DA, Levinson AJ, Garside S, Dupras DM, Erwin PJ, Montori VM. Internet-based learning in the health professions: a meta-analysis. JAMA 2008;300:1181-1196. [doi: 10.1001/jama.300.10.1181] [Medline: 18780847]
9. Cook DA, Levinson AJ, Garside S, Dupras DM, Erwin PJ, Montori VM. Instructional design variations in internet-based learning for health professions education: a systematic review and meta-analysis. Acad Med 2010;85:909-922. [doi: 10.1097/ACM.0b013e3181d6c319] [Medline: 20520049]
10. Lam-Antoniades M, Ratnapalan S, Tait G. Electronic continuing education in the health professions: an update on evidence from RCTs. J Contin Educ Health Prof 2009;29:44-51. [doi: 10.1002/chp.20005] [Medline: 19288566]
11. Sinclair P, Kable A, Levett-Jones T, Booth D. The effectiveness of Internet-based e-learning on clinician behaviour and patient outcomes: A systematic review. Int J Nurs Stud 2016;57:70-81. [doi: 10.1016/j.ijnurstu.2016.01.011] [Medline: 27045566]
12. Lahti M, Hätönen H, Välimäki M. Impact of e-learning on nurses' and student nurses knowledge, skills, and satisfaction: a systematic review and meta-analysis. Int J Nurs Stud 2014;51:136-149. [doi: 10.1016/j.ijnurstu.2012.12.017] [Medline: 23384695]
13. Voutilainen A, Saaranen T, Sormunen M. Conventional vs. e-learning in nursing education: a systematic review and meta-analysis. Nurse Educ Today 2017;50:97-103. [doi: 10.1016/j.nedt.2016.12.020] [Medline: 28038371]

14. Cook D, Garside S, Levinson AJ, Dupras DM, Montori VM. What do we mean by web-based learning? A systematic review of the variability of interventions. Med Educ 2010;44:765-774. [doi: 10.1111/j.1365-2923.2010.03723.x] [Medline: 20633216]
15. Crowley R, Legowski E, Medvedeva O, Tseytlin E, Roh E, Jukic D. Evaluation of an intelligent tutoring system in pathology: effects of external representation on performance gains, metacognition, and acceptance. J Am Med Inform Assoc 2007;14:182-190 [FREE Full text] [doi: 10.1197/jamia.M2241] [Medline: 17213494]
16. Samulski T, La T, Wu RI. Adaptive eLearning modules for cytopathology education: a review and approach. Diagn Cytopathol 2016;44:944-951. [doi: 10.1002/dc.23558] [Medline: 27534838]
17. Gaberson K, Oermann M. Clinical Teaching Strategies in Nursing. New York, New York: Springer; 2010.
18. Cook D, Hatala R, Brydges R, Zendejas B, Szostek JH, Wang AT, et al. Technology-enhanced simulation for health professions education: a systematic review and meta-analysis. JAMA 2011;306:978-988. [doi: 10.1001/jama.2011.1234] [Medline: 21900138]
19. Bloom B. Effects of continuing medical education on improving physician clinical care and patient health: a review of systematic reviews. Int J Technol Assess Health Care 2005;21:380-385. [Medline: 16110718]
20. Brusilovsky P, Peylo S. Adaptive and intelligent web-based educational systems. International Journal of Artificial Intelligence in Education 2003;13:159-172.
21. Knutov E, De Bra P, Pechenizkiy M. AH 12 years later: a comprehensive survey of adaptive hypermedia methods and techniques. New Rev Hypermedia Multimed 2009;15:5-38. [doi: 10.1080/13614560902801608]
22. Brown E, Cristea A, Stewart C, Brailsford RJ. Patterns in authoring of adaptive educational hypermedia: a taxonomy of learning styles. J Educ Technol Soc 2005;8:77-90.
23. Akbulut Y, Cardak CS. Adaptive educational hypermedia accommodating learning styles: A content analysis of publications from 2000 to 2011. Comp Educ 2012;58:835-842. [doi: 10.1016/j.compedu.2011.10.008]
24. Ma W, Adesope OO, Nesbit JC, Liu Q. Intelligent tutoring systems and learning outcomes: a meta-analysis. J Educ Psychol 2014;106:901-918. [doi: 10.1037/a0037123]
25. Steenbergen-Hu S, Cooper H. A meta-analysis of the effectiveness of intelligent tutoring systems on K–12 students' mathematical learning. J Educ Psychol 2013;105:970-987. [doi: 10.1037/a0032447]
26. Kulik J, Fletcher JD. Effectiveness of intelligent tutoring systems: a meta-analytic review. Rev Educ Res 2015;86:42-78. [doi: 10.3102/0034654315581420]
27. VanLehn K. The relative effectiveness of human tutoring, intelligent tutoring systems, and other tutoring systems. Educ Psychol 2011;46:197-221. [doi: 10.1080/00461520.2011.611369]
28. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev 2015:1 [FREE Full text] [doi: 10.1186/2046-4053-4-1] [Medline: 25554246]
29. EPOC Cochrane Review Group. What study designs should be included in an EPOC review and what should they be called?. 2014. URL: https://epoc.cochrane.org/sites/epoc.cochrane.org/files/public/uploads/EPOC [accessed 2017-06-27] [WebCite Cache ID 6rXc2WZjv]
30. Knutov E, De Bra P, Pechenizkiy M. Generic adaptation framework: a process-oriented perspective. Journal of Digital Information 2011;12:1-22.
31. Miller GE. The assessment of clinical skills/competence/performance. Acad Med 1990(suppl 2):S63-S67. [Medline: 2400509]
32. Moja L, Moschetti I, Cinquini M, Sala V, Compagnoni A, Duca P, et al. Clinical evidence continuous medical education: a randomised educational trial of an open access e-learning program for transferring evidence-based information - ICEKUBE (Italian Clinical Evidence Knowledge Utilization Behaviour Evaluation) - study protocol. Implement Sci 2008:37 [FREE Full text] [doi: 10.1186/1748-5908-3-37] [Medline: 18637189]
33. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS Med 2009;6:e1000100 [FREE Full text] [doi: 10.1371/journal.pmed.1000100] [Medline: 19621070]
34. EPOC Cochrane Review Group. Data extraction and management: EPOC resources for review authors. 2013. URL: http://epoc.cochrane.org/epoc?specific?resources?review?authors [accessed 2017-06-27] [WebCite Cache ID 6rXcQqGgu]
35. Higgins J, Green S. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0: The Cochrane Collaboration. London, United Kingdom: The Cochrane Collaboration; 2011.
36. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ 2003;327:557-560 [FREE Full text] [doi: 10.1136/bmj.327.7414.557] [Medline: 12958120]
37. Guyatt G, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ 2008;336:924-926 [FREE Full text] [doi: 10.1136/bmj.39489.470347.AD] [Medline: 18436948]
38. Schünemann H. Chapter 12: Interpreting results and drawing conclusions. In: Higgins JPT, Green S, editors. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0. London, United Kingdom: The Cochrane Collaboration; 2011:359-387.

Abbreviations

AEE: adaptive e-learning environment
EPOC: effective practice and organisation of care
GRADE: grading of recommendations assessment, development and evaluation
PRISMA-P: preferred reporting items for systematic review and meta-analysis protocols
RCT: randomized control trial

Edited by G Eysenbach; submitted 21.05.17; peer-reviewed by J Apolinário-Hagen, L DelSignore; comments to author 14.06.17; accepted 17.06.17; published 05.07.17.

Please cite as:
Fontaine G, Cossette S, Maheu-Cadotte MA, Mailhot T, Deschênes MF, Mathieu-Dupuis G
Effectiveness of Adaptive E-Learning Environments on Knowledge, Competence, and Behavior in Health Professionals and Students: Protocol for a Systematic Review and Meta-Analysis
JMIR Res Protoc 2017;6(7):e128
URL: http://www.researchprotocols.org/2017/7/e128/
doi:10.2196/resprot.8085
PMID:28679491

Protocol

Sharing Annotated Audio Recordings of Clinic Visits With Patients—Development of the Open Recording Automated Logging System (ORALS): Study Protocol

Paul J Barr[1], MSc, PhD; Michelle D Dannenberg[1], MPH; Craig H Ganoe[2], MS; William Haslett[2], PhD; Rebecca Faill[2]; Saeed Hassanpour[2,3,4], MMath, PhD; Amar Das[1,2], MD, PhD; Roger Arend[5], BS; Meredith C Masel[6], MSW, PhD; Sheryl Piper[7]; Haley Reicher[8], BA; James Ryan[9], DO; Glyn Elwyn[1], MSc, MD, PhD

[1]The Dartmouth Institute for Health Policy and Clinical Practice, Geisel School of Medicine, Dartmouth College, Lebanon, NH, United States

[2]Department of Biomedical Data Science, Geisel School of Medicine, Dartmouth College, Lebanon, NH, United States

[3]Department of Computer Science, Dartmouth College, Hanover, NH, United States

[4]Department of Epidemiology, Geisel School of Medicine, Dartmouth College, Lebanon, NH, United States

[5]Patient Partner, Hanover, NH, United States

[6]Oliver Center for Patient Safety and Quality Healthcare, University of Texas Medical Branch, Galveston, TX, United States

[7]Patient Partner, Ludington, MI, United States

[8]Dartmouth College, Hanover, NH, United States

[9]Ryan Family Practice, Ludington, MI, United States

Corresponding Author:
Paul J Barr, MSc, PhD
The Dartmouth Institute for Health Policy and Clinical Practice
Geisel School of Medicine
Dartmouth College
Level 5, Williamson Translational Research Building, Rm 555
One Medical Center Drive
Lebanon, NH,
United States
Phone: 1 603 653 0863
Fax: 1 603 653 0896
Email: paul.j.barr@dartmouth.edu

Abstract

Background: Providing patients with recordings of their clinic visits enhances patient and family engagement, yet few organizations routinely offer recordings. Challenges exist for organizations and patients, including data safety and navigating lengthy recordings. A secure system that allows patients to easily navigate recordings may be a solution.

Objective: The aim of this project is to develop and test an interoperable system to facilitate routine recording, the Open Recording Automated Logging System (ORALS), with the aim of increasing patient and family engagement. ORALS will consist of (1) technically proficient software using automated machine learning technology to enable accurate and automatic tagging of in-clinic audio recordings (tagging involves identifying elements of the clinic visit most important to patients [eg, treatment plan] on the recording) and (2) a secure, easy-to-use Web interface enabling the upload and accurate linkage of recordings to patients, which can be accessed at home.

Methods: We will use a mixed methods approach to develop and formatively test ORALS in 4 iterative stages: case study of pioneer clinics where recordings are currently offered to patients, ORALS design and user experience testing, ORALS software and user interface development, and rapid cycle testing of ORALS in a primary care clinic, assessing impact on patient and family engagement. Dartmouth's Informatics Collaboratory for Design, Development and Dissemination team, patients, patient partners, caregivers, and clinicians will assist in developing ORALS.

Results: We will implement a publication plan that includes a final project report and articles for peer-reviewed journals. In addition to this work, we will regularly report on our progress using popular relevant Tweet chats and online using our website, www.openrecordings.org. We will disseminate our work at relevant conferences (eg, Academy Health, Health Datapalooza, and

the Institute for Healthcare Improvement Quality Forums). Finally, Iora Health, a US-wide network of primary care practices (www.iorahealth.com), has indicated a willingness to implement ORALS on a larger scale upon completion of this development project.

Conclusions: Upon the completion of this project we will have developed a novel recording system that will be ready for large-scale testing. Our long-term goal is for ORALS to seamlessly fit into a clinic's and patient's daily routine, increasing levels of patient engagement and transparency of care.

(JMIR Res Protoc 2017;6(7):e121) doi:10.2196/resprot.7735

KEYWORDS

audiovisual aids; patient engagement; machine learning; disease management; caregivers; patients

Introduction

Background

Higher recall of medical information is associated with improved disease management, treatment adherence, and higher patient satisfaction; however, recall of medical information is often low, with 40% to 80% of medical information from a clinical visit forgotten immediately by patients [1-5]. Poor knowledge of medical conditions has been identified as a significant barrier to self-management of health conditions associated with lower health status [6]. Difficulty recalling health information is amplified when patients are emotionally charged [7-10]. Lack of health literacy—the ability to perform basic reading and numerical tasks required to function in a health care environment [10]—exacerbates the challenge of patient recall and understanding of health information and affects 59% of adults over 65 years in the United States [11]. Low health literacy is associated with a reduction in the ability of patients to self-manage and interpret health messages and medication labels [12-16]. When patients find it difficult to comprehend health care information during the visit, they are in turn less able to recall information following the visit [17-19].

There have been several advances toward addressing this information recall problem [20]. Providing patients with an after visit summary (AVS) within 3 days of the clinic visit is a key requirement of Meaningful Use of an electronic health record (EHR), stage 1 [21]. Allowing patients to have access to clinician notes through OpenNotes after the visit makes patients feel more in control of their care and improves information recall and medication adherence [22]. Patients also share these notes with family members, which can enhance decision-making skills and care because families can better support a patient through difficult decisions and treatments when they have all the necessary medical information [23]. Note-taking during the visit or specific written instructions postvisit are other methods proposed to improve recall and improve treatment engagement [24-26]. However, strategies dependent on written material are much less effective when the patient has basic health literacy [17,27-29], and the act of note-taking can be distracting to both the patient and the physician.

An alternative approach, based on 40 years of research, is to share audio or video recordings of clinic visits. Patients value listening to and sharing recordings of clinic visits with their families; access to recordings leads to increased patient and family engagement, understanding, recall of health care information, and treatment adherence and reduced decisional regret [8,30-45]. This is also a benefit for caregivers, who are better prepared to provide care, which could in turn reduce caregiver morbidity associated with a perceived lack of self-efficacy related to the provision of care [46,47].

Despite evidence of benefit, patients are rarely offered recordings, yet demand is high as evidenced by the rise of patients secretly recording clinic visits [32,48]. In a recent study of 130 respondents from the general public in the United Kingdom, 15% reported covertly recording a clinic visit, and 77% would like their clinic to offer recordings [49]. The main motivation for recording was to improve understanding and involve family members in care, and the patients who did record reported greater engagement and empowerment. However, patients felt that the absence of a safe, secure, and efficient recording system was a significant barrier. Navigating lengthy recordings was also considered a problem because getting the benefit "depends on picking out...the crucial points..." [32]. A secure system that allows patients to easily navigate recordings by tagging elements of the clinic visit that are most important to them (eg, diagnosis, treatment plan) may be a solution.

Aims

The purpose of this project is to develop and test an interoperable system to facilitate routine tagged recordings—Open Recording Automated Logging System (ORALS)—with the aim of increasing patient and family engagement in care. ORALS will consist of 2 key elements: (1) technically proficient software using automated machine learning technology to enable accurate and automatic tagging of in-clinic audio recordings and (2) a secure, easy-to-use Web interface enabling the upload and accurate linkage of recordings to patients that can be accessed at home. Our team consists of a range of stakeholders including the Informatics Collaboratory for Design, Development, and Dissemination (ic3d) at Dartmouth; Geisel School of Medicine at Dartmouth; patients; caregivers; and clinicians.

The expected outcome of this project is the development of a widely accepted and scalable recording system, ORALS, that can be used by patients and their families, leading to higher patient and family engagement.

We will use a mixed methods and agile software development approach, which involves the early and frequent engagement of end-users, to develop and conduct formative testing of ORALS in 4 iterative stages: a case study of pioneer clinics where recordings are currently offered to patients, ORALS

design and user experience testing, the development of ORALS software and user interface, and rapid cycle testing of ORALS in a primary care clinic (Figure 1).

Methods

Stage 1: Case Study

Overview

To gain a deeper understanding of phenomena in their context of use, a case study methodology is recommended [50]. The case study will be guided by Yin's [51,52] approach, using 5 components: research questions, propositions or purpose, units of analysis, determination of how the data are linked to the propositions, and criteria to interpret the findings. The first step to developing ORALS is to gain a deep understanding of existing approaches to recording visits (see Table 1). We will conduct site visits to the Ryan Family Practice, Ludington, MI; University of Texas Medical Branch Cancer Center Victory Lakes, League City, TX; and Barrow Neurosurgical Institute, Phoenix, AZ. Each of these sites has a unique approach to recording visits and thus important insight to share that will help guide the development of ORALS.

Purpose

Our purpose is to gain insight from pioneer clinics to guide the development of ORALS. In stages 2, 3, and 4, we will use case study findings to develop ORALS and test the software in a human-computer interaction laboratory and in clinic settings. The ic3d team and patient representatives will be involved in stage 1 by guiding the study design and interpreting findings. Figure 2 illustrates the critical steps, from the challenges of accurate physical recording to creating a secure data store for safe multiple use access.

Figure 1. Stages of Open Recording Automated Logging System development.

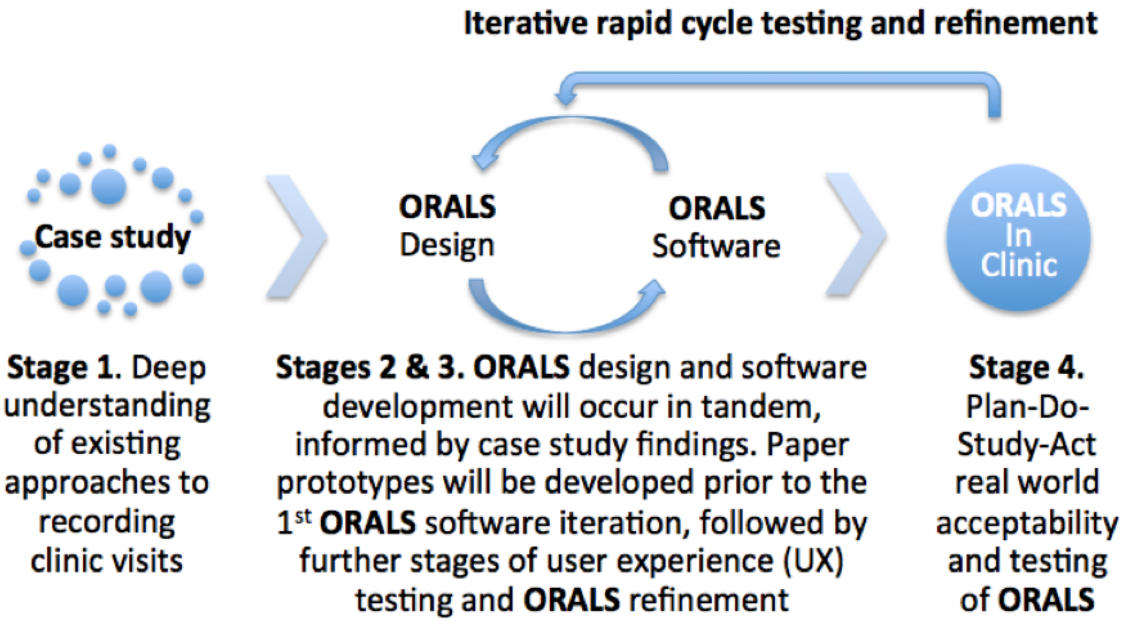
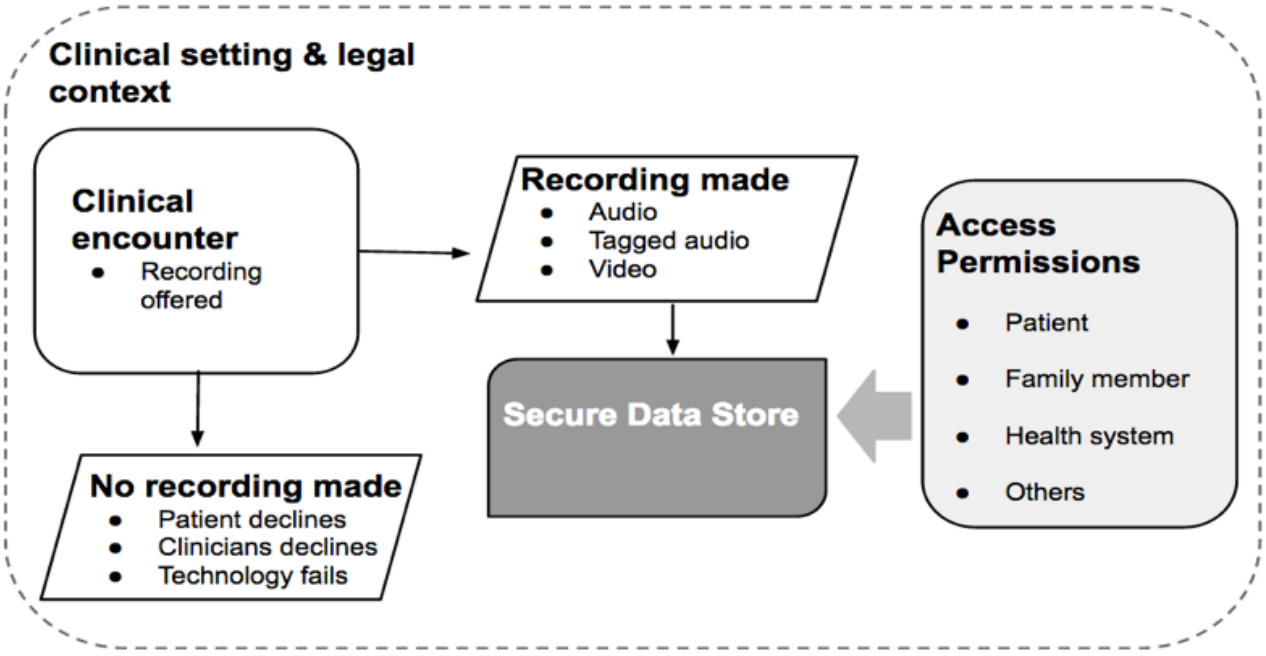


Table 1. Case study research guide (informed by our previous research [53]).

Research questions	Data sources
RQ1. What are the technological aspects of successful recording software and user interface?	Interview (clinicians, patients, family members, software developers, clinic management and administrators); documentation (study reports, specifications of software and hardware), direct observation (use of recording technology)
RQ2. Why and how was the recording and sharing of clinical visits with patients adopted?	Interview (clinicians, clinic management and administrators, patients), documentation (policy documents, consent forms, survey data, publications), archival (proportion of clinicians who offer recording, log of recording use)
RQ3. How are recordings used?	Interview (clinicians, patients, family members, clinic management and administrators), documentation (survey data, publications), direct observation (use of recording technology)
RQ4. What is the added value of tagging recordings and what are the most important moments to tag?	Interview (clinicians, patients, family members, clinic management and administrators), documentation (survey data), archival (log of system use)

Figure 2. A conceptual path to recording, tagging, and sharing the clinical encounter.



Design

We will adopt a multiple case design including 3 sites where recordings of medical visits are shared with patients [51]. Each recording system represents a case (ie, the unit of analysis). Embedded in each case will be clinicians who support recording and those who do not, patients and their families, and clinic management and administrative staff.

Settings

Clinic 1: Ryan Family Practice, Ludington, Michigan

This primary care practice consists of a clinician, medical assistant, secretary, and a 2000-patient panel, with 120 patient visits per week. Dr James Ryan and Kevin Perdue have developed an electronic medical record system called the small brain records project that supports contemporaneous tagging of audio recordings as Dr Ryan enters patient data (eg, medication change). These tagged encounters and audio recordings are shared with patients and caregivers via a secure Web portal. While Dr Ryan plans to record all of his patient visits, he currently records approximately 50% of patient visits.

Clinic 2: University of Texas Medical Branch, Cancer Center Victory Lakes, League City, Texas

The University of Texas Medical Branch (UTMB) Cancer Center in Victory Lakes consists of 14 clinicians who each treat approximately 40 to 50 patients per week. Dr Meredith Masel of the Oliver Center for Patient Safety and Quality Healthcare, UTMB, Galveston, TX, has pioneered the routine implementation of audiorecording in UTMB Cancer Clinics through the "Taking the Message and the Medicine Home" program. Patients are offered a digital device to record visits or are educated about recording and using their own device.

Clinic 3: Barrow Neurological Institute, Phoenix, Arizona

Barrow Neurological Institute (BNI) is a large neurological disease institute. Each of its 27 neurosurgeons treats 50 patients per week. Currently 10 clinicians use the Medical Memory video recording service, developed by Dr Randall Porter, to record the visit and share with patients via a secure Web portal.

Ethics

This research has received Institutional Review Board (IRB) approval from the Committee for the Protection of Human Subjects at Dartmouth College (Study #29380).

Participants

Participants will include patients, family members, clinical staff, management, and administrators. We will use key contacts to arrange interviews and include clinicians who have chosen not to offer patients recordings. Interviewees will be 18 years or older and able to communicate in English. We plan to conduct a minimum of 6 interviews per stakeholder group at each site until data saturation is reached [53].

Data Collection

Overview

Yin [51] identifies 6 primary sources of evidence for case study research. Using multiple sources of evidence per research question increases the precision of findings through a process of triangulation, taking different angles toward studying the same phenomena. Four of these sources can be used to answer the research questions described above (Table 1). A study database will be created using ATLAS.ti qualitative data analysis and research software (Scientific Software Development GmbH), increasing the reliability of findings by creating a chain of evidence from data collected, coding, and linkages to research questions [51]. Further details of theses sources are described below.

Semistructured Interviews

Semistructured interviews will be conducted and audiorecorded. We plan to conduct the majority of interviews over 5-day site visits. Our information technology (IT) team will conduct

interviews with technology experts at each site. Topic guides have been developed with patient representatives and IT staff (Multimedia Appendix 1). All interviews will be transcribed by Acusis medical transcription service.

Documentation and Archival Sources

Relevant documents will be requested from clinic staff (eg, clinic recording policies, patient information sheets). We will liaise with the IT team to assess technical barriers (eg, interoperability challenges) and, where available, the proportion of patients with recordings, length of recordings, and playback frequency.

Direct Observation

We will observe the process from introduction to recording, its completion, and sharing with the patient.

Analysis

Audio recordings will be transcribed verbatim. Data analysis will take place simultaneously with data collection, which, in turn, will assist in the iterative development of the interview guides. We will use a framework approach to analyze the data. This approach consists of 6 steps: familiarizing ourselves with the data, identifying a framework, and indexing, charting, mapping, and interpreting the data [54,55]. The research questions will provide the analytic framework with thematic comparisons across cases. Identifying recurring themes across sites is a strength of the multiple case study design. Two researchers will apply an initial codebook, and they will meet and include new codes into a revised codebook before conducting a secondary assessment of interview data. Emergent codes will be added to existing codes. Codes, memos, and short narrative summations of data will be entered into ATLAS.ti.

Stage 2: Open Recording Automated Logging System Design

Overview

Case study information will determine the scope and functionality of Open Recording Automated Logging System (ORALS) and the user interface designed using usability engineering [56].

Purpose

Usability engineering will provide iterative, formative feedback from ORALS target users. Vinter et al [57] reported that usability errors dominate 60% of software problem reports. Myers and Rosson [58] reported that about half of code development is devoted to user interface design. To mitigate these challenges, early stakeholder engagement in ORALS design before initial software development and iteratively thereafter is crucial.

Design

A member of the interaction design team will be embedded in stage 1 of the case study. We will analyze which moments during the clinic visit matter most to patients and their families (RQ4, Table 1) to arrive at a standardized set of tags for the user interface (eg, test result, treatment plan). This set will be categorized into terms such as specific medical conditions or treatments and topics such as treatment decisions and plans. Case study data will also support the development of a set of activity scenarios and associated tasks for participants to complete using prototypes. This will include tasks such as authenticating into ORALS to allow the secure linkage of recordings to patients, controlling recordings (eg, starting and stopping), finding a recent appointment, finding tagged information in the recordings, and other derived tasks.

Paper prototyping activities will guide early software development cycles by engaging potential ORALS users. This work creates an interactive interface by using paper, pens, markers, Post-It notes, and other media to mock up multiple screens and overlays for users [59]. As users complete tasks, a member of the design team responds by changing the paper interface screens and overlays. This prototyping process offers the benefits of getting users involved in the design early, when there is evidence that users are much more likely to offer feedback because the interface appears more malleable and capable of change.

The design team will develop a usability specification for the set of tasks and define the expected interaction paths and the amount of time to complete each task. The usability specification will be used as a baseline for determining changes. Survey questions will be used to collect demographics, preassessment of user expectations of the system, posttask design feedback, and postassessment of user impressions of the system.

We anticipate 3 rounds of ORALS usability evaluation with stakeholder users: (1) paper prototyping as described, (2) formative evaluation with an early software prototype midway in the software development cycle, and (3) summative evaluation at the end of the development cycle to understand how the ORALS will work in the field and guide final changes.

Settings

Facilitator-led paper prototyping activities will take place in person with prospective users in the human-computer interaction lab, ic3d lab, Geisel School of Medicine; observers will take notes. For formative and summative usability evaluation, activities can be conducted in person or facilitated remotely using Web conferencing tools. We will use a software usability evaluation product called Morae (TechSmith Corp), which supports screen recording of software use and a log of mouse and keyboard interactions. Each session will be designed to last about an hour.

Participants

We will work with a minimum of 6 potential users, patients, and clinicians in each design round. Participants will be identified both from local clinics and the in-clinic test site at UTMB. Participants will receive $25 for their participation.

Data Collection

Paper prototyping sessions will provide data through observational notes, think-aloud statements, and resulting design artifacts from changes in each session. Software evaluation sessions will collect performance measures, think-aloud statements, survey responses, and recordings of the user interactions with the system.

- Design artifacts: Modifications made to the design on the paper prototype will be photographed/scanned for review during analysis.
- Performance measures: Morae will capture time to task completion, successes, and failures.
- Survey responses: Morae will introduce and store survey questions during each task. Questions will focus on user roles and experience, ease of use for tasks, understanding of visual information, and known design tradeoff decisions.
- Screen and input recordings: Morae will produce a screen and audio recording of the session by task with an associated log of user input and any real-time codes entered by the facilitator.
- Observation: The facilitator and/or an observer will take notes during the session of any design-related events that take place during the user interactions with ORALS.
- Think aloud: Session participants will be instructed on how to think aloud during the session [60]. This will involve users verbally narrating their goals and plans for interacting with ORALS and reactions to the system's responses to their input.

Analysis

The primary evaluation goal is to refine the user interface design, providing a layout, interface controls, and workflow for creating and reviewing recordings in ORALS. A member of the research team with expertise in user design (CG) will analyze the results of the paper prototyping sessions for themes. CG will also review recordings of the software session for usability issues, including deviations from the expected interaction paths. Finally, CG will analyze performance measures, coded sessions, and survey responses. Modifications and enhancements to the interface will be based on commonality of themes.

System Prototyping

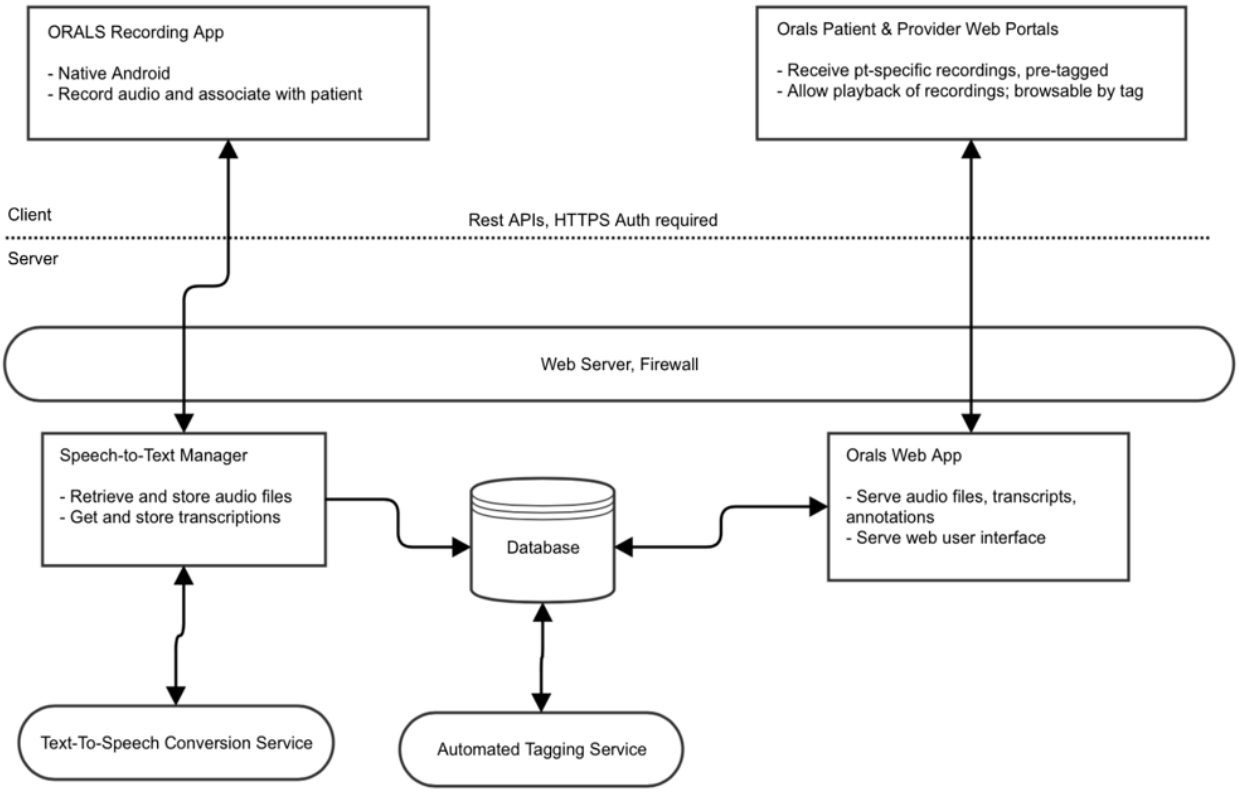
After the first round of usability evaluation through paper prototyping, we will create a set of software requirements for the initial ORALS prototype, and we will modify and improve the user interfaces for the software prototype based on feedback from the second and third rounds of usability evaluation.

Stage 3: Open Recording Automated Logging System Tagging Software

Overview

ORALS software will be developed and implemented as a secure Web-based system consisting of user interfaces (stage 2) supported by recording, transcribing, and automated tagging software (stage 3). User-facing portions (stage 2) of the software will be implemented in the Ruby on Rails Web development framework; the automated-tagging portion of the system will be written in the Python language (see Figure 3). The automated tagging software will have 2 components: speech recognition and tag identification. Speech recognition software has improved considerably in accuracy over the past 2 decades and is used in clinical settings for medical transcription [61]. We will use voice-to-text and text analytics approaches from IBM Research for speech-to-text transcription. For tag identification, we will use Weka [62] and SciKit [63], both open-source and widely used machine learning libraries.

Figure 3. Open Recording Automated Logging System high-level architecture.



Purpose

In this stage, our goal is to take the text output from the speech recognition component and develop machine learning methods that will support accurate tag identification.

Design

As noted in stage 2, we will formalize a list of standard tags that are either terms or topics. To capture the context of terms and phrases in text in our tagging system, first we apply a named-entity recognition system on input text to identify medical concepts and their corresponding classes. For this named-entity recognition task we will use Apache cTAKES information extraction framework [64] and Unified Medical Language System (UMLS) [65]. cTAKES is open-source software that identifies terms and phrases in text that correspond to UMLS concepts in high-level classes such as anatomy, symptom, procedure, disorder, and drug. To identify topics of interest within the transcriptions, we will use a supervised machine learning classifier based on a support vector machine (SVM) framework [66]. The text, extracted concepts, and their associated classes will be provided as input features to the SVM classifier. This classifier will identify the texts that are most related to a topic based on these features. If the accuracy of the SVM approach is less than 90%, we will try the alternative approach of Hidden Markov Model (HMM) [67]. We will implement the automated tagging software using the Weka, Natural Language Toolkit, and SciKit libraries in Python.

Transcription Evaluation

We have access to a set of 120 existing patient audio recordings from a primary care setting and will apply the speech-to-text software to translate the recordings into written text using voice-to-text and text analytics approaches from IBM Research. The accuracy of the automated speech-to-text transcriptions will be measured as the percentage of words correctly transcribed. This will be measured by first formatting all transcripts into a one-word-per-row format, then applying the OpenDiff tool to count the number of differences between the manual and software-generated transcripts. Percent correct will be expressed as the number of differences divided by the total number of words per transcript. We expect that an accuracy rate of 90% will be needed in order to have acceptable transcription performance for automated tagging.

Manual Tagging Evaluation

Four medical students will act as reviewers and will manually annotate the tags of interest in the text. Tags of interest will be derived through case study interviews with patients, caregivers, and clinicians. Students will work in pairs and will review 60 recordings each. An annotation guide will be created with a primary care clinician, who will also assist in training medical students in annotation. We will measure the Cohen's kappa coefficient between the 2 sets of reviewers and assess the interrater reliability, with a target kappa of >.8 [68]. Discrepancies will be resolved by consensus with other members of the research team.

Automated Tagging Evaluation

To automatically identify the tags related to terms, we will apply an SVM classifier to the transcriptions and their corresponding annotations using Apache cTAKES named-entity recognition method. We use 10-fold cross-validation to evaluate the classifier against the manual annotations (our reference standard). In this evaluation, we measure accuracy, precision, recall, and F1 score of our method. If the accuracy is below 90%, we will consider and evaluate the performance of other machine learning approaches for topic identification in text, such as an HMM.

Development

The usability testing and machine learning efforts in stages 2 and 3 will overlap so that the ORALS system can be developed and tested in an iterative agile approach. After paper prototyping is completed in stage 2, we will implement the initial Web-based prototype, which will include the manually tagged recordings, for the planned formative evaluation. For the planned summative evaluation, the ORALS system will include patient recordings that have been automatically tagged with terms and topics.

We will undertake 2 steps to ensure the privacy of the patient and physician participants who provided the initial recordings in our testing with other patient participants in usability evaluation. First, the project team will rerecord the transcription for the subset of recordings used in usability testing so that recording will be in the voices of project team members and not the original patient or clinician. Second, we will ensure that all protected health information defined by the Health Insurance Portability and Accountability Act (HIPAA) is removed from these recordings.

System Deployment

We will develop ORALS as a secure stand-alone Web-based application that can be accessed via the Internet from a home computer. The system will be hosted on HIPAA-compliant servers within Dartmouth College. For deployment and testing in stage 4, patient participants will access their individual recordings through authenticated log-in over an https secure online connection, ensuring the recording is linked to the correct patient. In addition, we will design audiorecording control interfaces that can be used from a native Android app on any compatible device. The interface will allow for the collection of the recording in the exam room via the Android device and the uploading of the recording in an encrypted manner directly to the ORALS database server.

Stage 4: Open Recording Automated Logging System In Clinic

Overview

The final stage will involve rapid cycle testing of ORALS using the Model of Improvement approach, which consists of 3 improvement questions and Plan-Do-Study-Act (PDSA) cycles [69] (described below). The Centers for Medicaid and Medicare Innovations recommends this approach for testing innovative interventions. PDSA cycles are iterative small-scale tests of change consisting of a hypothesis for improvement (Plan), study protocol to implement and test the proposed improvement (Do),

analysis and interpretation of the data (Study), and iteration of what to do next based on the study (Act) [69-72].

Goals

Our aim is to produce a version of ORALS that is widely accepted by clinicians and used by patients and their families. Each cycle will lead to refinements of ORALS, improving performance, usability, and acceptability. The introduction of ORALS will be considered a success if all of the following occur:

1. Patients are engaged in the system as evidenced by their use of ORALS. Use will be assessed by measuring (1) the proportion of eligible patients who consent to recording, (2) the proportion of consenting patients who access their recording (and playback frequency), (3) proportion of consenting patients who use tags, (4) proportion of patients who share their recording (and sharing frequency), and (5) time spent listening.
2. Accuracy of tagging is high. Patients will be asked to listen and indicate if ORALS accurately tagged the visit or not. We aim for 90% accuracy of topics.
3. Patient engagement increases. Patient engagement will be assessed using the Patient Activation Measure short form (PAM-SF, a 13-item patient-reported survey) (Multimedia Appendix 2) administered before and after recording playback [73].
4. Family members are better prepared to support the patient. We anticipate that family members will be better prepared to support the patient and will assess this using the Preparedness for Caregiving Scale (PCS, a 9-item caregiver-reported survey) (Multimedia Appendix 3) administered before and after recording playback [74,75].
5. ORALS is accepted by clinicians and patients. Acceptance will be assessed by semistructured interviews with end-users (patients, caregivers, and clinicians).

Setting

We will test ORALS in the 3 clinics of UTMB Family Medicine—Dickinson, Island East, and Island West—that are served by approximately 40 clinicians, with 15 to 25 daily patient visits per clinician. We will focus testing in one of these clinics, to be decided in conjunction with UTMB in year 2. UTMB has a dedicated quality improvement team with experience in rapid cycle testing that will assist in this stage.

Participants

Patients aged 18 years and older with access to the Internet who can communicate in English will be eligible for inclusion. Clinicians from the selected UTMB Family Practice clinic will be eligible for inclusion.

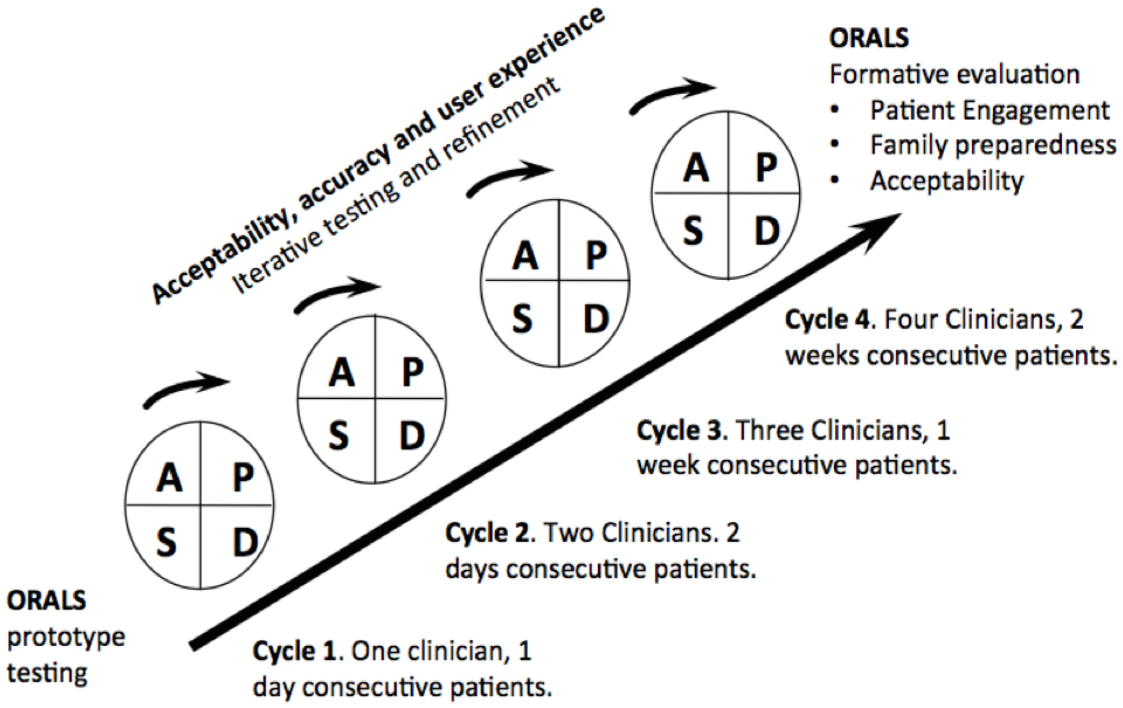
Plan-Do-Study-Act Cycles

Iteration Plan

Prior to PDSA cycles, recording hardware and ORALS software will be set up in the UTMB exam rooms and tested for audio quality. We will use written scripts from previously validated recordings read out loud in the exam room.

After testing, we will introduce ORALS for 1 day with consenting patients of a single UTMB clinician. A new clinician will be added per PDSA cycle, with 4 PDSA cycles in total (Figure 4). Each cycle will be used to refine ORALS, with results reported back to the IT team. PDSA cycles 1 and 2 will each take 1 month, and cycles 3 and 4 will each take approximately 2 months.

Figure 4. Plan-Do-Study-Act cycles: development of Open Recording Automated Logging System.



Assessment and Data Collection

Information on patient use of ORALS will be collected automatically within the system. This will include the number of patients who access their recordings, playback frequency, duration of use, time to first use, use of tags, and sharing frequency.

All users can leave feedback in an open text box. A selection of patients and family members (n=6-12) will be invited to take part in semistructured phone interviews within 1 week of their visit, each receiving $20 for participation. Clinician experience of ORALS will be assessed through semistructured interviews after each PDSA cycle.

Patient engagement will be measured with PAM-SF. Family engagement will be measured using the PCS. Surveys will be administered twice in the ORALS system, once prior to accessing recordings and again after ORALS use.

We will assess the accuracy of the tagging software by asking interviewed patients to relisten to their entire recording and verify each tag or identify missed tags, after which patients will be offered an additional $20.

Analysis

We will transcribe interviews and identify commonly reported issues and solutions in each cycle. A descriptive analysis of ORALS usage will be conducted with continuous data presented as means and standard deviations and categorical data as proportions and ranges. Paired *t* tests will compare PAM-SF and PCS scores before and after ORALS use. PAM-SF will be our primary outcome of interest. We will analyze PAM-SF on a continuous scale; scores range from 0 (low activation) to 100 (high activation). On average, interventions to promote engagement have required a 3- to 6-point change in PAM-SF to be a minimally important clinical difference [76,77]. With 200 patients, we will have 80% power to detect a 3-point change in PAM-SF with an alpha level of 0.05. We will aim for a minimum of 200 patients (25 patients per clinician per week) in the final cycle of PDSA testing. All data analysis will be conducted using Stata 14 (StataCorp LLC).

Results

At the completion of this research, we will have developed an innovative platform for patients and their caregivers, consisting of easy-to-navigate recordings of clinic visits. We will implement a publication plan that includes a final project report and articles for peer-reviewed journals. In addition to this work, we will regularly report on our progress using popular relevant Tweet chats and online using our website, www.openrecordings.org. We will disseminate our work at relevant conferences (eg, Academy Health, Health Datapalooza, and the Institute for Healthcare Improvement Quality Forums). Finally, Iora Health, a US-wide network of primary care practices (www.iorahealth.com), has indicated a willingness to implement ORALS on a larger scale upon completion of this development project.

Discussion

ORALS will offer patients and their families secure access to tagged recordings of health care encounters and will offer clinics a technically sound, interoperable, and secure system to facilitate routine recording. The proposed research is closely aligned with several of the strategies outlined in “A Roadmap for Patient and Family Engagement in Healthcare” [78].

Patient and Family Preparation

The availability of recordings can “educate, prepare, and empower patients and families to engage effectively in their health and healthcare” [78]. ORALS can catalyze this increased engagement by providing recordings of clinic visits with key information, as identified by patients, tagged in an easy-to-navigate system and, in turn, creating an electronic library of their care history. For patients with low literacy, these audio recordings will be easier to navigate than written text. Additionally, caregivers often suffer from morbidity resulting from a perceived lack of self-efficacy related to the provision of care. ORALS will better prepare caregivers, often family, to engage in care by providing the information on the health condition and treatment plan and allow them to do this at distance. For example, a mother from Harrisburg, PA, can share a recording with her son in Los Gatos, CA.

Transparency

“Nothing works well without transparency” [78]. There is no greater level of transparency and accountability than providing patients with access to recordings of clinical visits. This moves beyond giving patients access to the medical record, which still involves barriers for patients with low health literacy. Offering recordings of clinical visits appears to be the next step in transparency. Tagging recordings adds more value by providing structure based on the information that matters most to patients. Tagging is ubiquitous in today’s society bringing order and structure to masses of data—for example, the use of hashtags in Twitter groups tweets. ORALS will apply this same logic to health care recordings.

Care and System Redesign

ORALS will facilitate information sharing and, in turn, the potential of greater care coordination across the health care system. ORALS will enable families to become a bigger part of the care team by allowing them secure access to health information. Recordings could also be shared with health professionals who receive a referral, increasing care integration. The fragmentation of health information technology is a significant barrier to sharing information within and between organizations, clinicians, and patients. ORALS will be an interoperable platform, offering a scalable solution designed to operate in any health information technology setting.

Clinical and Leadership Preparation

Currently, many clinicians in training receive feedback based on a sample of visit recordings. Despite its value, this detailed feedback rarely occurs posttraining. ORALS could provide an opportunity for more routine performance assessment and

feedback based on recorded visits in a safe and secure environment.

Measurement and Research

The availability of detailed recordings would allow both patients and their families to provide feedback to clinicians on their performance. The availability of routinely collected recordings would also provide an opportunity for researchers, clinicians, and clinics to evaluate clinician performance.

The proposed ORALS aligns with the strategies outlined in "A Roadmap for Patient and Family Engagement in Healthcare" and has the potential to contribute to Gordon and Betty Moore Foundation's Patient Care Program's goals, and, thereby, the Triple Aim of better patient experience, better outcomes, and decreased cost. "We can't keep patients in the dark and then call them stupid for not having enough information" [78]. ORALS offers an opportunity to address this major information imbalance and bring patients and their families out of the dark.

The Team

Our multidisciplinary team is uniquely positioned to successfully complete the proposed project. We have extensive experience in successfully developing technological solutions in health care and implementing novel interventions in primary care. We have a track record of engaging patient partners and other stakeholders as equal members of our research teams. Importantly, our patient partners and stakeholders have been engaged from the outset and represent a spectrum of perspectives including our target population, experience recording visits and accessing recordings as caregivers, clinician partners, knowledge of health IT regulatory and system requirements, and experience disseminating research findings to target audiences.

Patient Engagement Activities

In addition to having patient partners as equal members of our research team, we will be holding "Lunch and Listen" exercises with patients from Dartmouth-Hitchcock's volunteer support group. During these 90-minute sessions, 6 to 8 participants will have the opportunity to comment on the research design and share their views on recording. These exercises will be co-led by our 2 patient partners and occur on an annual basis.

Conclusions

Upon the completion of this project we will have developed a novel recording system that will be ready for large-scale testing. Our long-term goal is for ORALS to seamlessly fit into a clinic's and patient's daily routine, increasing levels of patient engagement and transparency of care.

Acknowledgments

This work is supported through a Patient and Family Engagement Early-Career Investigator Award from the Gordon and Betty Moore Foundation (GBMF #4952).

Conflicts of Interest

Glyn Elwyn has been a consultant to Emmi Solutions LLC, which develops patient decision support tools; National Quality Forum on certification of decision support tools; Washington State Health Department on certification of decision support tools; PatientWisdom LLC; SciMentum LLC, Amsterdam; and Access Community Health Network, Chicago. He receives royalties on sales of the books *Shared Decision Making* (Oxford University Press) and *Groups: A Guide to Small Group Work in Healthcare, Management, Education and Research* (Radcliffe Press). Glyn Elwyn initiated and leads the Collaborative, which produces and publishes patient knowledge tools in the form of comparison tables (optiongrid.org) and has part ownership of the registered trademark. He owns copyright in CollaboRATE, IntegRATE, and Observer OPTION measures of shared decision making and care integration. These measures are freely available for use. Amar Das is the director of Healthcare Effectiveness Research at the IBM TJ Watson Research Center. The other authors have no conflicts to declare.

Multimedia Appendix 1

Interview topic guide.

[PDF File (Adobe PDF File), 101KB - resprot_v6i7e121_app1.pdf]

Multimedia Appendix 2

Patient Activation Measure-Short Form.

[PDF File (Adobe PDF File), 63KB - resprot_v6i7e121_app2.pdf]

Multimedia Appendix 3

The Preparedness for Caregiving Scale.

[PDF File (Adobe PDF File), 90KB - resprot_v6i7e121_app3.pdf]

References

1. Watson PW, McKinstry B. A systematic review of interventions to improve recall of medical advice in healthcare consultations. J R Soc Med 2009 Jun;102(6):235-243 [FREE Full text] [doi: 10.1258/jrsm.2009.090013] [Medline: 19531618]
2. Ley P. Memory for medical information. Br J Soc Clin Psychol 1979 Jun;18(2):245-255. [Medline: 454984]
3. Kessels RP. Patients' memory for medical information. J R Soc Med 2003 May;96(5):219-222 [FREE Full text] [Medline: 12724430]
4. Jansen J, Butow PN, van Weert JC, van Dulmen S, Devine RJ, Heeren TJ, et al. Does age really matter? Recall of information presented to newly referred patients with cancer. J Clin Oncol 2008 Nov 20;26(33):5450-5457. [doi: 10.1200/JCO.2007.15.2322] [Medline: 18936478]
5. McCarthy DM, Waite KR, Curtis LM, Engel KG, Baker DW, Wolf MS. What did the doctor say? Health literacy and recall of medical instructions. Med Care 2012 Apr;50(4):277-282 [FREE Full text] [doi: 10.1097/MLR.0b013e318241e8e1] [Medline: 22411440]
6. Bayliss EA, Ellis JL, Steiner JF. Barriers to self-management and quality-of-life outcomes in seniors with multimorbidities. Ann Fam Med 2007 Sep;5(5):395-402 [FREE Full text] [doi: 10.1370/afm.722] [Medline: 17893380]
7. Seider MI, Damato BE. Digital audio recording of initial patient visits to an ocular oncology clinic: a pilot study. Ophthalmic Surg Lasers Imaging Retina 2015 May;46(5):597-599. [doi: 10.3928/23258160-20150521-16] [Medline: 26057768]
8. Ford S, Fallowfield L, Hall A, Lewis S. The influence of audiotapes on patient participation in the cancer consultation. Eur J Cancer 1995 Dec;31(13-14):2264-2269. [doi: 10.1016/0959-8049(95)00336-3]
9. Stacey D, Bennett CL, Barry MJ, Col NF, Eden KB, Holmes-Rovner M, et al. Decision aids for people facing health treatment or screening decisions. Cochrane Database Syst Rev 2011(10):CD001431. [doi: 10.1002/14651858.CD001431.pub3] [Medline: 21975733]
10. Ad Hoc Committee on Health Literacy for the Council on Scientific Affairs, American Medical Association. Health literacy: report of the Council on Scientific Affairs. JAMA 1999 Feb 10;281(6):552-557. [Medline: 10022112]
11. Kutner M. The health literacy of America's adults: results from the 2003 National Assessment of Adult Literacy. 2006. URL: https://nces.ed.gov/pubs2006/2006483.pdf [accessed 2017-06-09] [WebCite Cache ID 6r6Xo0r1l]
12. Williams MV, Baker DW, Parker RM, Nurss JR. Relationship of functional health literacy to patients' knowledge of their chronic disease. A study of patients with hypertension and diabetes. Arch Intern Med 1998 Jan 26;158(2):166-172. [Medline: 9448555]
13. Williams MV, Baker DW, Honig EG, Lee TM, Nowlan A. Inadequate literacy is a barrier to asthma knowledge and self-care. Chest 1998 Oct;114(4):1008-1015. [Medline: 9792569]
14. Gazmararian JA, Williams MV, Peel J, Baker DW. Health literacy and knowledge of chronic disease. Patient Educ Couns 2003 Nov;51(3):267-275. [Medline: 14630383]
15. Dewalt DA, Berkman ND, Sheridan S, Lohr KN, Pignone MP. Literacy and health outcomes: a systematic review of the literature. J Gen Intern Med 2004 Dec;19(12):1228-1239 [FREE Full text] [doi: 10.1111/j.1525-1497.2004.40153.x] [Medline: 15610334]
16. Berkman ND, Sheridan SL, Donahue KE, Halpern DJ, Crotty K. Low health literacy and health outcomes: an updated systematic review. Ann Intern Med 2011 Jul 19;155(2):97-107. [doi: 10.7326/0003-4819-155-2-201107190-00005] [Medline: 21768583]
17. Schillinger D, Piette J, Grumbach K, Wang F, Wilson C, Daher C, et al. Closing the loop: physician communication with diabetic patients who have low health literacy. Arch Intern Med 2003 Jan 13;163(1):83-90. [Medline: 12523921]
18. Nair EL, Cienkowski KM. The impact of health literacy on patient understanding of counseling and education materials. Int J Audiol 2010 Feb;49(2):71-75. [doi: 10.3109/14992020903280161] [Medline: 20151879]
19. Wali H, Hudani Z, Wali S, Mercer K, Grindrod K. A systematic review of interventions to improve medication information for low health literate populations. Res Social Adm Pharm 2016 Nov;12(6):830-864. [doi: 10.1016/j.sapharm.2015.12.001] [Medline: 26926671]
20. van der Meulen N, Jansen J, van Dulmen DS, Bensing J, van Weert J. Interventions to improve recall of medical information in cancer patients: a systematic review of the literature. Psychooncology 2008 Sep;17(9):857-868. [doi: 10.1002/pon.1290] [Medline: 18050149]
21. Hummel J, Evans P. Providing clinical summaries to patients after each office visit: a technical guide. 2012. URL: https://www.healthit.gov/sites/default/files/measure-tools/avs-tech-guide.pdf [accessed 2017-06-09] [WebCite Cache ID 6r6YAVqNa]
22. Delbanco T, Walker J, Bell SK, Darer JD, Elmore JG, Farag N, et al. Inviting patients to read their doctors' notes: a quasi-experimental study and a look ahead. Ann Intern Med 2012 Oct 2;157(7):461-470 [FREE Full text] [doi: 10.7326/0003-4819-157-7-201210020-00002] [Medline: 23027317]
23. Jackson SL, Mejilla R, Darer JD, Oster NV, Ralston JD, Leveille SG, et al. Patients who share transparent visit notes with others: characteristics, risks, and benefits. J Med Internet Res 2014 Nov 12;16(11):e247 [FREE Full text] [doi: 10.2196/jmir.3363] [Medline: 25405911]
24. Blinder D, Rotenberg L, Peleg M, Taicher S. Patient compliance to instructions after oral surgical procedures. Int J Oral Maxillofac Surg 2001 Jun;30(3):216-219. [doi: 10.1054/ijom.2000.0045] [Medline: 11420904]

25. McPherson CJ, Higginson IJ, Hearn J. Effective methods of giving information in cancer: a systematic literature review of randomized controlled trials. J Public Health Med 2001 Sep;23(3):227-234. [Medline: 11585196]
26. Belkora JK, Loth MK, Chen DF, Chen JY, Volz S, Esserman LJ. Monitoring the implementation of consultation planning, recording, and summarizing in a breast care center. Patient Educ Couns 2008 Dec;73(3):536-543 [FREE Full text] [doi: 10.1016/j.pec.2008.07.037] [Medline: 18755564]
27. Houts P, Doak C, Doak L, Loscalzo MJ. The role of pictures in improving health communication: a review of research on attention, comprehension, recall, and adherence. Patient Educ Couns 2006 May;61(2):173-190. [doi: 10.1016/j.pec.2005.05.004] [Medline: 16122896]
28. Pavlik V, Brown AE, Nash S, Gossey JT. Association of patient recall, satisfaction, and adherence to content of an electronic health record (EHR)-generated after visit summary: a randomized clinical trial. J Am Board Fam Med 2014;27(2):209-218 [FREE Full text] [doi: 10.3122/jabfm.2014.02.130137] [Medline: 24610183]
29. Root J, Oster NV, Jackson SL, Mejilla R, Walker J, Elmore JG. Characteristics of patients who report confusion after reading their primary care clinic notes online. Health Commun 2016;31(6):778-781. [doi: 10.1080/10410236.2014.990078] [Medline: 26529325]
30. Tsulukidze M, Durand M, Barr PJ, Mead T, Elwyn G. Providing recording of clinical consultation to patients—a highly valued but underutilized intervention: a scoping review. Patient Educ Couns 2014 Jun;95(3):297-304. [doi: 10.1016/j.pec.2014.02.007] [Medline: 24630697]
31. Davison BJ, Degner LF. Empowerment of men newly diagnosed with prostate cancer. Cancer Nurs 1997 Jun;20(3):187-196. [Medline: 9190093]
32. Elwyn G, Buckman L. Should doctors encourage patients to record consultations? BMJ 2015 Jan 08;350:g7645. [Medline: 25569249]
33. Ong LM, de Haes JC, Kruyver IP, de Reijke TM, Lammes FB. [Providing patients with an audio recording of the outpatient oncological consultation; experiences of patients and physicians]. Ned Tijdschr Geneeskd 1995 Jan 14;139(2):77-80. [Medline: 7838223]
34. Butt HR. A method for better physician-patient communication. Ann Intern Med 1977 Apr;86(4):478-480. [Medline: 848814]
35. Mishra PK, Mathias H, Millar K, Nagrajan K, Murday A. A randomized controlled trial to assess the effect of audiotaped consultations on the quality of informed consent in cardiac surgery. Arch Surg 2010 Apr;145(4):383-388. [doi: 10.1001/archsurg.2010.45] [Medline: 20404290]
36. Knox R, Butow PN, Devine R, Tattersall MH. Audiotapes of oncology consultations: only for the first consultation? Ann Oncol 2002 Apr;13(4):622-627. [Medline: 12056714]
37. Leahy M, Douglass J, Barley V, Jarman M, Cooper G. Audiotaping the heart surgery consultation: qualitative study of patients' experiences. Heart 2005 Nov;91(11):1469-1470 [FREE Full text] [doi: 10.1136/hrt.2004.048769] [Medline: 16230447]
38. Tattersall MH, Butow PN. Consultation audio tapes: an underused cancer patient information aid and clinical research tool. Lancet Oncol 2002 Jul;3(7):431-437. [Medline: 12142173]
39. Rodriguez M, Morrow J, Seifi A. Ethical implications of patients and families secretly recording conversations with physicians. JAMA 2015 Apr 28;313(16):1615-1616. [doi: 10.1001/jama.2015.2424] [Medline: 25763514]
40. Santo A, Laizner AM, Shohet L. Exploring the value of audiotapes for health literacy: a systematic review. Patient Educ Couns 2005 Sep;58(3):235-243. [doi: 10.1016/j.pec.2004.07.001] [Medline: 16054796]
41. Hack TF, Pickles T, Bultz BD, Ruether JD, Weir LM, Degner LF, et al. Impact of providing audiotapes of primary adjuvant treatment consultations to women with breast cancer: a multisite, randomized, controlled trial. J Clin Oncol 2003 Nov 15;21(22):4138-4144. [doi: 10.1200/JCO.2003.12.155] [Medline: 14615442]
42. Wolderslund M, Kofoed P, Holst R, Ammentorp J. Patients' use of digital audio recordings in four different outpatient clinics. Int J Qual Health Care 2015 Dec;27(6):466-472. [doi: 10.1093/intqhc/mzv069] [Medline: 26403974]
43. Hack TF, Ruether JD, Weir LM, Grenier D, Degner LF. Promoting consultation recording practice in oncology: identification of critical implementation factors and determination of patient benefit. Psychooncology 2013 Jun;22(6):1273-1282. [doi: 10.1002/pon.3135] [Medline: 22821445]
44. Bruera E, Pituskin E, Calder K, Neumann CM, Hanson J. The addition of an audiocassette recording of a consultation to written recommendations for patients with advanced cancer: A randomized, controlled trial. Cancer 1999 Dec 01;86(11):2420-2425. [Medline: 10590386]
45. Lobb E, Butow P, Meiser B, Barratt A, Kirk J, Gattas M, et al. The use of audiotapes in consultations with women from high risk breast cancer families: a randomised trial. J Med Genet 2002 Sep;39(9):697-703 [FREE Full text] [Medline: 12205117]
46. Yee JL, Schulz R. Gender differences in psychiatric morbidity among family caregivers: a review and analysis. Gerontologist 2000 Apr;40(2):147-164. [Medline: 10820918]
47. Huis In Het Veld J, Verkaik R, Mistiaen P, van Meijel B, Francke AL. The effectiveness of interventions in supporting self-management of informal caregivers of people with dementia; a systematic meta review. BMC Geriatr 2015 Nov 11;15:147 [FREE Full text] [doi: 10.1186/s12877-015-0145-6] [Medline: 26561236]

48. Tsulukidze M, Grande SW, Thompson R, Rudd K, Elwyn G. Patients covertly recording clinical encounters: threat or opportunity? A qualitative analysis of online texts. PLoS One 2015;10(5):e0125824 [FREE Full text] [doi: 10.1371/journal.pone.0125824] [Medline: 25933002]
49. Elwyn G, Barr PJ, Grande SW. Patients recording clinical encounters: a path to empowerment? Assessment by mixed methods. BMJ Open 2015 Aug 11;5(8):e008566 [FREE Full text] [doi: 10.1136/bmjopen-2015-008566] [Medline: 26264274]
50. Runeson P, Höst M. Guidelines for conducting and reporting case study research in software engineering. Empir Softw Eng 2008;14:64.
51. Yin R. Case Study Research: Design and Methods, 3rd Edition. Thousand Oaks: Sage; 2003.
52. Brereton P, Kitchenham B, Budgen D. Using a protocol template for case study planning. 2008 Presented at: 12th International Conference on Evaluation and Assessment in Software Engineering; 2008; Bari.
53. Guest G. How many interviews are enough? An experiment with data saturation and variability. Field Methods 2006 Feb 01;18(1):59-82. [doi: 10.1177/1525822X05279903]
54. Ritchie J, Spencer L. Qualitative data analysis for applied policy research. In: Huberman AM, Miles MB, editors. Analyzing Qualitative Data. New York: Sage; 1994.
55. Pope C, Ziebland S, Mays N. Qualitative research in health care: analysing qualitative data. BMJ 2000 Jan 08;320(7227):114-116 [FREE Full text] [Medline: 10625273]
56. Nielsen J. Usability Engineering. Boston: Academic Press; 1993.
57. Vinter O. Experience-based approaches to process improvement. 2000 Presented at: Proceedings of the Thirteenth International Software Quality Week, Software Research; 2000; San Francisco.
58. Myers B, Rosson M. Survey on user interface programming. 1992 Presented at: Proceedings of the SIGCHI Conference on Human Factors in Computing Systems; 1992; Monterey p. 195-202.
59. Snyder C. Paper Prototyping: The Fast and Easy Way to Design and Refine User Interfaces. Burlington: Morgan Kaufmann; 2003.
60. Ericsson K, Simon H. Protocol Analysis: Verbal Reports as Data, Revised. Cambridge: MIT Press; 1993.
61. Zafar A, Overhage J. Continuous speech recognition for clinicians. J Am Med Inform Assoc 1999;6(3):204.
62. Hall M, Frank E, Holmes G. The WEKA data mining software: an update. ACM SIGKDD 2009:10-18.
63. Buitinck L, Louppe G, Blondel M. API design for machine learning software: experiences from the scikit-learn project. 2013. URL: https://dtai.cs.kuleuven.be/events/lml2013/papers/lml2013_api_sklearn.pdf [accessed 2017-06-09] [WebCite Cache ID 6r6aGiamo]
64. Savova GK, Masanz JJ, Ogren PV, Zheng J, Sohn S, Kipper-Schuler KC, et al. Mayo clinical Text Analysis and Knowledge Extraction System (cTAKES): architecture, component evaluation and applications. J Am Med Inform Assoc 2010;17(5):507-513 [FREE Full text] [doi: 10.1136/jamia.2009.001560] [Medline: 20819853]
65. Bodenreider O. The Unified Medical Language System (UMLS): integrating biomedical terminology. Nucleic Acids Res 2004 Jan 1;32(Database issue):D267-D270 [FREE Full text] [doi: 10.1093/nar/gkh061] [Medline: 14681409]
66. Cortes C, Vapnik V. Support-vector networks. 1995. URL: http://image.diku.dk/imagecanon/material/cortes_vapnik95.pdf [accessed 2017-06-09] [WebCite Cache ID 6r6aRftGG]
67. Xu R, Supekar K, Huang Y, Das A, Garber A. Combining text classification and Hidden Markov Modeling techniques for categorizing sentences in randomized clinical trial abstracts. AMIA Annu Symp Proc 2006:824-828 [FREE Full text] [Medline: 17238456]
68. McHugh M. Interrater reliability: the kappa statistic. Biochem Medica 2012;22:82.
69. Speroff T, O'Connor GT. Study designs for PDSA quality improvement research. Qual Manag Health Care 2004;13(1):17-32. [Medline: 14976904]
70. Berwick DM. Developing and testing changes in delivery of care. Ann Intern Med 1998 Apr 15;128(8):651-656. [Medline: 9537939]
71. Langley G. The Improvement Guide: A Practical Approach to Enhancing Organizational Performance. San Francisco: Jossey-Bass Publishers; 1996.
72. Nelson E, Batalden P, Godfrey M. Value By Design: Developing Clinical Microsystems to Achieve Organizational Excellence. Hoboken: Wiley; 2011.
73. Hibbard JH, Mahoney ER, Stockard J, Tusler M. Development and testing of a short form of the patient activation measure. Health Serv Res 2005 Dec;40(6 Pt 1):1918-1930 [FREE Full text] [doi: 10.1111/j.1475-6773.2005.00438.x] [Medline: 16336556]
74. Archbold PG, Stewart BJ, Greenlick MR, Harvath T. Mutuality and preparedness as predictors of caregiver role strain. Res Nurs Health 1990 Dec;13(6):375-384. [Medline: 2270302]
75. Zwicker D. Mov Disord. Preparedness for caregiving scale URL: https://consultgeri.org/try-this/general-assessment/issue-28.pdf [accessed 2017-06-09] [WebCite Cache ID 6r6b0hnvo]
76. Hibbard JH, Greene J. What the evidence shows about patient activation: better health outcomes and care experiences; fewer data on costs. Health Aff (Millwood) 2013 Feb;32(2):207-214. [doi: 10.1377/hlthaff.2012.1061] [Medline: 23381511]
77. Insignia Health. Patient Activation Measure. 2015. URL: http://www.insigniahealth.com/products/pam-survey [accessed 2017-06-09] [WebCite Cache ID 6r6b7NV4k]

78. Carman KL, Dardess P, Maurer ME, Workman T, Ganachari D, Pathek-Sen E. A roadmap for patient and family engagement in healthcare practice and research.: American Institutes for Research; 2014. URL: http://patientfamilyengagement.org/roadmap.php [accessed 2017-06-09] [WebCite Cache ID 6r6ThdNoj]

Abbreviations

AVS: after visit summary
BNI: Barrow Neurological Institute
EHR: electronic health record
HIPAA: Health Insurance Portability and Accountability Act
HMM: Hidden Markov Model
ic3d: Informatics Collaboratory for Design, Development, and Dissemination
IRB: Institutional Review Board
IT: information technology
ORALS: Open Recording Automated Logging System
PAM-SF: Patient Activation Measure-Short Form
PSC: Preparedness for Caregiving Scale
PDSA: Plan-Do-Study-Act
SVM: support vector machine
UMLS: Unified Medical Language System
UTMB: University of Texas Medical Branch

Edited by G Eysenbach; submitted 24.03.17; peer-reviewed by J Bian, P Wicks; comments to author 09.05.17; revised version received 22.05.17; accepted 23.05.17; published 06.07.17.

Please cite as:
Barr PJ, Dannenberg MD, Ganoe CH, Haslett W, Faill R, Hassanpour S, Das A, Arend R, Masel MC, Piper S, Reicher H, Ryan J, Elwyn G
Sharing Annotated Audio Recordings of Clinic Visits With Patients—Development of the Open Recording Automated Logging System (ORALS): Study Protocol
JMIR Res Protoc 2017;6(7):e121
URL: http://www.researchprotocols.org/2017/7/e121/
doi:10.2196/resprot.7735
PMID:28684387

Proposal

Natural Compounds for the Treatment of Psoriatic Arthritis: A Proposal Based on Multi-Targeted Osteoclastic Regulation and on a Preclinical Study

Shiqiang Deng[1*], BMed, PhD; Jianwen Cheng[1,2,3*], BMed, PhD; Jinmin Zhao[1,2,3], BMed, PhD; Felix Yao[1], MBBS, PhD; Jiake Xu[1,2,3], MBBS, PhD

[1]Molecular Laboratory, School of Biomedical Sciences, The University of Western Australia, Perth, Australia

[2]Research Centre for Regenerative Medicine and Guangxi Key Laboratory of Regenerative Medicine, Guangxi Medical University, Nanning, China

[3]Department of Orthopaedic Surgery, The First Affiliated Hospital of Guangxi Medical University, Nanning, China

[*]these authors contributed equally

Corresponding Author:
Jiake Xu, MBBS, PhD
Molecular Laboratory
School of Biomedical Sciences
The University of Western Australia
Room 1.4H, M Block, QEII Medical Centre, Nedlands
35 Stirling Highway
Perth, WA 6009
Australia
Phone: 61 (08) 6457 2739
Fax: 61 (08) 6457 2891
Email: jiake.xu@uwa.edu.au

Abstract

Background: Psoriatic arthritis (PsA) is a chronic inflammatory arthritis affecting approximately 2% to 3% of the population globally, and is characterized by both peripheral articular manifestations and axial skeletal involvement. Conventional therapies for PsA have not been fully satisfactory, though natural products (NPs) have been shown to be highly effective and represent important treatment options for psoriasis. PsA is a multigenic autoimmune disease with both environmental and genetic factors contributing to its pathogenesis. Accordingly, it is likely that the use of natural compounds with a multi-targeted approach will enable us to develop better therapies for PsA and related disorders.

Objective: PsA, either on joint damage or on bone erosion, has been shown to respond to anti-psoriatic pharmacotherapy (APP), APP-like NPs, and their natural compounds. This study aims to uncover specific natural compounds for improved PsA remedies. Specifically, by targeting bone erosion caused by increased osteoclastic bone resorption, we aim to predict the key signaling pathways affected by natural compounds. Further, the study will explore their anti-arthritis effects using an in silico, in vitro, and in vivo approach. Following the signaling pathway prediction, a preclinical efficacy study on animal models will be undertaken. Collectively, this work will discover lead compounds with improved therapeutic effects on PsA.

Methods: We hypothesize that 9 potential APP-like NPs will have therapeutic effects on arthritis via the modulation of osteoclast bone resorption and signaling pathways. For in silico identification, the Latin name of each NP will be identified using the Encyclopedia of Traditional Chinese Medicine (Encyclopedia of TCM). The biological targets of NPs will be predicted or screened using the Herbal Ingredients' Targets (HIT) database. With the designed search terms, DrugBank will be used to further filter the above biological targets. Protein ANnotation THrough Evolutionary Relationship (PANTHER) will be used to predict the pathways of the natural compound sources. Subsequently, an in vitro sample preparation including extraction, fractionation, isolation, purification, and bioassays with high-speed counter-current chromatography-high-performance liquid chromatography-diode array detection (HSCCC-HPLC-DAD) will be carried out for each identified natural source. In vitro investigations into the effect of NPs on osteoclast signaling pathways will be performed. The experimental methods include cell viability assays, osteoclastogenesis and resorption pit assays, quantitative reverse transcription polymerase chain reaction (RT-PCR), western blot, and luciferase reporter gene assays. Finally, an in vivo preclinical efficacy on a collagen-induced arthritis rat model will be carried out using a treatment group (n=10), a control group (n=10), and a non-arthritis group (n=10). Main outcome measure

assessments during intervention include daily macroscopic scores and a digital calipers measurement. Post-treatment tissue measurements will be analyzed by serological testing, radiographic imaging, and histopathological assessment.

Results: Studies are currently underway to evaluate the in silico data and the in vitro effects of compounds on osteoclastogenesis and bone resorption. The preclinical study is expected to start a year following completion of the in silico analysis.

Conclusions: The in silico rapid approach is proposed as a more general method for adding value to the results of a systematic review of NPs. More importantly, the proposed study builds on a multi-targeted approach for the identification of natural compounds for future drug discovery. This innovative approach is likely to be more precise, efficient, and compatible to identify the novel natural compounds for effective treatment of PsA.

(JMIR Res Protoc 2017;6(7):e132) doi:10.2196/resprot.7636

KEYWORDS

arthritis; osteoclast; RANKL signaling pathways; anti-psoriatic pharmacotherapy (APP); multi-target; natural compounds; in silico screening; preclinical study

Introduction

Psoriatic arthritis (PsA) is a chronic inflammatory arthritis characterized by both peripheral articular manifestations and axial skeletal involvement [1-3]. It affects approximately 2% to 3% of the population globally, with the majority of patients experiencing a chronic, progressive course of disease developing to a destructive, disabling form of arthritis over time [1]. Conventional therapies for psoriasis have not been fully satisfactory and natural products (NPs)—anecdotally known to be highly effective (though with little formal scientific research evidence)—represent important treatment options for psoriasis [4-8]. PsA is considered a systemic inflammatory disease with multifactorial (environmental and genetic) factors contributing to its pathogenesis. Accordingly, a lead compound which simultaneously effects different targets would be ideal for the improved treatment of PsA [4,9]. The practice of combining NPs into formulations, a common method in Chinese medicine, could prove to be an effective alternative approach for the development of multi-compound, multi-target therapies [10].

For PsA, joint damage results from the release of the direct bone-resorbing factors osteoclasts (OCs) and metalloproteinases. An increased frequency of osteoclast precursor (OCP) is found in most patients with PsA and correlates with the extent of radiographic damage observed in affected patients. In osteoclastogenesis, peripheral OCPs and cluster of differentiation (CD) 14^+ monocytes differentiate to OCs [11]. Disordered osteoclastogenesis leads to altered bone remodeling causing bone erosion and joint damage, represented by increased osteoclast precursors numbers, radiographic damage scores, and disease activity index [3,12]. Typically, this correlates with increased serum levels of the following cellular biomarkers: (1) macrophage-colony stimulating factor (M-CSF); (2) tumor necrosis factor alpha (TNF-α); (3) osteoprotegerin (OPG); (4) receptor activator of nuclear factor-κB ligand (RANKL); (5) $CD14^+/CD11b^+/CD16^+$; and (7) interleukin (IL-23/IL-17) [3,11,12]. Accordingly, our research direction will focus on the impact of NPs on the above biomarkers, osteoclastogenesis, and joint damage/erosion associated with PsA.

There exists an intrinsic connection between psoriasis and PsA. PsA, either on joint damage or on bone erosion, may respond to anti-psoriatic pharmacotherapy (APP), APP-like NPs, and their natural compounds. A psoriasis study recently developed a novel approach for the identification of promising NPs for psoriasis therapy based on an extensive literature review of current clinical evidence available, followed by an in silico screening of biological targets for APP and drug development. This approach extends beyond psoriasis and can be applied to similar diseases with multifactorial causes for which multi-compound, multi-target therapies are emerging as the therapeutic norm. This approach has been successfully applied in psoriasis and generated robust preliminary data identifying potential NP targets and pathways [13-17]. We have also previously undertaken in vitro and in vivo studies screening for natural compounds that affect osteoclast differentiation and osteoclast-mediated osteolysis, and identified NPs which may have therapeutic potential for the treatment of bone lytic disorders [18-22].

With this project, we aim to (1) identify specific lead natural compounds with therapeutic effects on PsA and/or other autoimmune joint disorders with a multi-target in silico, in vitro, and in vivo approach; (2) provide an overview of the relevant signaling pathways and mechanisms of action; and (3) present therapeutic targets and preclinical efficacy evaluation of APP-like NPs and their natural compounds.

Methods

Preliminary Data

Previous work included the development of a novel approach to identify promising NPs for psoriasis treatment based on available clinical evidence followed by in silico screening for biological targets for APP and drug development. Using this combined approach, 9 APP-like NPs have been identified as promising candidates for psoriasis therapy (Table 1) [13-17].

Table 1. Promising natural products for psoriasis (N=12) including 9 anti-psoriatic pharmacotherapy-like natural products.

Scientific name	Study design	Administration	APP[a]-like NPs[b]
Sophora flavescens	NPM[c] and APP vs APP	External	Yes
Cnidium monnieri	NPM and APP vs APP	External	No
Dictamnus dasycarpus	NPM and APP vs APP	External	No
Borneolum syntheticum	NPM and APP vs APP	External	No
Aloe vera	Single NP vs APP/placebo	External	Yes
Indigo naturalis	Single NP vs APP/placebo	External	Yes
Camptotheca acuminata	Single NP vs APP/placebo	External	Yes
Mahonia aquifolium	Single NP vs APP/placebo	External	Yes
Sophora flavescens	NP formula vs APP/placebo	External	Yes
Lithospermum erythrorhizon	NP formula vs APP/placebo	External	Yes
Oldenlandia diffusa	NP formula vs APP/placebo	Internal	Yes
Rehmannia glutinosa	NP formula vs APP/placebo	Internal	Yes
Salvia miltiorrhiza	NP formula vs APP/placebo	Internal	Yes

[a]APP: anti-psoriatic pharmacotherapy.

[b]NP: natural product.

[c]NPM: natural product medication.

The effect of the above NPs on bone erosion and arthritis are still unknown. We hypothesize that these NPs will have therapeutic effects on arthritis via the modulation of osteoclastic bone resorption and signaling pathways. Therefore, the aims of the study consist of the following 4 specific parts: (1) in silico compound identification; (2) in vitro sample preparation; (3) in vitro mechanism investigation; and (4) in vivo preclinical efficacy evaluation (Figure 1).

In Silico Identification of Prospective Natural Compounds

The preliminary data will return a shortlist of promising NPs for an in silico molecular investigation on PsA. In addition to the Encyclopedia of Traditional Chinese Medicine (Encyclopedia of TCM), the Herbal Ingredients' Targets database (HIT, China), DrugBank (Canada), and Protein ANnotation THrough Evolutionary Relationship (PANTHER, USA) will be applied in the in silico identification procedure (Figure 2). All are available in English [13].

The Encyclopedia of TCM can successively locate the relevant Latin names and the contained chemical compounds with the individual and unique plant code of each promising NP species. Subsequently, HIT can access the relevant biological targets with their individual name identification (ID) and types in an Excel spreadsheet. With a dedicated search term(s) (eg, psoriatic arthritis), DrugBank can induce the reference targets (together with the previous cellular biomarkers) to be further filtered by the above biological targets.

For each identified natural compound, their known protein targets will be entered into the keyword search using the “homo sapiens” setting. For each target, the identified Gene ID will be saved a Notepad (txt) file. One Notepad file is created for each species. This file contains all the Gene IDs for all the known therapeutic targets of all the compounds that are known to be active in the species. Each file will be sequentially uploaded into the Gene List Analysis field in PANTHER. This will report the following 5 aspects in Excel for the particular species: (1) molecular function(s), (2) biological processes, (3) cellular component(s), (4) protein class, and (5) pathway(s). The Excel files will be sorted to identify the most commonly identified pathway for each species. For each of the most commonly identified pathways, all the identified proteins, excluding upstream and downstream proteins, will be entered into Excel. Since the nomenclatures used by PANTHER and by HIT differ, cross-referencing will be undertaken regarding the short and long names used for the proteins in both databases.

Figure 1. Flowchart of study progression. NI: non-intervention, NP: natural product, PsA: psoriatic arthritis, CIA: collagen-induced arthritis, TCM: traditional Chinese medicine.

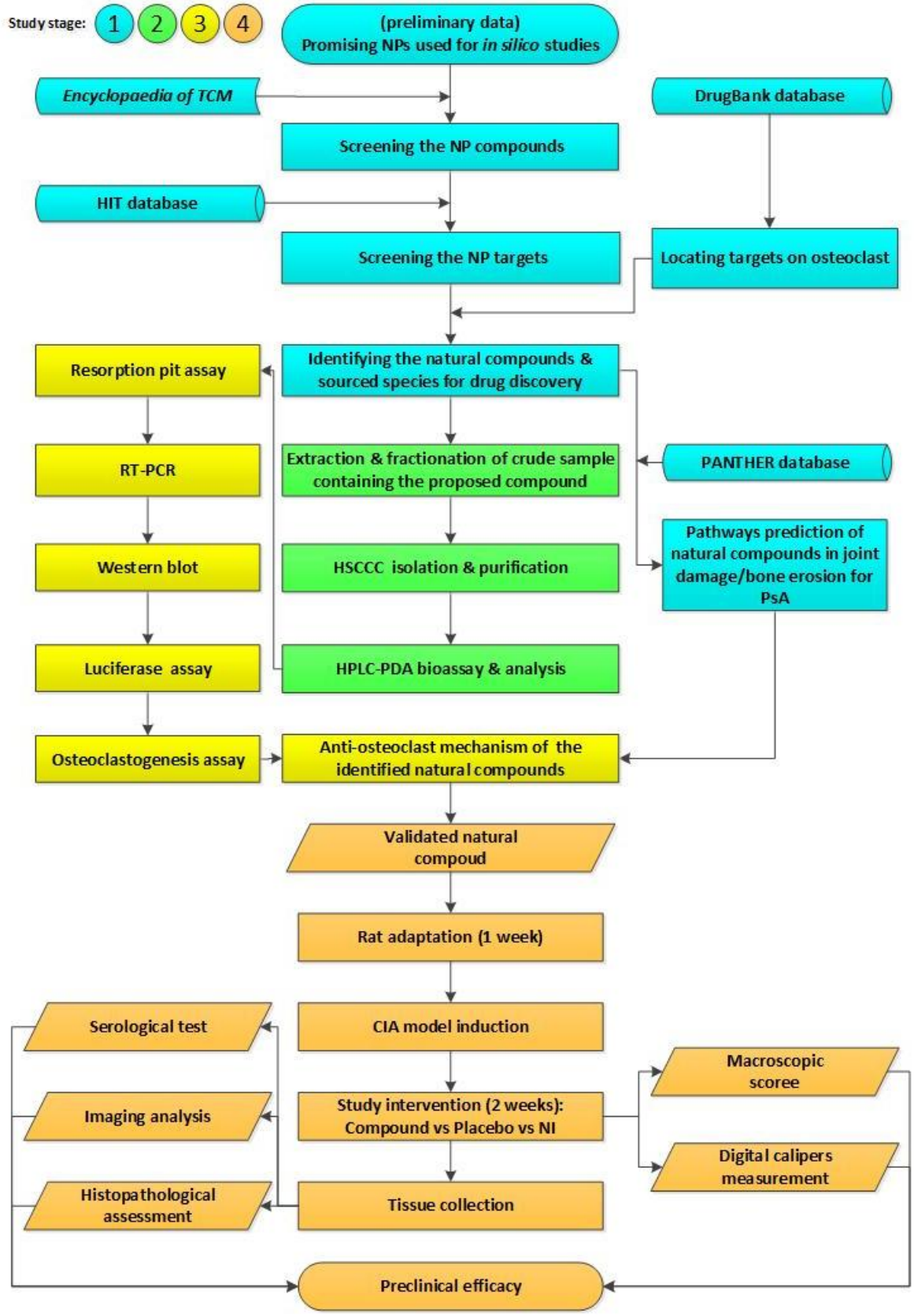
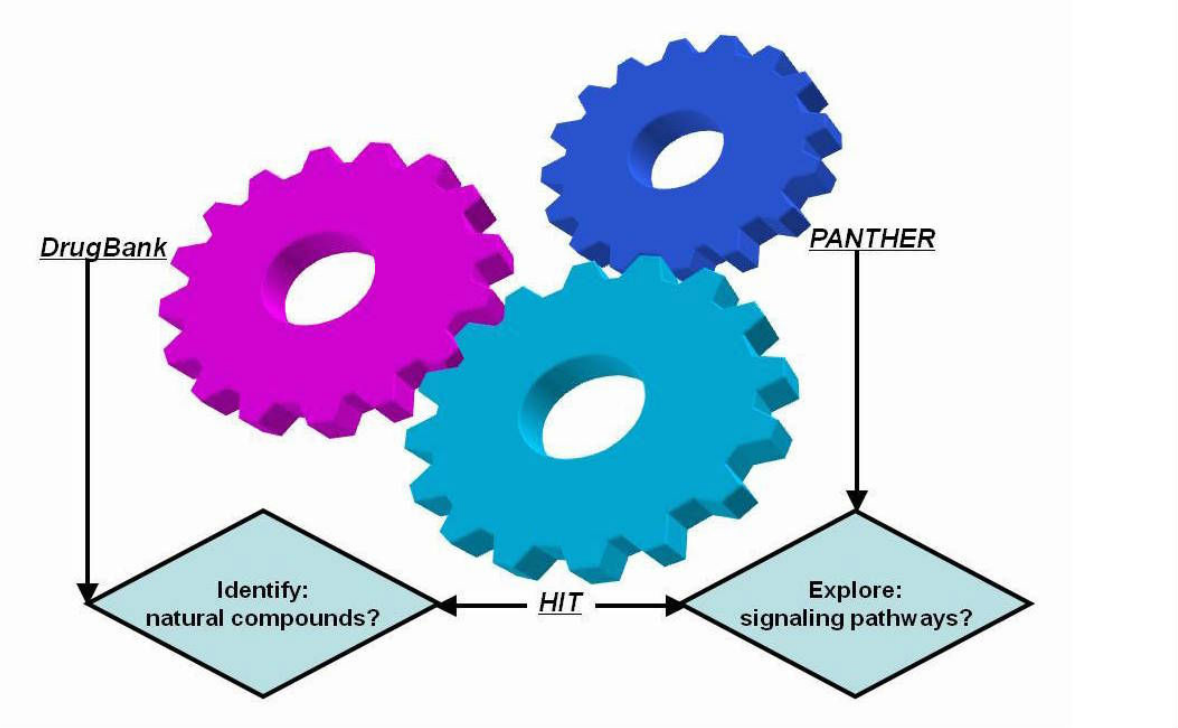


Figure 2. Target-directed in silico identification.



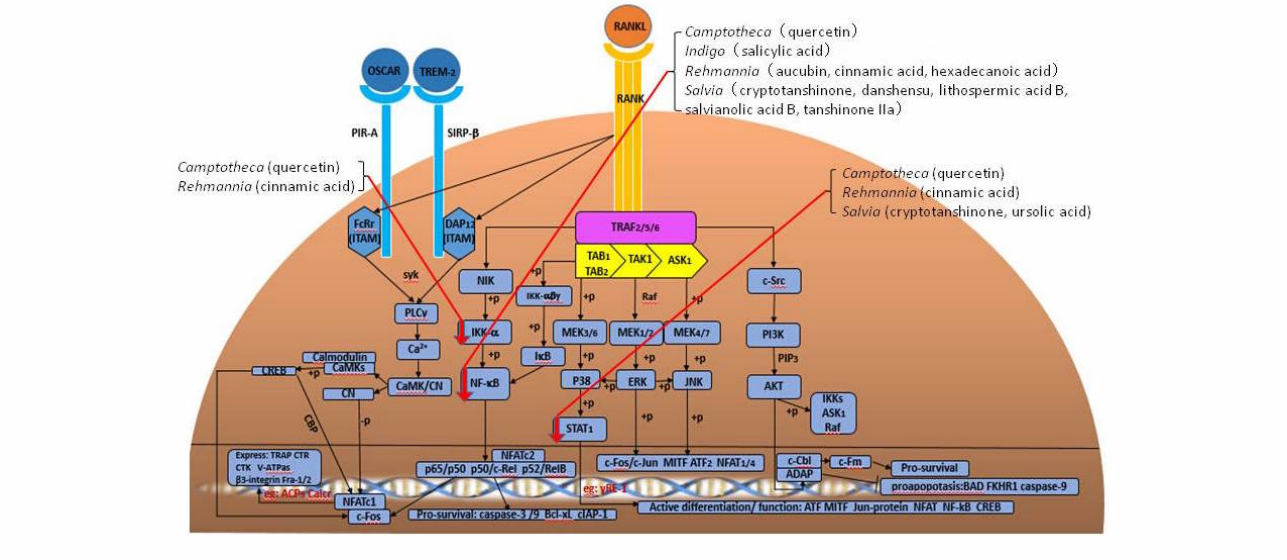
In Vitro Sample Preparation Using the Identified Compound Sources for Drug Development

This stage includes the extraction, fractionation, isolation, purification, and the formation of a series of bioassays for the identified compounds. The extraction method is specific to the nature of the source material and target compound. It typically involves a process of drying, grinding, homogenization, or maceration of the plant. For a pure single compound, the crude extract initially needs to be fractionated into various discrete fractions containing compounds in similar polarities or molecular sizes. NP isolation is also subject to the nature of the target compound(s) presented in the crude extract or fraction. Part sample compounds may be purchased from the market or supported by the relevant group. Qualitative chemical tests, preliminary thin-layer chromatography (TLC), and/or high performance liquid chromatography-photodiode array hyphenated technique (HPLC-PDA) can be used to obtain spectral profiles from molecular mixtures or chromatographically separated samples [23]. For isolation and purification, an efficient on-line purity monitoring strategy based on on-line coupling of high-speed counter-current chromatography (HSCCC) with high performance liquid chromatography-diode array detection (HPLC-DAD) will be performed. In summary, this part of project consists of the preparation of a crude extract, preparation of a 2-phase solvent system, HSCCC separation, and HPLC-DAD purity analysis of counter-current chromatography (CCC) peak fractions [24].

In Vitro Investigation of Drug Candidates

We will perform in vitro studies on compounds prepared in stage 2 to investigate their effects on osteoclastogenesis and bone resorption (Figure 3). For osteoclast formation, 1×10^4 bone marrow macrophage (BMM) cells per well will be isolated from the femur and tibiae of 6-week-old C57BL/6 mice and will be cultured in media containing macrophage-colony stimulating factor (M-CSF) (30 ng/mL) and RANKL (100 ng/mL). After a cell viability evaluation, further investigations will be carried out using resorption pit assays, quantitative reverse transcription polymerase chain reactions (RT-PCR), western blot analysis, luciferase reporter gene activity assays, and osteoclastogenesis assays. For statistical analysis, the student Newmane-Keuls test will be applied with mean (SD) for data expression and *P* less than .05 for statistical significance [25].

Figure 3. Natural compound inhibitors of the RANKL pathway.



Preclinical Efficacy Evaluation Using Animal Models

The collagen-induced arthritis (CIA) model is regarded as the best-studied animal model for PsA [26] and will be used in this study to determine the anti-arthritic effects of NPs (as utilized in previously published work by this laboratory) [19,21].

A total of 30, 9-week old female Dark Agouti (DA) rats will be used with 10 assigned to the non-arthritic control group (C). The remaining 20 rate will be induced following the CIA protocol and will be randomly assigned to either the treatment group (A) or the placebo group (B) when PsA symptoms first appear. Groups A and B will be subject to a subcutaneous injection of the purified natural compound (1 mg/kg in 0.9% saline) or 0.9% saline control every second day from onset of symptoms (clinical score 2 or greater), until tissue collection at day 14. Natural compounds differ in their bioavailability and solubility in water. As such, the proposed dosage and/or administration of may be further adjusted if required. All rats will be raised with water, 0.9% sodium chloride (NaCl) and standard rodent food ad libitum in a 22°C and 12h illuminated daily environment. Main outcome measures include a daily macroscopic scoring system and digital calipers to measure dorsal to plantar thickness (3 times per week) of each paw. Groups will be compared with (1) serological tests including serum albumin, alanine transaminase (ALT), aspartate transaminase (AST), and bilirubin using a clinical biochemical analyzer; (2) micro-computed tomography (micro-CT) image analysis of hind paws and femora and contact radiographs for both hind feet; and (3) histopathological assessment using tartrate-resistant acid phosphatase (TRAP) staining [27] of serial 5 µm sagittal sections through the digits. The latter requires at least 2 digits randomly taken from each rat. Each digit will have distal interphalangeal (DIP), proximal interphalangeal (PIP), and metatarsophalangeal (MTP) joints intact for scoring by 2 independent observers. Analysis of variance (ANOVA) and Fishers' protected least significant difference (PLSD) tests will be applied for statistical analyses (using StatView 4.0) with *P* values less than .05 indicating statistical significance.

Results

This 4-stage study will take approximately 4 years to complete and proposes to discover the effects of natural compounds against PsA through the identification of relevant signaling pathways and preclinical efficacy evaluations using animal models (Figure 4). Currently, we are in the early stages of evaluating the in silico data and detailing the in vitro effects of compounds on osteoclastogenesis and bone resorption. The findings from this research are expected to be published when the proposed studies are fully completed.

Figure 4. Study timelines. Green squares represent scheduled parts.

Expected findings	Timeline Duration (4 years): 8 units							
	1	2	3	4	5	6	7	8
1. Natural compounds and sourced species for in vitro study								
2. Extracted samples and their bioassay for drug development								
3. Signaling pathway prediction on osteoclast investigation								
4. Anti-arthritis effects on preclinical animal study								

Discussion

Significance of Findings

Anecdotal evidence suggests that promising NPs are able to act on specific targets regulating osteoclast function and here they constitute the compounds identified for PsA drug discovery. For each identified compound, its extracted sample will be validated in a preparation bioassay such as HPLC. This can directly prove or discount a previous PANTHER prediction by demonstrating the signaling pathways associated with joint damage and/or bone erosion. Further preclinical studies will demonstrate the anti-arthritic effects of validated natural compounds. The principal methods and findings of this project can be further applied in the search of other natural compounds effective against other arthropathies.

In Silico, Multi-Targeted Approach

The in silico, multi-targeted approach is a target-directed large-scale analysis using multiple databases [13]. It is able to locate biological targets for NPs and APPs. Consequently, the consolidated list of APP targets could be used to screen NPs target lists. This approach could also be used to further identify APP-like NPs by filtering out those targets irrelevant to any of the APPs. This can “fish” out a specific target across NPs and APPs. The identification of protein targets related to a specific natural compound can also reflect its therapeutic molecular mechanisms and hint at potential side effects. However, the number of estimated potential targets on the human genome is huge [28]. Therefore, an in silico model is necessary for large-scale data analysis to elucidate potential protein targets associated with natural compounds (including their formulae) effective against a certain disease.

That the HIT database contains a list of NPs along with their active ingredient makes this model innovative and broadens the scope of searches, ensuring the inclusion of all potentially relevant proteins [13]. An additional novelty is the “APP-like” NP identification and the NP/APP property exploration. With such a database cluster, the NP target list can be matched against potential APP drug targets to identify APP-like NPs. This may provide a direct biological and/or pharmaceutical comparison between NPs and APPs, in terms of their possible effects on specific proteins, for the same disorder.

The Reliability of In Silico Screening Data

The in silico solution extensively uses frequency effects in target identification, which provides an objective approach to short listing targets and facilitates the reliability of the in silico data to a considerable extent. On the other hand, popular targets often reflect the hot topics previously undertaken in natural product research. Due to a number of studies and reports on natural products in chronic inflammation with PsA, some inflammatory targets may be presented in high frequency within the identified data sets. It is also noted that multiple terms of a single potential target often exist in the above main databases (HIT, DrugBank, and PANTHER) [13]. The variable nomenclature in different databases may impact the reliability of data when locating a crossing target. Structure-based drug docking has emerged as a valuable tool to identify lead compounds and to facilitate drug development.

Following the in silico work, we will undertake in vitro studies and an in vivo CIA preclinical trial to individually validate the anti-arthritic effects of the identified natural compounds which have shown promise to be effective against PsA . During this part of the project, we will adopt standardized quality control over procedures, a high performance analysis approach, and employ established animal models to ensure the study’s success and feasibility.

Conclusion

The in silico rapid approach is proposed as a more general method for adding value to the results of a systematic review of NPs. More importantly, the proposed study builds on a multi-targeted approach for the identification of natural compounds for future drug discovery. This innovative approach is likely to be more precise, efficient, and compatible to identify the novel natural compounds for effective treatment of PsA.

Acknowledgments

We thank Ms Karen Dalby for her contribution to this manuscript.

Authors' Contributions

All authors contributed to the design of the study and have read, commented on, revised, and approved the manuscript. Shiqiang Deng and Jianwen Cheng contributed equally to this study.

Conflicts of Interest

None declared.

References

1. Haroon M, FitzGerald O. Psoriatic arthritis: complexities, comorbidities and implications for the clinic. Expert Rev Clin Immunol 2016;12(4):405-416. [doi: 10.1586/1744666X.2016.1139453] [Medline: 26735626]
2. Myers WA, Gottlieb AB, Mease P. Psoriasis and psoriatic arthritis: clinical features and disease mechanisms. Clin Dermatol 2006;24(5):438-447. [doi: 10.1016/j.clindermatol.2006.07.006] [Medline: 16966023]

3. Xue Y, Jiang L, Cheng Q, Chen H, Yu Y, Lin Y, et al. Adipokines in psoriatic arthritis patients: the correlations with osteoclast precursors and bone erosions. PLoS One 2012;7(10):e46740 [FREE Full text] [doi: 10.1371/journal.pone.0046740] [Medline: 23144698]
4. Chen X, Decker M. Multi-target compounds acting in the central nervous system designed from natural products. Curr Med Chem 2013;20(13):1673-1685. [Medline: 23410166]
5. Kwak HB, Lee BK, Oh J, Yeon J, Choi S, Cho HJ, et al. Inhibition of osteoclast differentiation and bone resorption by rotenone, through down-regulation of RANKL-induced c-Fos and NFATc1 expression. Bone 2010 Mar;46(3):724-731. [doi: 10.1016/j.bone.2009.10.042] [Medline: 19900598]
6. Newman DJ, Cragg GM, Snader KM. Natural products as sources of new drugs over the period 1981-2002. J Nat Prod 2003 Jul;66(7):1022-1037. [doi: 10.1021/np030096l] [Medline: 12880330]
7. Wang YN, Zhang Y, Wang Y, Zhu DX, Xu LQ, Fang H, et al. The beneficial effect of total glucosides of paeony on psoriatic arthritis links to circulating Tregs and Th1 cell function. Phytother Res 2014 Mar;28(3):372-381. [doi: 10.1002/ptr.5005] [Medline: 23610010]
8. Zhai ZJ, Li HW, Liu GW, Qu XH, Tian B, Yan W, et al. Andrographolide suppresses RANKL-induced osteoclastogenesis in vitro and prevents inflammatory bone loss in vivo. Br J Pharmacol 2014 Feb;171(3):663-675 [FREE Full text] [doi: 10.1111/bph.12463] [Medline: 24125472]
9. Chen HS, Qi SH, Shen JG. One-compound-multi-target: combination prospect of natural compounds with thrombolytic therapy in acute ischemic stroke. Curr Neuropharmacol 2017;15(1):134-156 [FREE Full text] [Medline: 27334020]
10. Sucher NJ. The application of Chinese medicine to novel drug discovery. Expert Opin Drug Discov 2013 Jan;8(1):21-34. [doi: 10.1517/17460441.2013.739602] [Medline: 23170842]
11. Paek SY, Han L, Weiland M, Lu C, McKinnon K, Zhou L, et al. Emerging biomarkers in psoriatic arthritis. IUBMB Life 2015 Dec;67(12):923-927 [FREE Full text] [doi: 10.1002/iub.1453] [Medline: 26602058]
12. Dalbeth N, Pool B, Smith T, Callon KE, Lobo M, Taylor WJ, et al. Circulating mediators of bone remodeling in psoriatic arthritis: implications for disordered osteoclastogenesis and bone erosion. Arthritis Res Ther 2010;12(4):R164 [FREE Full text] [doi: 10.1186/ar3123] [Medline: 20796300]
13. Deng S. Chinese herbal medicine for psoriasis: evaluation of clinical evidence and investigation of the anti-psoriatic effects of specific Chinese medicinal herbs. Melbourne: RMIT University; 2014 Feb 28. URL: https://researchbank.rmit.edu.au/eserv/rmit:160799/Deng.pdf [accessed 2016-10-30] [WebCite Cache ID 6le18berB]
14. Deng S, May BH, Zhang AL, Lu C, Xue CC. Topical herbal medicine combined with pharmacotherapy for psoriasis: a systematic review and meta-analysis. Arch Dermatol Res 2013 Apr;305(3):179-189. [doi: 10.1007/s00403-013-1316-y] [Medline: 23354931]
15. Deng S, May BH, Zhang AL, Lu C, Xue CC. Plant extracts for the topical management of psoriasis: a systematic review and meta-analysis. Br J Dermatol 2013 Oct;169(4):769-782. [doi: 10.1111/bjd.12557] [Medline: 23909714]
16. Deng S, May BH, Zhang AL, Lu C, Xue CC. Phytotherapy in the management of psoriasis: a review of the efficacy and safety of oral interventions and the pharmacological actions of the main plants. Arch Dermatol Res 2014 Apr;306(3):211-229. [doi: 10.1007/s00403-013-1428-4] [Medline: 24253308]
17. Deng S, May BH, Zhang AL, Lu C, Xue CC. Topical herbal formulae in the management of psoriasis: systematic review with meta-analysis of clinical studies and investigation of the pharmacological actions of the main herbs. Phytother Res 2014 Apr;28(4):480-497. [doi: 10.1002/ptr.5028] [Medline: 23817996]
18. Huang J, Zhou L, Wu H, Pavlos N, Chim SM, Liu Q, et al. Triptolide inhibits osteoclast formation, bone resorption, RANKL-mediated NF- B activation and titanium particle-induced osteolysis in a mouse model. Mol Cell Endocrinol 2015 Jan 05;399:346-353. [doi: 10.1016/j.mce.2014.10.016] [Medline: 25448849]
19. Liu Q, Zhao J, Tan R, Zhou H, Lin Z, Zheng M, et al. Parthenolide inhibits pro-inflammatory cytokine production and exhibits protective effects on progression of collagen-induced arthritis in a rat model. Scand J Rheumatol 2015 May;44(3):182-191. [doi: 10.3109/03009742.2014.938113] [Medline: 25439190]
20. Song F, Zhou L, Zhao J, Liu Q, Yang M, Tan R, et al. Eriodictyol inhibits RANKL-induced osteoclast formation and function via inhibition of NFATc1 activity. J Cell Physiol 2016 Sep;231(9):1983-1993. [doi: 10.1002/jcp.25304] [Medline: 26754483]
21. Zhou C, You Y, Shen W, Zhu Y, Peng J, Feng H, et al. Deficiency of sorting nexin 10 prevents bone erosion in collagen-induced mouse arthritis through promoting NFATc1 degradation. Ann Rheum Dis 2016 Jun;75(6):1211-1218. [doi: 10.1136/annrheumdis-2014-207134] [Medline: 26141367]
22. Zhou L, Liu Q, Yang M, Wang T, Yao J, Cheng J, et al. Dihydroartemisinin, an anti-malaria drug, suppresses estrogen deficiency-induced osteoporosis, osteoclast formation, and RANKL-induced signaling pathways. J Bone Miner Res 2016 May;31(5):964-974 [FREE Full text] [doi: 10.1002/jbmr.2771] [Medline: 26684711]
23. Sarker SD, Nahar L. An introduction to natural products isolation. Methods Mol Biol 2012;864:1-25. [doi: 10.1007/978-1-61779-624-1_1] [Medline: 22367891]
24. Zhou T, Zhu Z, Wang C, Fan G, Peng J, Chai Y, et al. On-line purity monitoring in high-speed counter-current chromatography: application of HSCCC-HPLC-DAD for the preparation of 5-HMF, neomangiferin and mangiferin from

Anemarrhena asphodeloides Bunge. J Pharm Biomed Anal 2007 May 09;44(1):96-100. [doi: 10.1016/j.jpba.2007.01.050] [Medline: 17349768]
25. Nie S, Xu J, Zhang C, Xu C, Liu M, Yu D. Salicortin inhibits osteoclast differentiation and bone resorption by down-regulating JNK and NF-κB/NFATc1 signaling pathways. Biochem Biophys Res Commun 2016 Jan 29;470(1):61-67. [doi: 10.1016/j.bbrc.2015.12.115] [Medline: 26740180]
26. Weitz JE, Ritchlin CT. Mechanistic insights from animal models of psoriasis and psoriatic arthritis. Curr Rheumatol Rep 2013 Nov;15(11):377. [doi: 10.1007/s11926-013-0377-4] [Medline: 24072605]
27. Minkin C. Bone acid phosphatase: tartrate-resistant acid phosphatase as a marker of osteoclast function. Calcif Tissue Int 1982 May;34(3):285-290. [Medline: 6809291]
28. Zheng CJ, Han LY, Yap CW, Ji ZL, Cao ZW, Chen YZ. Therapeutic targets: progress of their exploration and investigation of their characteristics. Pharmacol Rev 2006 Jun;58(2):259-279 [FREE Full text] [doi: 10.1124/pr.58.2.4] [Medline: 16714488]

Abbreviations

APP: anti-psoriatic pharmacotherapy
CD: cluster of differentiation
CIA: collagen-induced arthritis
DAD: diode array detection
Encyclopedia of TCM: Encyclopedia of Traditional Chinese Medicine
HIT: Herbal Ingredients' Targets database
HPLC: high-performance liquid chromatography
HSCCC: high-speed counter-current chromatography
ID: identification
IL: interleukin
NPM: natural product medication
RANKL: receptor activator of nuclear factor-κB ligand
TRAP: tartrate-resistant acid phosphatase

Edited by G Eysenbach; submitted 03.03.17; peer-reviewed by M Liu, P Kurizky; comments to author 19.04.17; revised version received 30.04.17; accepted 30.04.17; published 11.07.17.

Please cite as:
Deng S, Cheng J, Zhao J, Yao F, Xu J
Natural Compounds for the Treatment of Psoriatic Arthritis: A Proposal Based on Multi-Targeted Osteoclastic Regulation and on a Preclinical Study
JMIR Res Protoc 2017;6(7):e132
URL: http://www.researchprotocols.org/2017/7/e132/
doi:10.2196/resprot.7636
PMID:28698171

Original Paper

Integrated Care in Prostate Cancer (ICARE-P): Nonrandomized Controlled Feasibility Study of Online Holistic Needs Assessment, Linking the Patient and the Health Care Team

Veronica Nanton[1], BA (Comb Hons), PGDip, MSc, PhD; Rebecca Appleton[1], BA (Hons), BPsS; Jeremy Dale[1], BA, MA, MBBS (Hons), PhD, FRCGP; Julia Roscoe[1], MSc; Thomas Hamborg[1], MSc, Mphil; Sam H Ahmedzai[2], BSc, MBChB, FCRP, FFPM; Theodoros N Arvanitis[3], RT, DPhil, CEng, FRSM; Douglas Badger[4], BA, MA; Nicholas James[5], BSc, MBBS, MRCP, FRCR, PhD, FRCP; Richard Mendelsohn[6], MBChB, FFPH, MRCGP; Omar Khan[3], MEng (Hons); Deepak Parashar[1], BSc (Hons), BSc, MSc, MASt, PhD; Prashant Patel[7], MBBS, MS, FRCSEd, PhD, FRCSEd(Urol)

[1]Division of Health Sciences, Warwick Medical School, University of Warwick, Coventry, United Kingdom

[2]Medical School, University of Sheffield, Sheffield, United Kingdom

[3]Institute of Digital Healthcare, WMG, University of Warwick, Coventry, United Kingdom

[4]South Warwickshire Prostate Support Association, Stratford, United Kingdom

[5]The Cancer Centre, University Hospital Birmingham NHS Foundation Trust, Birmingham, United Kingdom

[6]Birmingham South Central CCG, Birmingham, United Kingdom

[7]Department of Urology, University Hospital Birmingham NHS Foundation Trust, Birmingham, United Kingdom

Corresponding Author:
Veronica Nanton, BA (Comb Hons), PGDip, MSc, PhD
Division of Health Sciences
Warwick Medical School
University of Warwick
Coventry
Coventry, CV4 7AL
United Kingdom
Phone: 44 02476 574025
Fax: 44 02576 461606
Email: V.Nanton@warwick.ac.uk

Abstract

Background: The potential of technology to aid integration of care delivery systems is being explored in a range of contexts across a variety of conditions in the United Kingdom. Prostate cancer is the most common cancer in UK men. With a 10-year survival rate of 84%, there is a need to explore innovative methods of care that are integrated between primary health care providers and specialist teams in order to address long-term consequences of the disease and its treatment as well as to provide continued monitoring for recurrence.

Objective: Our aim was to test the feasibility of a randomized controlled trial to compare a model of prostate cancer continuing and follow-up care integration, underpinned by digital technology, with usual care in terms of clinical and cost-effectiveness, patient-reported outcomes, and experience.

Methods: A first phase of the study has included development of an online adaptive prostate specific Holistic Needs Assessment system (HNA), training for primary care-based nurses, training of an IT peer supporter, and interviews with health care professionals and men with prostate cancer to explore views of their care, experience of technology, and views of the proposed intervention. In Phase 2, men in the intervention arm will complete the HNA at home to help identify and articulate concerns and share them with their health care professionals, in both primary and specialist care. Participants in the control arm will receive usual care. Outcomes including quality of life and well-being, prostate-specific concerns, and patient enablement will be measured 3 times over a 9-month period.

Results: Findings from phase 1 indicated strong support for the intervention among men, including those who had had little experience of digital technology. Men expressed a range of views on ways that the online system might be used within a clinical

pathway. Health care professionals gave valuable feedback on how the output of the assessment might be presented to encourage engagement and uptake by clinical teams. Recruitment to the second phase of the study, the feasibility trial, commenced March 2017.

Conclusions: To our knowledge, this study is the first in the United Kingdom to trial an online holistic needs assessment for men with prostate cancer, with data shared between patients and primary and secondary care providers. This study addresses recommendations in recent policy documents promoting the importance of data sharing and enhanced communication between care providers as a basis for care integration. We anticipate that this model of care will ultimately provide important benefits for both patients and the National Health Service.

Trial Registration: International Standard Randomized Controlled Trial Number (ISRCTN): 31380482; http://www.isrctn.com/ISRCTN31380482 (Archived by WebCite at http://www.webcitation.org/6s8I42u5N)

(JMIR Res Protoc 2017;6(7):e147) doi:10.2196/resprot.7667

KEYWORDS

Internet; prostate cancer; holistic needs assessment; integrated care

Introduction

Increasing numbers of cancer patients and cancer survivors represent a growing demand on overstretched specialist secondary care services in the United Kingdom. Evidence indicates that these services often fail to meet the various needs of survivors [1-4]. The potential role for primary care in addressing these needs and reducing the demand on specialist services is now widely recognized [5]. In response, there has been a rapid increase in recent years in interventions aiming to introduce and evaluate integrated and shared approaches to care, in which primary care services take on an extended role in the care of patients during or following treatment [6,7]. Macmillan Cancer Support has promoted greater primary care involvement with patients with cancer and has developed and rolled out a training program in cancer follow-up for practice nurses [8].

Prostate cancer is the most common cancer in men, with over 47,000 men diagnosed each year in the United Kingdom [9]. With current 10-year survival rates of 84% [10], there are over 330,000 men in the United Kingdom living with and after prostate cancer. Men with prostate cancer follow a range of treatment pathways depending on factors such as the stage their cancer was diagnosed, comorbidities, and patient choice. They often live with the direct consequences of their illness or treatment, such as urinary, sexual and bowel problems, as well as fatigue. These symptoms can have a negative impact on men's quality of life [11-14]. Men on hormone treatment also face an increased risk of osteoporosis and cardiovascular events [15-18]. In addition, men are often affected by indirect consequences of their cancer such as social, financial, and psychological difficulties [4,19,20]. In particular, men may suffer from anxiety and depression, both during initial treatment and thereafter [21,22]. These may be especially pronounced if they have a lack of positive support, detrimental interactions, and a high perceived threat of cancer [23]. This may contribute to men with prostate cancer reporting a worse experience of care and follow-up than those with other cancers [24,25]. There is also evidence that problems may remain unrecognized and unaddressed and may persist for many years [26-28].

While high survival rates in prostate cancer are extremely encouraging, there remains a need for greater attention to quality of life. As well as treatment of the disease and its physical symptoms, methods to identify men's emotional and psychological concerns, or "holistic needs," are required. Care pathways that are designed to address these from an early stage are needed.

A Role for Primary Care

While protocols vary widely throughout the United Kingdom, the National Institute for Health and Care Excellence (NICE) has recommended that after 2 years of secondary care based follow-up, care should be transferred to the general practitioner (GP) as long as there are no concerning symptoms or treatment complications [29]. Many specialist services currently transfer care of men with "stable" disease either after surgery or on hormone treatment to primary care providers under locally enhanced or incentivized service arrangements with provision for men to return to specialist care if necessary. Primary care clinicians appear willing to undertake an early role in follow-up [30-32]. Interventions that increase communication between primary and secondary specialist services have been shown to facilitate the transfer of care process [33].

Practice nurses and other primary care team members are well placed to understand the wide ranging needs of men with prostate cancer with their knowledge of each patient's comorbidities, family, and social circumstances. They are also better placed to provide opportunistic support, as GP consultation rates for men with prostate cancer are around three times higher than those of their peers [34]. Much of their expertise and skills in the care of patients with chronic conditions in relation to supporting self-management may be transferable to prostate cancer care. Primary care staff may also have detailed knowledge of local resources that may be of value to the patient, and GPs may make direct referrals to community support services. Evaluation within one Clinical Commissioning Group, where follow-up for stable patients has been transferred to primary care, has demonstrated benefits in terms of patient experience and costs and barriers to the pathway redesign including issues around primary and secondary care communication [35].

Holistic Needs Assessment

In recognition of the changing needs of cancer patients throughout their cancer journey, "holistic needs assessment" as a method of identifying, assessing, and planning appropriate care has been widely promoted for use in the specialist secondary care setting. The National Cancer Survivorship Initiative's "Living with and beyond cancer programme" recommended that all cancer patients should have access to a Holistic Needs Assessment (HNA) and Care Plan [36]. The program promotes the use of the HNA for encouraging patients to self-manage during and after their treatment. A recent National Prostate Cancer Audit [37] has also highlighted the importance of identifying the needs of men with prostate cancer and linking men to appropriate services. While there is general agreement regarding the potential of the HNA, there is little evidence of effectiveness [38,39]. Adoption of the HNA with respect to men with prostate cancer has also been shown to be uneven, with staff identifying barriers including the time needed for completion in clinic (Prostate Cancer UK unpublished report). To address the limitations of a paper-based system [40], Macmillan Cancer Support has developed an electronic generic HNA. Evaluation has demonstrated acceptability of the electronic format to both patients and staff but pointed out difficulties of implementation within the secondary care setting [41]. To date, there is little indication of uptake of such assessments tools within general practice.

Information Technology

The use of information technology (IT) in cancer patient follow-up and primary care has been explored in the United States [42], Norway [43,44], and Australia [45] but has as yet received limited attention within the United Kingdom. However, technology now well embedded within general practice management is increasingly incorporated into patient care in a variety of forms and across a range of conditions (eg [6,46-50]). The GP Forward View policy document describing the National Health Service (NHS) plans for developing general practice in the next 5 years emphasizes its increasing importance and includes a key policy aim to support the design and adoption of technology that enables patient self-care and self-management. The document also highlights the central role of technology in improving primary and secondary care communication and the provision of integrated care [51]. Secondary care adoption of IT, however, has been comparatively slow and the need for secondary care digitization, including patient-facing systems, has recently been highlighted by the National Advisory Group on Health Information Technology in England [52].

In order to better address the ongoing needs of men with prostate cancer and to try to reduce the pressures on specialist services, we have designed an innovative study that brings together IT, HNA, and primary care involvement throughout the cancer pathway. Our intervention aims to promote an integrated approach to care through enhanced communication between the patient and health care providers. This protocol describes a feasibility study in which an online prostate-specific HNA is shared between patient and their clinical teams. In addition, our study involves training for practice nurses in collaboration with Macmillan Cancer Support and ongoing support from specialist teams. To our knowledge, this is the first UK-based study in which IT provides the basis for a primary care based intervention in prostate cancer and the first UK-based study that seeks to develop an integrated and holistic approach to care for all men with prostate cancer from diagnosis onwards.

Methods

Design

This study involves a complex intervention [53] that includes both the development of patient self-efficacy and the implementation of organizational change [54]. Hence, we have adopted a mixed-methods, two-phase design. Phase 1 of the study (March-November 2016) was designed to include technical development, training, recruitment, and qualitative interviews. Phase 2 is a nonrandomized cluster controlled trial of the intervention. Follow-up interviews will be undertaken with patient participants and health professionals to explore their experience of the trial.

Population, Setting, and Inclusion Criteria

Our study population extends to all men who have ever had a diagnosis of prostate cancer. The selection of this population offers the opportunity for participation to any man who may have problems related to prostate cancer, whether currently receiving treatment, monitoring, or follow-up. This will allow us to identify the wide range of short- and long-term concerns that may occur during or following different treatment regimens.

The study is set in 14 general practices including 10 intervention and 4 control practices within one Clinical Commissioning Group (CCG) in the West Midlands and one specialist secondary care site within an NHS Foundation Trust hospital. Eligibility for general practices is determined by location within the participating CCG and a referral pathway to the specialist center. Practices must also be willing to support a practice nurse taking part in the Macmillan training program and the prostate specific training or to enable a primary care research nurse who has undergone the training to run the study within the practice.

Patient eligibility for each of the study phases requires registration with any of the participating practices and diagnosis of prostate cancer or treatment at any time at the participating specialist center. Men must be able to read written and understand spoken English and be able and willing to give informed consent. GPs' screening of the list of potentially eligible men ensures capacity to participate.

Men are ineligible for inclusion if they are aged under 18 years, unable to give informed consent, unable to complete outcome measures, living in a care setting, suffer from mental health problems, or are unable to communicate in English.

Practice nurses and GPs from participating practices are eligible to take part in interviews prior to or following the intervention.

Phase 1 Summary

During Phase 1, the HNA has been finalized and installed on a secure study website at the participating Trust. Participating patients, associated clinicians in secondary and primary care,

and members of the study team have access to the site. Ten intervention and 4 control general practices within the participating CCG have been recruited. Five Macmillan trained nurses recruited to the study have undertaken additional prostate cancer training at the specialist secondary care center. One volunteer peer supporter has been recruited and trained in order to help men complete the HNA if needed. Qualitative semistructured interviews have been undertaken with 8 primary care based health care professionals and 10 patient participants recruited through their general practices. The purpose of the interviews was to determine variation in delivery and experience of usual care and to identify barriers and facilitators to implementation of the intervention and to assess the views of health care professionals and patients on the online HNA.

Findings from Phase 1 demonstrate an enthusiasm for the project among patients. Men who have had little experience with IT have expressed a willingness to take part, in some cases despite a lack of access to the Internet. We have responded to this potential barrier by equipping the ITmate peer supporter with an Internet-enabled tablet computer. Health professionals have also been supportive of the study and acknowledged the potential of the intervention. GPs in particular expressed the importance of a brief output from the HNA, hence the summary document generated by the assessment has been designed to be concise and easily interpreted.

Aims and Objectives

The aim of the trial is to test the feasibility of undertaking a future cluster randomized controlled trial (RCT) comparing a model of integrated prostate cancer continuing care and follow-up care with usual care in terms of clinical and cost-effectiveness, patient-reported outcomes, and experience.

Trial objectives are to (1) assess the fidelity of intervention delivery, and the acceptability and utility of the intervention by patients and primary and secondary care clinicians, (2) test patient recruitment, data collection, and retention in both intervention and control practices, (3) analyze how the HNA is used by men over a 9-month period, with self-assessment completed at baseline, 3 months, and 6 months, (4) test the willingness of clinicians and patients to provide qualitative and quantitative data including process data and measurement of outcomes, (5) test the feasibility of collecting use of resource data and process data, including numbers of primary and specialist contacts and consultations, (6) identify the most suitable primary outcome measure and refine secondary outcome measures for a future cluster RCT, and (7) estimate parameters for a sample size calculation for cluster RCT.

The Holistic Needs Assessment Instrument

The HNA is an online self-assessment tool designed to capture the needs of men who have had a diagnosis of prostate cancer. It is composed of 11 different sections, including Physical Health, Emotional and Psychological Issues, Independence and Activity, and Access to Services. These can be used flexibly so that men can complete all of the sections or only the ones they feel are relevant to them, in any order, and in their own time. As men work through the assessment, they are shown links to advice pages or videos on websites such as Prostate Cancer UK, with the aim of encouraging and enabling self-management. This system shows a “red flag” if a patient reports having any physical or psychological symptoms of serious concern, for example, “blood in urine” or “thoughts of ending it all” with a prompt to visit their GP as soon as possible. The system will also alert the clinician to these red flags when they access the output from their patient’s HNA. At the end of each section, men have the facility to disclose additional concerns, and this text is inserted into the summary generated on completion of the assessment. This summary auto-populates the first pages of a Care Plan to be completed with a health professional.

The system has been designed to be attractive and easy to navigate. Figures 1 and 2 illustrate two of the initial screens. The online HNA has been finalized following an iterative process of user and patient testing (Prostate Cancer UK unpublished report). It has been installed on a study website hosted on a Trust server and penetration tested to ensure security.

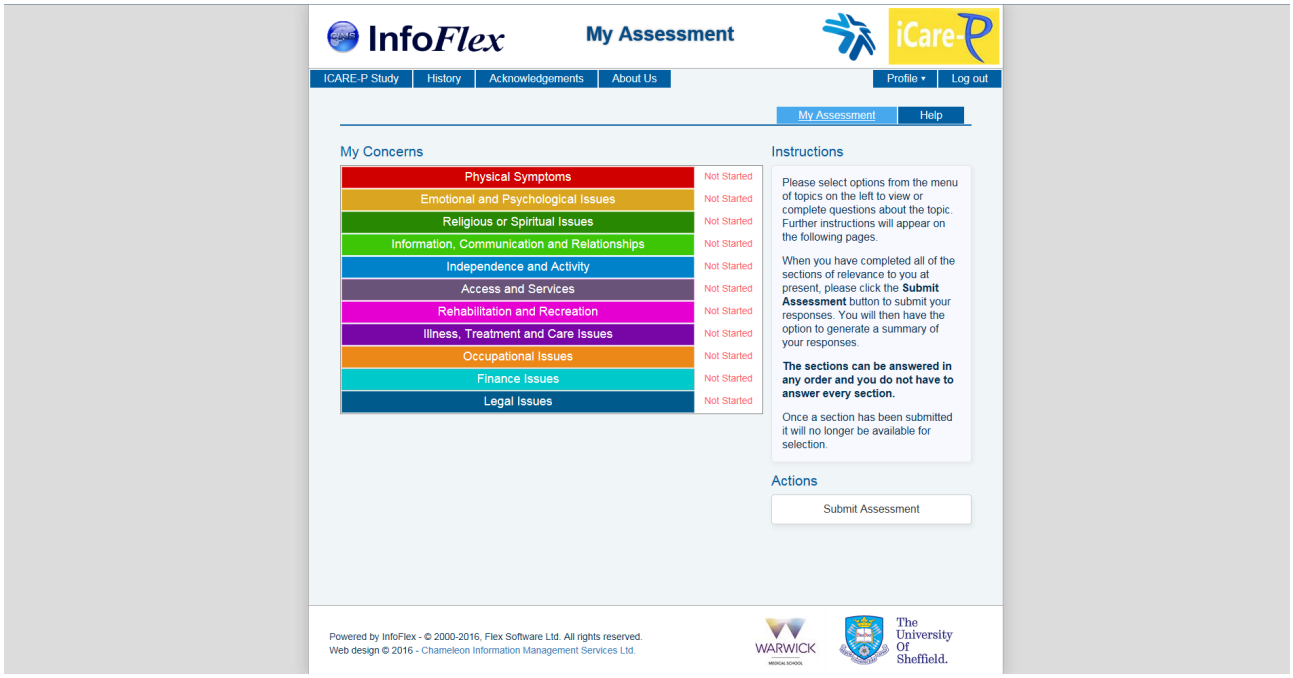
The project platform incorporates three elements: (1) a Web app for patients to complete the holistic needs assessments, (2) a Web app for nurses to review those assessments and record care plans, and (3) a windows app design to allow administration of the project such as adding patient or nurse users and monitoring completion of study stages by the research team.

Intervention

Participants in the intervention group will be invited to complete the HNA three times in a 9-month period. Following submission of the assessment, men will be invited to make an appointment with the nurse to discuss any concerns identified and to complete and personalize the care plan. The care plan will summarize any topics discussed, outcomes or referrals, actions taken regarding any “red flag” symptoms, and actions to be undertaken by the man himself. The document will be generated and a copy given to participants and added to their patient notes. Where specific clinical concerns are identified, sharing of the online data with the secondary care team will enable rapid specialist advice or referral. If the participants attend the surgery between the three study appointments, practice nurses or GPs will be encouraged to undertake opportunistic reinforcement of the care plan, for example, checking whether the man has undertaken any actions he has agreed to in the plan or whether referrals made have led to appointments.

Figure 1. The HNA login screen.

Figure 2. Assessment page showing the different sections of the HNA.



If the participant is a patient undergoing ongoing treatment at the specialist center, study participation will be flagged in his notes. Relevant secondary care clinicians will be able to access the participants assessment summary and care plan prior to or during an appointment. If any concerns other than clinical issues related to the prostate cancer arise in the consultation (eg, occupational or family concerns, worries over comorbidities), the secondary care clinician may, with the participant's permission, contact the primary care based nurse.

Usual Care

Usual care comprises a community-based, stable prostate clinical care pathway. Men with advanced disease on hormone treatment are also largely seen in primary care for their injections and will be seen only in secondary care if their prostate specific antigen (PSA) rises above a threshold or other complications occur. Care of men by specialist teams continues up until 3 years postcurative treatment and is reintroduced if a clinical need arises (symptoms that are suggestive of prostate cancer progression, eg, significant rise in PSA, suspected metastases, pain or treatment complication, deteriorating renal function). Men on active surveillance are excluded from this pathway. Men who do not meet the criteria continue to be seen by secondary care teams.

Recruitment

The GP and practice nurse will search for eligible patients, who will then be sent a participant information sheet and a covering

letter of invitation to participate signed by the GP. If patients are considering taking part in the study or have decided to do so, they will return an enclosed reply slip to the study team. If there has been no response after 2 weeks from the initial contact, the practice nurse will telephone to check whether the patient is interested. Patients can also be invited to take part on an opportunistic basis, such as during a routine appointment. Written consent will be taken by a member of the study team.

Data Collection

Participants in the intervention group will complete the HNA at baseline, as well as 3 months and 6 months later. We will use six validated questionnaires to measure unmet need, quality of life, and general health and well-being of participants: the Cancer Survivors Unmet Needs instrument [55], the Patient Activation Measure [56], the Expanded Prostate Cancer Index Composite [57], the EuroQol five dimensions questionnaire (EQ5D) [58], the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ) [59], and the Warwick and Edinburgh Mental Well-being Scale [60], as participants in the intervention group progress through the study. At baseline and 9 months later, participants in both the intervention and control groups will complete all the outcome measures. Participants in the intervention group will also complete a smaller subset of outcome measures before consultations at 3 and 6 months. Men can either complete these online or fill out paper copies for postal return.

A small number of patients from the intervention group (n<10) will be followed up at the end of the study for an interview about their experiences of the intervention. We will also invite participants to complete an HNA technology acceptance and usability questionnaire developed by members of the study team.

Outcomes

Patient and feasibility outcomes will be assessed. In order to determine feasibility of carrying out a larger scale RCT to compare the intervention with usual care, we will evaluate this study in terms of >25% eligible men consenting to participate in the study and >70% of participants in the intervention group completing the HNA and the patient outcome measures at each time point.

Figure 3 illustrates the study pathway.

Analysis

Quantitative

The analyses will be exploratory and mainly descriptive. Point estimates and corresponding 90% confidence intervals will be calculated for all outcome measures in both arms, and their distributions will be assessed to identify appropriate statistical analysis methods for a future RCT. Hierarchical mixed models accounting for within GP practice correlation will be fitted for potential primary outcomes to explore the effect of the intervention relative to usual care at a single time point as well as over time (repeated measures model). Propensity score matching and regression adjustment techniques will be used as sensitivity analyses and to minimize potential bias in outcomes estimates due to the nonrandomized nature of the study.

Data will be downloaded from the HNA database to assess completion rates at each time period, sequential completion over a year, and analysis of the needs identified.

Qualitative

Thematic analysis of the interviews will also take place with the audiorecorded data transcribed and entered into a software analysis package (NVivo 10). Members of the research team will each identify broad themes from close reading of the interview transcripts. Further themes and subthemes will be developed through an iterative process of coding, categorization, and discussion between team members. Topics to be explored include men's experiences of the new model of care, advantages and disadvantages of the intervention, and any impact on heath and confidence in self-management.

Health Economic Analysis

Completion rates for collecting resource utilization data, contacts with health care professionals and referrals to hospitals and other community health and social care providers will be evaluated. Data collected at each time point will be analyzed to provide preliminary indications of the costs associated with the intervention over the 9-month period.

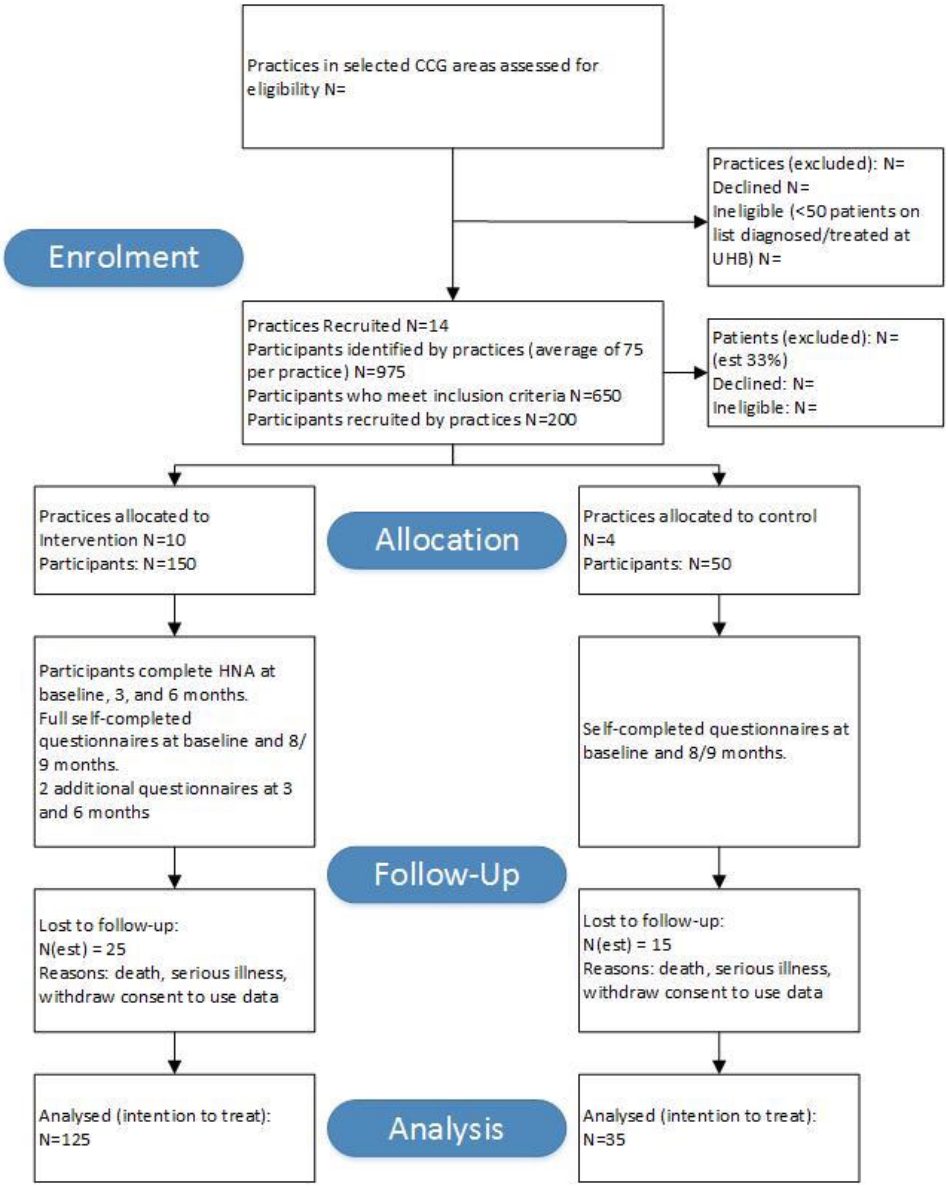
Intervention Fidelity

Researchers within the project team are able to access the ICARE-P admin site. This will allow the tracking of completion of HNAs and Care Plans and to identify how the software has been used by participants and health professionals. Content of the HNAs and Care Plans are also accessible to these members of the research team. Analysis of Care Plans and referral data retrieved from practices will allow assessment of intervention fidelity.

Ethics

Phase 1 of the study was approved by NHS Research Ethics Committee proportionate review process (ref: 15/EM/0534). Phase 2 was considered and approved under full review (ref: 16/YH/0278).

Figure 3. Flowchart for ICARE-P Adapted from CONSORT guidelines for randomized controlled trials.



Discussion

Principal Considerations

The online HNA that forms the cornerstone of our intervention puts the patient at the center of care [61], enabling him to identify and express concerns to both primary care and specialist teams, as well as encouraging and facilitating self-management. The adaptive nature of the HNA ensures its suitability for men from early diagnosis onwards regardless of treatment modality or their stage in the care pathway. The online system offers an opportunity for integrated care allowing all linked clinicians access to the HNA output in which prostate specific clinical issues, broader concerns, or issues related to comorbidities are summarized.

Integration between primary and specialist secondary care services and the role of technology in supporting this aim represent key themes of the five-year forward policy document [51]. Integrated services offer advantages to patients in terms of continuity and coordination together with a potential for streamlining of provision. Interoperability of systems that allow easy data sharing are critical to integration, and the implementation of such systems has been identified as priority in a recent report by the National Advisory Group on Health Information Technology in England [52]. Primary care clinicians interviewed in Phase 1 of our study endorsed the need for improvements in communication with specialist colleagues, expressing frustration at the speed of current systems. The report has also highlighted the relatively slow adoption of digital technology in secondary care compared with high levels of primary care digitization and has emphasized the need for secondary care implementation. Barriers identified include extreme caution in relation to data security and a lack of attention to the needs of the end user when systems have been developed and put in place. Our HNA and Care Plan have been designed for ease of use by patients and clinicians, and they aim to be comprehensive yet relevant. We have provided training for participating clinicians in the use of the system to

encourage engagement with the study. To overcome any difficulties patients may experience, we have the trained ITmate available to assist them. We have met the need to conform to rigorous data security standards and have worked collaboratively with our participating NHS Trust, our institution, and our IT partners to ensure all requirements are met.

A further recommendation of the report is a stepwise approach to digitization. We recognize the importance of such an approach both from the technological and the behavioral standpoints. This study introduces an innovative approach to the care of men with prostate cancer; however, more can be achieved.

If feasibility aims are met in terms of recruitment (>25% of eligible men and >70% retention) and usability and acceptability testing with patients and clinical teams indicate support for the intervention, further technical development of the HNA is proposed prior to a full effectiveness trial. This development will involve full integration of the HNA within the Trusts' own clinical data management system and the development of an enhanced communication pathway between specialist and primary care teams enabling automated alerts and notifications.

Limitations

As a feasibility study, the sample size involved is limited. A nonrandomized controlled trial may result in some biases (in particular confounding and allocation bias). We aim to reduce these biases through the use of regression adjustment and propensity score matching.

Conclusion

This study is the first of its kind to trial an online HNA for men with prostate cancer with data shared between patients and primary and secondary care providers. We anticipate that this system will ultimately provide important benefits for patients in terms of addressing unmet needs, identifying concerning symptoms, and enabling self-management, and benefits to the NHS in terms of effective use of resources and appropriate use of skills.

Acknowledgments

This paper presents independent research funded by the National Institute for Health Research (NIHR) under its Research for Patient Benefit Programme (grant reference #PB-PG-0214-33092). The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR, or the Department of Health.

A project to develop the adaptive prostate-specific HNA was funded by the Movember Foundation in collaboration with Prostate Cancer UK.

The HNA and ICARE-P project platform were developed and configured by Chameleon Information Management Services Ltd free of charge. The ICARE-P platform is hosted by the University Hospital Birmingham NHS Foundation Trust.

Conflicts of Interest

None declared.

References

1. Richards M, Corner J, Maher J. The National Cancer Survivorship Initiative: new and emerging evidence on the ongoing needs of cancer survivors. Br J Cancer 2011 Nov 08;105 Suppl 1:S1-S4 [FREE Full text] [doi: 10.1038/bjc.2011.416] [Medline: 22048027]
2. Davies NJ, Batehup L. Towards a personalised approach to aftercare: a review of cancer follow-up in the UK. J Cancer Surviv 2011 Jun;5(2):142-151. [doi: 10.1007/s11764-010-0165-3] [Medline: 21253881]
3. Carey M, Lambert S, Smits R, Paul C, Sanson-Fisher R, Clinton-McHarg T. The unfulfilled promise: a systematic review of interventions to reduce the unmet supportive care needs of cancer patients. Support Care Cancer 2012 Feb;20(2):207-219 [FREE Full text] [doi: 10.1007/s00520-011-1327-1] [Medline: 22089430]
4. Ream E, Quennell A, Fincham L, Faithfull S, Khoo V, Wilson-Barnett J, et al. Supportive care needs of men living with prostate cancer in England: a survey. Br J Cancer 2008 Jun 17;98(12):1903-1909 [FREE Full text] [doi: 10.1038/sj.bjc.6604406] [Medline: 18506142]
5. Buckland D. Role of primary care in the management of cancer patients. Prescriber 2016 May 20;27(4):45-49. [doi: 10.1002/psb.1453]
6. Tomasone JR, Brouwers MC, Vukmirovic M, Grunfeld E, O'Brien MA, Urquhart R, et al. Interventions to improve care coordination between primary healthcare and oncology care providers: a systematic review. ESMO Open 2016;1(5):e000077 [FREE Full text] [doi: 10.1136/esmoopen-2016-000077] [Medline: 27843639]
7. Kendall M, Mason B, Momen N, Barclay S, Munday D, Lovick R, et al. Proactive cancer care in primary care: a mixed-methods study. Fam Pract 2013 Jun;30(3):302-312 [FREE Full text] [doi: 10.1093/fampra/cms085] [Medline: 23382502]
8. Macmillan. Macmillan UK. 2013. Cancer as a long-term condition: Practice nurse pilot evaluation URL: https://www.macmillan.org.uk/documents/aboutus/health_professionals/primarycare/newslettermay2013/cancerasalongtermconditionfullevaluationreportfinal2.pdf [accessed 2017-07-21] [WebCite Cache ID 6s8IRGtTt]

9. Prostate Cancer UK. URL: http://prostatecanceruk.org/prostate-information/about-prostate-cancer [accessed 2016-12-13] [WebCite Cache ID 6mixDOd6y]
10. Cancer Research UK. URL: http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/prostate-cancer [accessed 2016-12-13] [WebCite Cache ID 6mixSVRG5]
11. Watson E, Shinkins B, Frith E, Neal D, Hamdy F, Walter F, et al. Symptoms, unmet needs, psychological well-being and health status in survivors of prostate cancer: implications for redesigning follow-up. BJU Int 2016 Jun;117(6B):E10-E19 [FREE Full text] [doi: 10.1111/bju.13122] [Medline: 25818406]
12. Pardo Y, Guedea F, Aguiló F, Fernández P, Macías V, Mariño A, et al. Quality-of-life impact of primary treatments for localized prostate cancer in patients without hormonal treatment. J Clin Oncol 2010 Nov 01;28(31):4687-4696. [doi: 10.1200/JCO.2009.25.3245] [Medline: 20921463]
13. Gavin AT, Drummond FJ, Donnelly C, O'Leary E, Sharp L, Kinnear HR. Patient-reported 'ever had' and 'current' long-term physical symptoms after prostate cancer treatments. BJU Int 2015 Sep;116(3):397-406 [FREE Full text] [doi: 10.1111/bju.13036] [Medline: 25597493]
14. Lehto U, Helander S, Taari K, Aromaa A. Patient experiences at diagnosis and psychological well-being in prostate cancer: A Finnish national survey. Eur J Oncol Nurs 2015 Jun;19(3):220-229. [doi: 10.1016/j.ejon.2014.10.018] [Medline: 25547457]
15. Potosky AL, Davis WW, Hoffman RM, Stanford JL, Stephenson RA, Penson DF, et al. Five-year outcomes after prostatectomy or radiotherapy for prostate cancer: the prostate cancer outcomes study. J Natl Cancer Inst 2004 Sep 15;96(18):1358-1367. [doi: 10.1093/jnci/djh259] [Medline: 15367568]
16. Resnick MJ, Koyama T, Fan K, Albertsen PC, Goodman M, Hamilton AS, et al. Long-term functional outcomes after treatment for localized prostate cancer. N Engl J Med 2013 Jan 31;368(5):436-445 [FREE Full text] [doi: 10.1056/NEJMoa1209978] [Medline: 23363497]
17. Daniell HW, Dunn SR, Ferguson DW, Lomas G, Niazi Z, Stratte PT. Progressive osteoporosis during androgen deprivation therapy for prostate cancer. J Urol 2000 Jan;163(1):181-186. [Medline: 10604342]
18. Nguyen PL, Je Y, Schutz FAB, Hoffman KE, Hu JC, Parekh A, et al. Association of androgen deprivation therapy with cardiovascular death in patients with prostate cancer: a meta-analysis of randomized trials. JAMA 2011 Dec 07;306(21):2359-2366. [doi: 10.1001/jama.2011.1745] [Medline: 22147380]
19. Armes J, Crowe M, Colbourne L, Morgan H, Murrells T, Oakley C, et al. Patients' supportive care needs beyond the end of cancer treatment: a prospective, longitudinal survey. J Clin Oncol 2009 Dec 20;27(36):6172-6179. [doi: 10.1200/JCO.2009.22.5151] [Medline: 19884548]
20. Weber BA, Sherwill-Navarro P. Psychosocial consequences of prostate cancer: 30 years of research. Geriatr Nurs 2005;26(3):166-175. [doi: 10.1016/j.gerinurse.2005.05.001] [Medline: 15973345]
21. Sharpley CF, Christie DRH. Patient information preferences among breast and prostate cancer patients. Australas Radiol 2007 Apr;51(2):154-158. [doi: 10.1111/j.1440-1673.2007.01687.x] [Medline: 17419861]
22. Korfage IJ, Essink-Bot M, Janssens ACJW, Schröder FH, de Koning HJ. Anxiety and depression after prostate cancer diagnosis and treatment: 5-year follow-up. Br J Cancer 2006 Apr 24;94(8):1093-1098 [FREE Full text] [doi: 10.1038/sj.bjc.6603057] [Medline: 16622434]
23. Mehnert A, Lehmann C, Graefen M, Huland H, Koch U. Depression, anxiety, post-traumatic stress disorder and health-related quality of life and its association with social support in ambulatory prostate cancer patients. Eur J Cancer Care (Engl) 2010 Nov;19(6):736-745. [doi: 10.1111/j.1365-2354.2009.01117.x] [Medline: 19832893]
24. Sinfield P, Baker R, Camosso‐Stefinovic J, Colman A, Tarrant C, Mellon J, et al. Men's and carers' experiences of care for prostate cancer: a narrative literature review. Health Expect 2009 Sep;12(3):301-312.
25. Department of Health. 2012. National Cancer Patient Experience Survey 2011/12 - National Report URL: https://www.quality-health.co.uk/resources/surveys/national-cancer-experience-survey/201112-national-cancer-patient-experience-survey-reports [accessed 2017-07-21] [WebCite Cache ID 6s8Jo861a]
26. Nanton V, Docherty A, Meystre C, Dale J. Finding a pathway: information and uncertainty along the prostate cancer patient journey. Br J Health Psychol 2009 Sep;14(Pt 3):437-458. [doi: 10.1348/135910708X342890] [Medline: 18718111]
27. O'Brien R, Rose P, Campbell C, Weller D, Neal RD, Wilkinson C, Prostate Cancer Follow-up Group. "I wish I'd told them": a qualitative study examining the unmet psychosexual needs of prostate cancer patients during follow-up after treatment. Patient Educ Couns 2011 Aug;84(2):200-207. [doi: 10.1016/j.pec.2010.07.006] [Medline: 20702055]
28. Morrison V, Henderson BJ, Zinovieff F, Davies G, Cartmell R, Hall A, et al. Common, important, and unmet needs of cancer outpatients. Eur J Oncol Nurs 2012 Apr;16(2):115-123. [doi: 10.1016/j.ejon.2011.04.004] [Medline: 21555246]
29. NICE.: National Institute for Health and Care Excellence; 2014. Prostate cancer: diagnosis and management URL: https://www.nice.org.uk/guidance/cg175 [accessed 2017-07-21] [WebCite Cache ID 6s8K1S2RK]
30. Watson EK, O'Brien R, Campbell C, Weller D, Neal RD, Wilkinson C, Prostate Cancer Follow-Up Study Group. Views of health professionals on the role of primary care in the follow-up of men with prostate cancer. Fam Pract 2011 Dec;28(6):647-654. [doi: 10.1093/fampra/cmr034] [Medline: 21693683]
31. Del Giudice ME, Grunfeld E, Harvey BJ, Piliotis E, Verma S. Primary care physicians' views of routine follow-up care of cancer survivors. J Clin Oncol 2009 Jul 10;27(20):3338-3345. [doi: 10.1200/JCO.2008.20.4883] [Medline: 19380442]

32. Jiwa M, McManus A, Dadich A. The impact of knowledge, attitudes and beliefs on the engagement of primary and community-based healthcare professionals in cancer care: a literature review. Curr Med Res Opin 2013 Nov;29(11):1475-1482. [doi: 10.1185/03007995.2013.838154] [Medline: 23998506]
33. Lewis RA, Neal RD, Williams NH, France B, Hendry M, Russell D, et al. Follow-up of cancer in primary care versus secondary care: systematic review. Br J Gen Pract 2009 Jul;59(564):e234-e247 [FREE Full text] [doi: 10.3399/bjgp09X453567] [Medline: 19566990]
34. Heins M, Schellevis F, Rijken M, van der Hoek L, Korevaar J. Determinants of increased primary health care use in cancer survivors. J Clin Oncol 2012 Nov 20;30(33):4155-4160. [doi: 10.1200/JCO.2012.41.9101] [Medline: 23071230]
35. NHS Transforming Cancer Services for London Team. NHS. 2016. Business Case: Primary Care Led Stratified Follow-up for Prostate Cancer Patients URL: https://www.myhealth.london.nhs.uk/sites/default/files/Stratified%20prostate%20pathway%20business%20case%20Aug%202016.pdf [accessed 2017-07-21] [WebCite Cache ID 6s8Ke8KXj]
36. Department of Health. 2013. Living with & Beyond Cancer: Taking Action to Improve Outcomes (an update to the 2010 The National Cancer Survivorship Initiative Vision) URL: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/181054/9333-TSO-2900664-NCSI_Report_FINAL.pdf [accessed 2017-07-21] [WebCite Cache ID 6s8KjAsKd]
37. National Prostate Cancer Audit. 2016. URL: http://www.npca.org.uk [WebCite Cache ID 6nx70UBq]
38. Richardson A, Medina J, Brown V, Sitzia J. Patients' needs assessment in cancer care: a review of assessment tools. Support Care Cancer 2007 Oct;15(10):1125-1144. [doi: 10.1007/s00520-006-0205-8] [Medline: 17235503]
39. Carlson LE, Waller A, Mitchell AJ. Screening for distress and unmet needs in patients with cancer: review and recommendations. J Clin Oncol 2012 Apr 10;30(11):1160-1177. [doi: 10.1200/JCO.2011.39.5509] [Medline: 22412146]
40. Richardson AS, Brown V, Medina JA. Patients' Needs Assessment Tools in Cancer Care: Principles and Practice. London, UK: King's College London; 2005. URL: https://pdfs.semanticscholar.org/3112/12ad3b6c512c8b24aea8c650891bc3896ab0.pdf [accessed 2017-07-21] [WebCite Cache ID 6s8LJe6d6]
41. IPSOS Mori. 2013. Evaluation of electronic holistic needs assessment: final report URL: https://www.macmillan.org.uk/_images/e-hna-evaluation-report-executive-summary_tcm9-283675.pdf [accessed 2017-07-21] [WebCite Cache ID 6s8LPFyJn]
42. Vickers AJ, Salz T, Basch E, Cooperberg MR, Carroll PR, Tighe F, et al. Electronic patient self-assessment and management (SAM): a novel framework for cancer survivorship. BMC Med Inform Decis Mak 2010 Jun 17;10:34 [FREE Full text] [doi: 10.1186/1472-6947-10-34] [Medline: 20565745]
43. Ruland CM, Andersen T, Jeneson A, Moore S, Grimsbø GH, Børøsund E, et al. Effects of an internet support system to assist cancer patients in reducing symptom distress: a randomized controlled trial. Cancer Nurs 2013;36(1):6-17. [doi: 10.1097/NCC.0b013e31824d90d4] [Medline: 22495503]
44. Wibe T, Hellesø R, Varsi C, Ruland C, Ekstedt M. How does an online patient-nurse communication service meet the information needs of men with recently diagnosed testicular cancer? ISRN Nurs 2012;2012:260975 [FREE Full text] [doi: 10.5402/2012/260975] [Medline: 23251816]
45. Jiwa M, McManus A, Dadich A, White J, Rieck A, Razmi S. Harnessing information technology to innovate in primary care. Qual Prim Care 2013;21(1):43-49. [Medline: 23735634]
46. Young AJ. New technologies and general practice. Br J Gen Pract 2016 Dec;66(653):601-602. [doi: 10.3399/bjgp16X688021] [Medline: 27884890]
47. Bodenheimer T, Grumbach K. Electronic technology: a spark to revitalize primary care? JAMA 2003 Jul 09;290(2):259-264. [doi: 10.1001/jama.290.2.259] [Medline: 12851283]
48. Meade B, Buckley D, Boland M. What factors affect the use of electronic patient records by Irish GPs? Int J Med Inform 2009 Aug;78(8):551-558. [doi: 10.1016/j.ijmedinf.2009.03.004] [Medline: 19375381]
49. McMillan B, Abdelgalil R, Madhuvrata P, Easton K, Mitchell C. Reducing the risk of type 2 diabetes mellitus in primary care after gestational diabetes: a role for mobile technology to improve current care. Br J Gen Pract 2016 Dec;66(653):631-632. [doi: 10.3399/bjgp16X688297] [Medline: 27884913]
50. Smith JJ, Mallard-Smith RJ, Beattie V, Beattie DK. Use of information technology in general practice. J R Soc Med 2003 Aug;96(8):395-397 [FREE Full text] [Medline: 12893856]
51. NHS England. 2016. General Practice 'Forward View' URL: https://www.england.nhs.uk/wp-content/uploads/2016/04/gpfv.pdf [accessed 2017-07-21] [WebCite Cache ID 6s8Lm4BcD]
52. Wachter R. Department of Health. 2016. Making IT Work: Harnessing the power of health information technology to improve care in England URL: https://www.gov.uk/government/publications/using-information-technology-to-improve-the-nhs/making-it-work-harnessing-the-power-of-health-information-technology-to-improve-care-in-england [accessed 2017-07-21] [WebCite Cache ID 6s8Lqb1oz]
53. Anderson R. New MRC guidance on evaluating complex interventions. BMJ 2008 Oct 22;337:a1937. [Medline: 18945728]
54. Plamping D. The NHS's 50 anniversary. Change and resistance to change in the NHS. BMJ 1998 Jul 04;317(7150):69-71 [FREE Full text] [Medline: 9651280]

55. Hodgkinson K, Butow P, Hunt GE, Pendlebury S, Hobbs KM, Lo SK, et al. The development and evaluation of a measure to assess cancer survivors' unmet supportive care needs: the CaSUN (Cancer Survivors' Unmet Needs measure). Psychooncology 2007 Sep;16(9):796-804. [doi: 10.1002/pon.1137] [Medline: 17177268]
56. Hibbard JH, Stockard J, Mahoney ER, Tusler M. Development of the Patient Activation Measure (PAM): conceptualizing and measuring activation in patients and consumers. Health Serv Res 2004 Aug;39(4 Pt 1):1005-1026 [FREE Full text] [doi: 10.1111/j.1475-6773.2004.00269.x] [Medline: 15230939]
57. Chang P, Szymanski KM, Dunn RL, Chipman JJ, Litwin MS, Nguyen PL, et al. Expanded prostate cancer index composite for clinical practice: development and validation of a practical health related quality of life instrument for use in the routine clinical care of patients with prostate cancer. J Urol 2011 Sep;186(3):865-872 [FREE Full text] [doi: 10.1016/j.juro.2011.04.085] [Medline: 21788038]
58. Herdman M, Gudex C, Lloyd A, Janssen M, Kind P, Parkin D, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). Qual Life Res 2011 Dec;20(10):1727-1736 [FREE Full text] [doi: 10.1007/s11136-011-9903-x] [Medline: 21479777]
59. Groenvold M, Klee MC, Sprangers MA, Aaronson NK. Validation of the EORTC QLQ-C30 quality of life questionnaire through combined qualitative and quantitative assessment of patient-observer agreement. J Clin Epidemiol 1997 Apr;50(4):441-450. [Medline: 9179103]
60. Tennant R, Hiller L, Fishwick R, Platt S, Joseph S, Weich S, et al. The Warwick-Edinburgh Mental Well-being Scale (WEMWBS): development and UK validation. Health Qual Life Outcomes 2007 Nov 27;5:63 [FREE Full text] [doi: 10.1186/1477-7525-5-63] [Medline: 18042300]
61. Dunn N. Practical issues around putting the patient at the centre of care. J R Soc Med 2003 Jul;96(7):325-327 [FREE Full text] [Medline: 12835443]

Abbreviations

GP: general practitioner
HNA: holistic needs assessment
ICARE-P: integrated system to improve patient outcomes and experience
IT: information technology
NHS: National Health Service
NICE: National Institute for Health and Care Excellence
RCT: randomized controlled trial

Edited by G Eysenbach; submitted 10.03.17; peer-reviewed by A Guttilla, M Stanciu; comments to author 26.04.17; revised version received 07.05.17; accepted 08.05.17; published 28.07.17.

Please cite as:
Nanton V, Appleton R, Dale J, Roscoe J, Hamborg T, Ahmedzai SH, Arvanitis TN, Badger D, James N, Mendelsohn R, Khan O, Parashar D, Patel P
Integrated Care in Prostate Cancer (ICARE-P): Nonrandomized Controlled Feasibility Study of Online Holistic Needs Assessment, Linking the Patient and the Health Care Team
JMIR Res Protoc 2017;6(7):e147
URL: http://www.researchprotocols.org/2017/7/e147/
doi:10.2196/resprot.7667
PMID:28754653

Original Paper

Apps for Health-Related Education in Pharmacy Practice: Needs Assessment Survey Among Patients Within a Large Metropolitan Area

Sean M Mirk[1*], PharmD, PMCHI, BCACP; Nicole Marie Wegrzyn[1,2,3*], PharmD, BCACP

[1]Department of Pharmacy Practice, Chicago College of Pharmacy, Midwestern University, Downers Grove, IL, United States

[2]Department of Pharmacy Practice, Albany College of Pharmacy and Health Sciences, Albany, NY, United States

[3]CareMore Health Plan, Tucson, AZ, United States

[*]all authors contributed equally

Corresponding Author:
Sean M Mirk, PharmD, PMCHI, BCACP
Department of Pharmacy Practice
Chicago College of Pharmacy
Midwestern University
555 31st Street
Downers Grove, IL, 60515
United States
Phone: 1 630 515 7330
Fax: 1 630 515 6958
Email: smirk@midwestern.edu

Abstract

Background: Patient education resources are crucial to the effectiveness of prescribed pharmacotherapy. However, user interest and patient preference for these materials is lacking. Regardless of the field, nearly every article on designing mHealth apps references the lack of end-user involvement as a key flaw to sustainable design. The traditional paper-based methods of patient education are difficult to tailor to a patient's specific needs and learning styles, but a customizable app might be beneficial.

Objective: Regarding a mobile app for patient education, the objectives of the study were to (1) quantify patient interest, (2) determine desirable features, and (3) determine if a relationship exists between patient variables and interest in an iPad app for patient education.

Methods: A paper-based questionnaire was developed and administered to consenting patients receiving care within three sites: two suburban outpatient sites where ambulatory care services are provided and one urban hospital site where ambulatory care transition services are provided.

Results: A total of 121 surveys were completed. Most respondents were female (64/120, 53.3%), between 50 and 70 years of age, white/Caucasian (94/120, 78.3%), owned at least one technology device, and knew what an iPad was. Diabetes was the most common disease state (43/120, 35.8%), followed by heart failure (27/120, 22.5%), history of venous thromboembolism (VTE) (21/120, 17.5%), and asthma/chronic obstructive pulmonary disease (17/120, 14.2%). Overall interest in a mobile health app for patient education was 63.7% (72/113). Interest increased to 68.4% (78/114) if a health care provider recommended it. Respondents with one chronic health condition were more likely to be interested in an app compared to those with two or more. Respondents with a history of VTE were mostly likely to be interested in using an app on their own accord, while respondents with diabetes were mostly likely to be interested if their health care provider recommended it.

Conclusions: This preliminary needs assessment identified that patients are interested in using mHealth apps for health-related education in pharmacy practice, particularly if their health care provider recommends it.

(JMIR Res Protoc 2017;6(7):e133) doi:10.2196/resprot.5886

KEYWORDS

patient education; mHealth; health information management; user-centered design

Introduction

Mobile devices are growing increasingly popular. Based on recent data from Pew Internet Research surveys, 32% of adults in the United States own an e-reader, 42% own a tablet, and 64% own a mobile phone [1-2]. In the past year, a large majority (62%) of mobile phone users have used their phones to look up health information. Furthermore, a larger number of individuals access the Internet from a mobile device than from a traditional computer [3].

Earlier studies have examined the use of personal digital assistants (PDAs) for health care professionals and patients. Most studies utilized PDAs for journaling or data collection [4-6]. These early studies demonstrate the usefulness of a mobile device to support daily clinical activities and as a preferred method for diary entries by patients. Mobile devices today (eg, mobile phones and tablets) have advanced capabilities and provide greater functionality; this has created a boon in mobile health apps.

The latest published information shows there are around 165,000 mobile health apps available in major app stores [7]. Patient-centered mobile health apps target major disease states (eg, diabetes, asthma, heart failure, and chronic pulmonary disorders), promote wellness and healthy habits, provide information and education, allow for tracking of health information, promote engagement with health care providers, and leverage social influence [8,9]. The growth of mobile apps for health-related purposes will continue to increase as mobile devices become more ubiquitous [10].

Despite the number of mobile health apps available, mobile apps used in health care are in their infancy. The majority of mobile health apps researched for mHealth interventions have focused on behavioral changes and self-management. Review of mobile health apps for diabetes, smoking cessation, asthma, and sexually transmitted disease and HIV prevention indicate that most of the available apps do not follow established guidelines; these apps may have questionable reliability, may lack comprehensive information, and may not be personalized [11-14]. Additionally, mobile health apps are often developed without the end user (ie, the patient or health care provider) in mind [8,15-17]. It is also unclear whether or not patients would be interested in a mobile health app as a means for a health care service. Regarding a mobile app for patient education, the objectives of this study were to (1) quantify patient interest, (2) determine desirable features, and (3) determine if a relationship exists between patient variables and interest in an iPad app for patient education.

Methods

Setting

The three study sites offered clinical pharmacy services in the Chicago metropolitan area and included two suburban outpatient sites where outpatient ambulatory care services (OACS) are provided and one urban hospital site where hospital-based ambulatory care transition services (HATS) are provided. At the OACS sites, clinical pharmacists provide face-to-face medication therapy management to patients who have been referred by their primary care provider. The OACS sites were comprised of one private internal medicine physician group and one primary care office associated with a patient-centered medical home. At the HATS site, clinical pharmacists provide medication reconciliation and counseling to patients at discharge from the hospital. These patients are being discharged from inpatient treatment on a cardiac medicine floor or one of three internal medicine floors.

Patients were recruited by a sample of convenience. Patients under the age of 18 or for whom English is not their primary language were excluded from the study. Return of the completed survey indicated consent.

Survey Instrument

A paper-based questionnaire was developed and administered to consenting patients receiving care within the three predetermined sites. The survey was comprised of 19 multiple-choice questions and one open-ended question for general comments. The multiple-choice component included eight questions related to background demographic information, five questions related to technology use, and six questions related to interest in iPad apps and app features. Two of the questions related to technology were only to be answered by respondents who indicated that they own or proficiently use a tablet device or mobile phone. Some questions allowed respondents to “check all that apply.”

To ensure a standardized baseline level of knowledge, a laminated information card titled “What is an iPad?” was provided to the patient after the patient’s knowledge of an iPad was assessed. The iPad was chosen as a platform identifier that the general public was thought to be familiar with at the time the survey was conducted.

The survey was pilot-tested by a group of pharmacy faculty, refined, then pilot-tested by patients prior to distribution.

Statistical Analysis

A total of 120 surveys were to be administered, split evenly between OACS and HATS, in order to investigate the relationship between certain patient demographics and an interest in an iPad app. The total number of surveys was estimated based on collecting approximately 10 surveys per variable of interest.

The authors identified 12 variables of interest: diabetes, heart failure, asthma/chronic obstructive pulmonary disease (COPD), history of venous thromboembolism (VTE), perceived level of health, knowledge of what an iPad is, types of technology used, age, sex, race/ethnicity, level of education, and type of health insurance. Any answer that was left blank by the survey respondent was not included in the analysis.

Variables of interest were collapsed into categories and analyzed as follows: presence or absence of each of the chronic disease states (ie, diabetes, heart failure, history of VTE, asthma/COPD); perceived level of health (ie, positive—excellent, very good, good—or negative—fair, poor, very poor); knowledge of what an iPad is (ie, yes or no); use of technology (ie, computer, game consoles, mobile phone, tablet device, other portable electronic

device, none); age (ie, <40, 40-49, 50-59, 60-69, 70-79, >79); sex (ie, male, female, other); race/ethnicity (ie, American Indian or Alaskan Native, Asian/Pacific Islander, black/African American, Hispanic American, white/Caucasian, other); level of education (ie, high school or less, some college or associate degree, bachelor's degree or higher); and type of health insurance (ie, Medicare/Medicaid, other public, private [employer sponsored], private [individually purchased], self pay). Descriptive statistics for all parameters were reported.

Ad hoc analyses of variables included number of chronic disease states (ie, 1, 2, 3, 4+, 1+); number of technology devices owned (ie, 1, 2, 3, 4, 5, 3+); age (ie, <50, 50-70, >70); race/ethnicity (ie, white, nonwhite); and type of health insurance (ie, government sponsored, private, self-pay).

This study was designated exempt by the Midwestern University Institutional Review Board.

Results

Survey collection was complete with 121 collected surveys. Data collection began in December 2012 and ended in July 2013.

Demographics and Background Information

The mean age of all respondents was 63.7 years and the majority of respondents were between 50 and 70 years old. Less than half of the respondents identified as male (56/120, 46.7%). The most predominant self-identified race/ethnicity was white/Caucasian (94/120, 78.3%), followed by black/African American (11/120, 9.2%). Of the four chronic health conditions identified as variables of interest, diabetes was the most common (43/120, 35.8%), followed by heart failure (27/120, 22.5%), history of VTE (21/120, 17.5%), and asthma/COPD (17/120, 14.2%). Most of the respondents owned at least one technology device and knew what an iPad was.

OACS patients were more likely to have fewer chronic health conditions, a more positive perception of health, and a history of VTE. They were also more likely to identify as white/Caucasian (52/60, 87%) and male (32/60, 53%). HATS patients were more likely to have asthma/COPD, have completed a high school diploma or less, and be racially/ethnically diverse. Additional demographics of the survey respondents are outlined in Table 1.

Interest in mHealth Apps

Overall interest in a mobile health app for patient education was 63.7% (72/113). Interest increased to 68.4% (78/114) if a health care provider recommended it. Compared to the general study population, HATS patients were slightly more interested on their own accord (68%) and 75% of this population would use a mobile app if a health care provider recommended it. Regardless of the variable of interest and population, in most cases, the respondent's interest in a mobile app increased if a health care provider recommended it (see Table 2).

Based on number of chronic health conditions, respondents with one condition were most likely to be interested in an app. More than 60% of patients with at least one disease state of interest were interested in using an app. Respondents with a history of VTE were mostly likely to be interested in using an app on their own accord, while respondents with diabetes were mostly likely to be interested if their health care provider recommended it. As the respondent's perception of their health decreased, their interest in an app lessened.

Respondents who knew what an iPad was were more likely to be interested in using an app (73.1% vs 45.5%). Number of technology devices owned was directly proportional to interest in a mobile app. Of respondents who owned three or more devices, 95.8% would use a mobile app if their health care provider recommended it.

Compared to those aged <50 and >70 years, respondents who were 50-70 years old were most likely to be interested in a mobile app. The two age groups with the highest interest in apps were 60-69 years old (86.5%) and <40 years old (83.3%). No notable differences in interest were identified based on the respondent's sex. Respondents who identified as white were less likely to be interested compared to nonwhite respondents (60.9% vs 77.3%) and were less likely to use the app if it was recommended by a health care provider (65.5% vs 86.4%). A vast majority of patients with employer-sponsored or privately purchased insurance was interested in an app (78.4%) and would use it if their health care provider recommended it (81.1%).

Many of the same patterns in the overall population were consistent within the OACS and HATS populations. However, OACS respondents <50 years old were slightly more interested than were respondents 50-70 years old and those >70 years old. OACS respondents with a negative perception of health were more likely to be interested in an app, while the opposite was true for HATS patients. Respondents within the HATS populations who had one or two chronic conditions had a very high likelihood (>80%) of using an app if recommended by a health care provider.

Table 1. Interest in mHealth app stratified by demographic and clinical characteristics of 120 respondents.

Variable	Interested in an app, n (%)	Interested in an app if recommended by health care professional, n (%)
Number of diseases		
One (n=28)	19 (68)	21 (75)
Two (n=27)	18 (67)	15 (56)
Three (n=32)	20 (63)	23 (72)
Four or more (n=55)	35 (64)	40 (73)
One or more (n=109)	71 (65.1)	75 (68.8)
Chronic disease states		
Diabetes (n=40)	27 (68)	32 (80)
Heart failure (n=23)	16 (70)	14 (61)
History of VTE[a] (n=20)	15 (75)	14 (70)
Asthma/COPD[b] (n=22)	13 (59)	14 (64)
Perceived level of health		
Positive (n=77)	51 (66)	53 (69)
Negative (n=34)	20 (59)	23 (68)
Knowledge of an iPad		
Yes (n=78)	57 (73)	61 (78)
No (n=33)	15 (45)	16 (48)
Technology		
No devices (n=20)	8 (40)	7 (35)
One device (n=39)	22 (56)	23 (59)
Two devices (n=24)	20 (83)	21 (88)
Three or more devices (n=24)	20 (83)	23 (96)
Sex		
Male (n=54)	35 (65)	36(67)
Female (n=57)	37 (65)	41(72)
Age in years		
<50 (n=18)	13 (72)	14 (78)
50-70 (n=51)	39 (76)	14 (86)
>70 (n=40)	19 (48)	17 (43)
Race		
White (n=87)	53 (61)	57 (66)
Nonwhite (n=22)	17 (77)	19 (86)
Education		
High school diploma or less (n=32)	18 (56)	18 (56)
Associate degree or some secondary education coursework (n=42)	30 (71)	33 (79)
Bachelor's degree or more (n=34)	23 (68)	24 (71)
Type of insurance		
Government sponsored (n=64)	37 (58)	41 (64)
Employer sponsored or purchased (n=37)	29 (78)	30 (81)
Self-pay (n=8)	4 (50)	4 (50)

[a]VTE: venous thromboembolism.

[b]COPD: chronic obstructive pulmonary disease.

Table 2. Patient interest in a mobile app for patient education in pharmacy practice increased if recommended by a health care professional.

Population variable	Interested in an app, n (%)	Interested in an app if recommended by health care professional, n (%)
All respondents	72/113 (63.7)	78/114 (68.4)
HATS[a] (n=57)	39 (68)	43 (75)
OACS[b] (n=55)	33 (60)	34 (62)

[a]HATS: hospital-based ambulatory care transition services.

[b]OACS: outpatient ambulatory care services.

Table 3. Desirable methods for using a mobile health app for patient education (n=109).

Options	n (%)
I want my health care provider to use and demonstrate the app	37 (33.9)
I want to have access to the app at home	58 (53.2)
Both	22 (20.2)

Technology Use Preferences

A majority of respondents (81.3%) owned at least one device, which was always a computer. Of those that owned two devices, the second device was almost always a mobile phone; of those that owned three devices, the most common combination was computer, mobile phone, and tablet. Mobile phone and tablet users indicated that they use their devices at least daily (86.2%). The most common apps used were weather apps, search tool apps, and news apps. Health and fitness apps were used by 30.9% of mobile device owners.

When asked how they prefer to receive information about their health, 5.7% of respondents indicated software apps. Less than half the respondents have seen an iPad used in a health care setting.

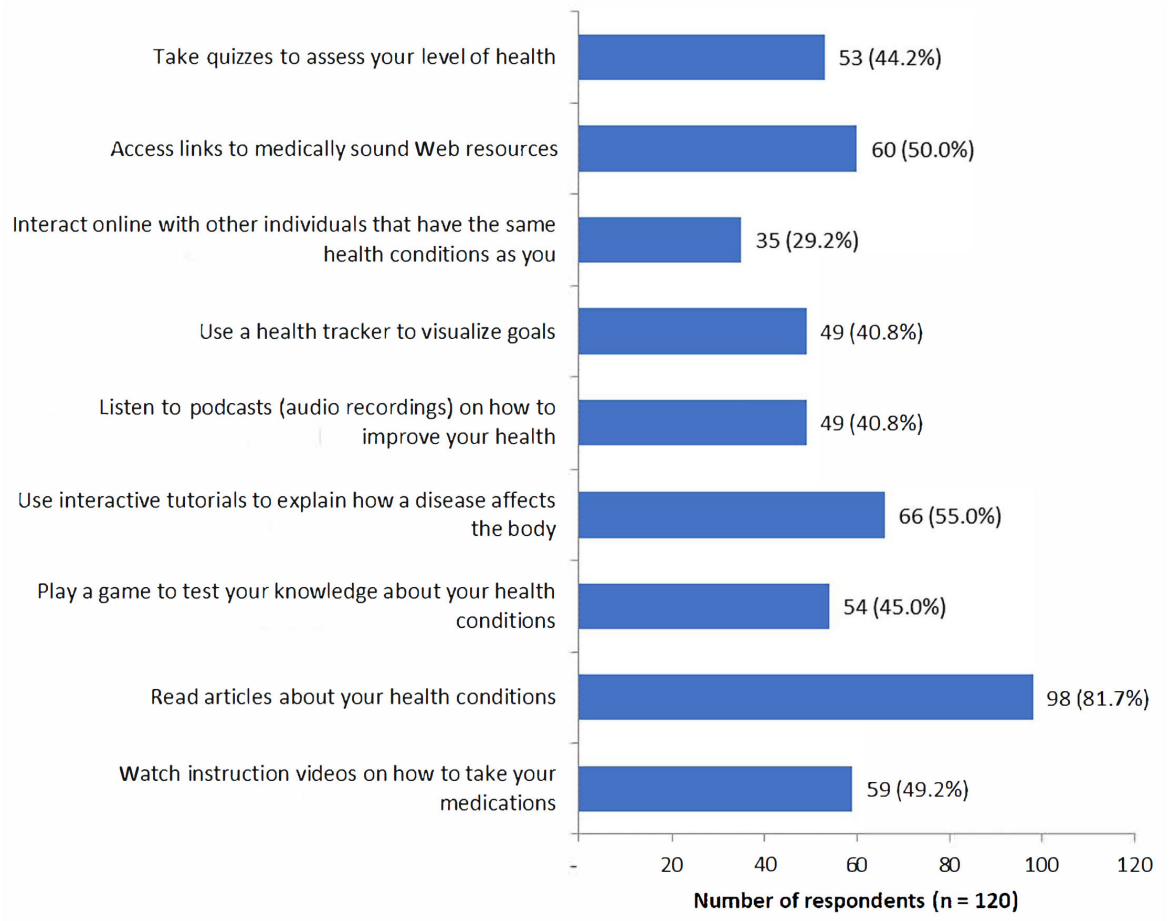
Regarding methods for using a mobile health app, the majority of respondents were more interested in having access to the app at home (58/109, 53.2%) compared to having the health care provider use and demonstrate the app (37/109, 33.9%); some patients would prefer both (22/109, 20.2%). Table 3 indicates the distribution of responses.

Respondents indicated an interest in a variety of health-related information, with the most common being information about the medications they are taking (see Table 4). The two most common methods to display information were articles with printed text (56/95, 59%) and images and diagrams (46/95, 48%), while the least common were podcasts and audio recordings (20/95, 21%).

Table 4. Types of information and methods to display information that patients would find beneficial in a mobile health app for patient education.

Information and methods of display	n (%)
Type of information (n=105)	
Medications	87 (82.9)
Health conditions	81 (77.1)
Lifestyle changes	58 (55.2)
Treatment options	68 (64.8)
Tools and resources to improve health	59 (56.2)
Methods to display information (n=95)	
Articles with printed text	56 (59)
Images and diagrams	46 (48)
Links to resources	41 (43)
Interactive tutorials	39 (41)
On-demand educational videos	27 (39)
Animation with narration	28 (30)
Podcasts or audio recordings	20 (21)

Figure 1. Actions respondents would be likely or very likely to take when using a mobile health app for patient education.



Respondents were also asked to identify their likelihood of performing various actions related to patient education as shown in Figure 1. Relevant comments written in response to the open-ended question included one comment asking for both Kindle and Blackberry software to be included.

Discussion

Principal Findings

Overall, a majority of respondents indicated that they were interested in a mobile app for patient education. Almost all patient variables indicated a large interest in an app. Interested respondents were younger, had some amount of secondary education, owned one or more devices, received private health care coverage, and had basic knowledge of an iPad. A digital divide grew as interest decreased dramatically for those over age 70, for those that do not own any mobile technology devices, and for those who pay for health care fully out of pocket (ie, self-pay).

Survey respondents were more likely to be interested in an app they could use at home versus a provider-driven, point-of-care app. A similar percentage of those who reported seeing a health care provider use an iPad were interested in an app at the point of care. This interest may increase as exposure to mobile technology increases. Concurrently, there may be an increased expectation from patients for health care providers to use mobile apps when providing care to patients.

If a health care provider recommended an app, there was an almost universal increase in interest. Power, size, portability, built-in features, access to the Internet, social and communication tools, personal affection, and a large marketplace makes using a mobile app for patient education attractive to patients [9]. These factors increase a health care professional's abilities to provide point-of-care or just-in-time services to patients, both in practice settings and remotely. This would also support the notion of app prescribing.

A potential starting place for health care providers to introduce mHealth apps into patient care is recommending specific apps to patients that they can access on their own device at any time. Health care providers may choose to target certain populations, such as younger patients with one chronic health condition and a positive perception of health, in deciding to whom they should recommend mHealth apps. Apps may not be best suited for patients with a preference for personal consultation from their provider, approximately a third of patients over 55 [18].

It is interesting to note that the perception of health influenced an interest in app technology in different ways based on the type of health care setting of the respondent. Ambulatory patients in primary care settings were more likely to be interested if they had a negative perception of their health. These individuals with poor health and many chronic conditions are usually the most vulnerable and tend to require extensive patient education. On the other hand, patients who were about to be discharged from the hospital, who had a positive perception of

health and only one chronic condition, were more likely to be interested in mobile apps for health-related information. Discharge counseling at this point in time is crucial for many patients because they are likely to be more receptive to information to promote a healthy lifestyle, prevent disease progression, and avoid readmission. Utilization of apps among these types of patients at discharge from the hospital may be beneficial.

When asked about what types of information they would find beneficial, respondents indicated that they want more information in a wide variety of areas and formats. We believe that this suggests that options for app developers are bountiful. Interestingly, respondents indicated most frequently that they are interested in articles, printed text, images, and diagrams as delivery methods for medical information. Use of these delivery methods for educating patients has been common practice for years. We wonder if this was due to familiarity and, furthermore, wonder if many of the respondents knew what podcasts and audio recordings are. With more education as to what podcasts and audio recordings are, patients may potentially be more interested in these as delivery methods within mobile apps for health-related information.

Limitations

The focus of the survey specifically on the iPad device may limit our ability to generalize this data to other mobile technology devices and mHealth apps. Additionally, the survey was conducted early in the adoption of the tablet devices. We chose to focus solely on the iPad as investigators felt it was the most recognizable mobile device on the market; inclusion of other devices could have confused patients, especially those that were not familiar with tablet devices and would have required an explanation of other tablet devices. Respondents who may be interested in receiving education through the use of other devices may not have identified an interest in the use of the iPad. There were several comments to this effect that were relayed verbally to the survey administrator, who is the primary author. We suspect that interest in the use of an iPad, or any tablet device, would not have decreased from the time that this study was conducted.

Of the surveyed population, approximately one-third did not know what an iPad was. For some of these respondents, the laminated information card could have provided enough information to trigger the respondent's memory. For other respondents that may not have ever encountered an iPad, it is possible that some of them may not have been able to conceptualize the device, even despite reading the description and viewing the life-size picture. Demonstrating the use of an iPad device and/or app to respondents was assessed during survey development, but ultimately was not utilized due to feasibility.

One question in particular was designed to provide app developers with more insight into what patients want in an app for patient education, as this has been suggested to be an important aspect of the design process [16]. Unfortunately, there was a low response rate for this question. The low response rate was likely due to the fact that the question was asked in a matrix and patients did not understand the format. With the data that we have, we are able to suggest some areas for app development based on the likelihood that patients would use certain features, but future research in this area is warranted.

The patient populations of each site are uniquely different and cover a broad range of demographics; therefore, inherent bias exists. Additionally, the study utilized a sample of convenience, as patients were not randomly selected. OACS patients report to clinic for appointments with clinical pharmacists. Those who adhere to appointments may be more likely to want additional education, though this survey was not conducted in a manner to assess this thought. Patients who did not show up for appointments were not able to complete a survey. Thus, the population of patients surveyed may not represent the entirety of the OACS patient population.

The population of survey respondents at HATS may have included some patients who were not actually discharged from the hospital setting. We made every attempt to capture patients that were ambulant and had a high likelihood of being discharged from the hospital. However, the clinical status changed for some of the patients and they continued to be hospitalized after survey completion. Surveys were deidentified and we were not able to exclude patients who were not discharged. It is notable that being hospitalized was not specifically addressed as an exclusion criterion for this study. Including surveys from a broad patient population in different health care settings may affect the homogeneity of the respondents, but it may also strengthen the results by reflecting the diverse opinion(s) patients have.

Strengths and Future Research

One of the strengths of this study is that it included patients who previously did not know what an iPad was. Despite this lack of prior knowledge, many of these respondents indicated an interest in obtaining health-related information via mobile apps. This counters a preconceived notion that those who are older and may not have used mobile devices or know what one is will be less likely to want to learn in this way.

Additionally, the responses suggested that patients would use apps for education if their health care providers recommended them. Given this data, providers should be guiding patients to resources. Health care professionals in primary care and transition-of-care settings should carefully weigh the pros and cons of utilizing this technology with their patients.

Despite patient interest and known benefits of patient education for chronic disease, not much is known regarding the utility of mHealth apps for patient education. Published studies assessing the impact of mHealth apps on clinically relevant health outcomes are limited. However, early data show promise [19-21].

Future areas of research include looking further into the desirable features of apps for patient education. Investigators and developers need to include patients and health care providers in this area of research. With more data in this area, it will be possible to develop and utilize an app for educational interventions that is tailored to a patient and/or a health care provider and that impacts health outcomes.

Conclusions

Interest in an mHealth app for patient education is high, regardless of patient variables. A health care provider's recommendation may increase the likelihood of a patient using an app. This emphasizes the need to develop evidence-based, medically sound, and reliable mobile apps that both patients and pharmacists can use and trust.

Acknowledgments

The authors would like to recognize Jill S Borchert, PharmD, BCPS, FCCP, for her contributions to protocol development, survey tool refinement, and manuscript editing.

Conflicts of Interest

None declared.

References

1. Zickuhr K, Rainie L. Pew Research Center. Washington, DC: Pew Internet & American Life Project; 2014 Jan 16. E-reading rises as device ownership jumps URL: http://www.pewinternet.org/files/2014/01/PIP_E-reading_011614.pdf [accessed 2017-05-19] [WebCite Cache ID 6qZvsgAkH]
2. Smith A, Page D. Pew Research Center. Washington, DC: Pew Internet & American Life Project; 2015 Apr 01. US smartphone use in 2015 URL: http://www.pewinternet.org/files/2015/03/PI_Smartphones_0401151.pdf [accessed 2017-05-19] [WebCite Cache ID 6qZw0ulnG]
3. Digital Government: Building a 21st Century Platform to Better Serve the American People. Washington, DC: The White House; 2012 May 23. URL: http://www.federalnewsradio.com/wp-content/uploads/pdfs/whitehousedigitalstrategy.pdf [accessed 2017-05-20] [WebCite Cache ID 6qbObgjG8]
4. Dale O, Hagen KB. Despite technical problems personal digital assistants outperform pen and paper when collecting patient diary data. J Clin Epidemiol 2007 Jan;60(1):8-17. [doi: 10.1016/j.jclinepi.2006.04.005] [Medline: 17161749]
5. Fischer S, Stewart TE, Mehta S, Wax R, Lapinsky SE. Handheld computing in medicine. J Am Med Inform Assoc 2003;10(2):139-149 [FREE Full text] [Medline: 12595403]
6. Lane SJ, Heddle NM, Arnold E, Walker I. A review of randomized controlled trials comparing the effectiveness of hand held computers with paper methods for data collection. BMC Med Inform Decis Mak 2006;6:23 [FREE Full text] [doi: 10.1186/1472-6947-6-23] [Medline: 16737535]
7. The Economist. 2016 Mar 10. Things are looking app URL: http://www.economist.com/news/business/21694523-mobile-health-apps-are-becoming-more-capable-and-potentially-rather-useful-things-are-looking [accessed 2017-05-19] [WebCite Cache ID 6qZw3tplV]
8. Jahns RG. Research2Guidance. The market for mHealth app services will reach $26 billion by 2017 URL: http://www.research2guidance.com/the-market-for-mhealth-app-services-will-reach-26-billion-by-2017/ [accessed 2017-05-19] [WebCite Cache ID 6qZw52G66]
9. Demiris G, Afrin LB, Speedie S, Courtney KL, Sondhi M, Vimarlund V, et al. Patient-centered applications: Use of information technology to promote disease management and wellness. A white paper by the AMIA knowledge in motion working group. J Am Med Inform Assoc 2008 Feb;15(1):8-13 [FREE Full text] [doi: 10.1197/jamia.M2492] [Medline: 17947617]
10. Klasnja P, Pratt W. Healthcare in the pocket: Mapping the space of mobile-phone health interventions. J Biomed Inform 2012 Feb;45(1):184-198 [FREE Full text] [doi: 10.1016/j.jbi.2011.08.017] [Medline: 21925288]
11. Frost & Sullivan. 2012 Jan 05. Unlocking the door to mobile health app opportunities URL: http://www.frost.com/prod/servlet/press-release.pag?docid=250559977 [accessed 2017-05-19] [WebCite Cache ID 6qZw6WlBr]
12. Abroms LC, Padmanabhan N, Thaweethai L, Phillips T. iPhone apps for smoking cessation: A content analysis. Am J Prev Med 2011 Mar;40(3):279-285 [FREE Full text] [doi: 10.1016/j.amepre.2010.10.032] [Medline: 21335258]
13. Chomutare T, Fernandez-Luque L, Arsand E, Hartvigsen G. Features of mobile diabetes applications: Review of the literature and analysis of current applications compared against evidence-based guidelines. J Med Internet Res 2011;13(3):e65 [FREE Full text] [doi: 10.2196/jmir.1874] [Medline: 21979293]
14. Huckvale K, Car M, Morrison C, Car J. Apps for asthma self-management: A systematic assessment of content and tools. BMC Med 2012;10:144 [FREE Full text] [doi: 10.1186/1741-7015-10-144] [Medline: 23171675]
15. 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;15(1):e1 [FREE Full text] [doi: 10.2196/jmir.2301] [Medline: 23291245]
16. McCurdie T, Taneva S, Casselman M, Yeung M, McDaniel C, Ho W, et al. mHealth consumer apps: The case for user-centered design. Biomed Instrum Technol 2012 Sep;Suppl:49-56 [FREE Full text] [doi: 10.2345/0899-8205-46.s2.49] [Medline: 23039777]

17. van Gemert-Pijnen JE, Nijland N, van Limburg M, Ossebaard HC, Kelders SM, Eysenbach G, et al. A holistic framework to improve the uptake and impact of eHealth technologies. J Med Internet Res 2011;13(4):e111 [FREE Full text] [doi: 10.2196/jmir.1672] [Medline: 22155738]
18. SlideShare. London, UK: Ruder Finn Healthcare Technology 2012 mHealth report URL: https://www.slideshare.net/ruderfinnuk/ruder-finn-mhealth-report-2012 [accessed 2017-05-19] [WebCite Cache ID 6qZw9kuEJ]
19. Powell AC, Landman AB, Bates DW. In search of a few good apps. JAMA 2014 May 14;311(18):1851-1852. [doi: 10.1001/jama.2014.2564] [Medline: 24664278]
20. Fiordelli M, Diviani N, Schulz PJ. Mapping mHealth research: A decade of evolution. J Med Internet Res 2013;15(5):e95 [FREE Full text] [doi: 10.2196/jmir.2430] [Medline: 23697600]
21. Lowres N, Neubeck L, Salkeld G, Krass I, McLachlan AJ, Redfern J, et al. Feasibility and cost-effectiveness of stroke prevention through community screening for atrial fibrillation using iPhone ECG in pharmacies. The SEARCH-AF study. Thromb Haemost 2014 Jun;111(6):1167-1176. [doi: 10.1160/TH14-03-0231] [Medline: 24687081]
22. Wicklund E. MobiHealthNews. 2014 Jun 11. ACO reaping mHealth benefits already URL: http://www.mobihealthnews.com/news/aco-reaping-mhealth-benefits-already-accountable-care-mobile-health [accessed 2017-05-20] [WebCite Cache ID 6qbR5Sypp]

Abbreviations

COPD: chronic obstructive pulmonary disease
HATS: hospital-based ambulatory care transition services
OACS: outpatient ambulatory care services
PDA: personal digital assistant
VTE: venous thromboembolism

Edited by G Eysenbach; submitted 19.04.16; peer-reviewed by A Powell, L Fernandez-Luque; comments to author 27.07.16; revised version received 15.11.16; accepted 27.02.17; published 19.07.17.

Please cite as:
Mirk SM, Wegrzyn NM
Apps for Health-Related Education in Pharmacy Practice: Needs Assessment Survey Among Patients Within a Large Metropolitan Area
JMIR Res Protoc 2017;6(7):e133
URL: http://www.researchprotocols.org/2017/7/e133/
doi:10.2196/resprot.5886
PMID:28724511

Original Paper

MotivATE: A Pretreatment Web-Based Program to Improve Attendance at UK Outpatient Services Among Adults With Eating Disorders

Sarah Muir[1], BA (Hons), PhD; Ciarán Newell[2], BA (Hons), PhD; Jess Griffiths[3], MBACP Dip.Counselling; Kathy Walker[4], BSc (Hons); Holly Hooper[5], BA(Hons), PGDip; Sarah Thomas[6], BSc (Hons), PhD; Peter W Thomas[6], BSc (Hons), PhD; Jon Arcelus[7], LMS, MSc, MRCPsych, PhD; James Day[5], BSc (Hons), MSc; Katherine M Appleton[5], BSc., PhD

[1]Bournemouth University, Psychology Department, Poole, United Kingdom

[2]Dorset Healthcare University NHS Foundation Trust, Poole, United Kingdom

[3]i*feel Organisation, Poole, United Kingdom

[4]Patient Safety, University Hospital Coventry and Warwickshire, Coventry, United Kingdom

[5]Research Centre for Behaviour Change, Psychology Department, Bournemouth University, Poole, United Kingdom

[6]Bournemouth University Clinical Research Unit, Faculty of Health and Social Sciences, Bournemouth, United Kingdom

[7]Institute of Mental Health, Nottingham University, Nottingham, United Kingdom

Corresponding Author:
Sarah Muir, BA (Hons), PhD
Bournemouth University
Psychology Department
Poole House, Talbot Campus
Fern Barrow,
Poole, BH12 5BB
United Kingdom
Phone: 44 01202961561
Fax: 44 01202965314
Email: swilliams@bournemouth.ac.uk

Abstract

Background: In the UK, eating disorders affect upward of 725,000 people per year, and early assessment and treatment are important for patient outcomes. Around a third of adult outpatients in the UK who are referred to specialist eating disorder services do not attend, which could be related to patient factors related to ambivalence, fear, and a lack of confidence about change. This lack of engagement has a negative impact on the quality of life of patients and has implications for service costs.

Objective: To describe the development of a Web-based program ("MotivATE") designed for delivery at the point of referral to an eating disorder service, with the aim of increasing service attendance.

Methods: We used intervention mapping and a person-based approach to design the MotivATE program and conducted a needs assessment to determine the current impact of service nonattendance on patients (via a review of the qualitative evidence) and services (through a service provision survey to understand current issues in UK services). Following the needs assessment, we followed the five steps of program development outlined by Bartholomew et al (1998): (1) creating a matrix of proximal program objectives; (2) selecting theory-based intervention methods and strategies; (3) designing and organizing the program; (4) specifying adoption and implementation plans; and (5) generating program evaluation plans.

Results: The needs assessment identified current nonattendance rates of 10%-32%. We defined the objective of MotivATE as increasing attendance rates at an eating disorder service and considered four key determinants of poor attendance: patient ambivalence about change, low patient self-efficacy, recognition of the need to change, and expectations about assessment. We chose aspects of motivational interviewing, self-determination theory, and the use of patient stories as the most appropriate ways to enable change. Think-aloud piloting with people with lived experience of an eating disorder resulted in positive feedback on the MotivATE program. Participants related well to the stories used. Nonetheless, because of feedback, we further modified the program in line with patients' stage of change and addressed issues with the language used. A consultation with service staff

meant that we could make clear implementation plans. Finally, a randomized controlled trial is currently underway to evaluate the MotivATE program.

Conclusions: Using intervention mapping, we have developed a novel pretreatment Web-based program that is acceptable to people with eating disorders. To our knowledge, this is the first such program. The model of development described here could be a useful template for designing further programs for other difficult-to-engage populations.

(JMIR Res Protoc 2017;6(7):e146) doi:10.2196/resprot.7440

KEYWORDS

Program Development; Program Evaluation; Internet; Patient Acceptance of Health Care; Assessment, Process; Feeding and Eating Disorders; Anorexia Nervosa; Bulimia Nervosa; Binge Eating Disorder

Introduction

Eating disorders (including anorexia nervosa, bulimia nervosa, other specified feeding or eating disorder, and binge eating disorder) have a prevalence rate of 1 in 600,000–725,000 people in the UK, affecting up to 6.4% of adults at any time [1,2]. These disorders are typically characterized by people over-evaluating themselves based on their weight and shape or by people engaging in eating behaviors as a mechanism for coping with difficult emotions or relationships [3,4]. Eating disorders have the highest mortality rate of all mental health conditions [5], and the number of affected individuals being diagnosed and admitted to inpatient care in the UK has been increasing by 7% each year since 2009 [2]. Early assessment and intervention are essential for patient outcomes [6,7] and the quality of life of patients and their carers [1], but it is reported that as many as 44% of people with eating disorders do not access mental health care treatment for their eating disorder [8].

After a person in the UK initially seeks help for his or her eating disorder (eg, from primary care), he or she is usually referred to a specialist eating disorder service for an initial assessment appointment. However, research highlights that up to a third of people referred for specialist psychological treatment do not access the services and that 16.4% of these people simply do not attend their first scheduled assessment appointment [9]. Reasons for this lack of engagement may include having had an eating disorder for a long time; laxative abuse; and symptoms of depression, substance abuse, or borderline personality disorder but predictors of nonattendance are still relatively unknown, as current quantitative studies report extremely low sample sizes [10]. Other barriers to psychological treatment may include stigma, poor mental health literacy, a perceived lack of a need for treatment, unhelpful past experiences with treatment, a fear of change, low motivation to change, service restrictions, and cost [11]. Aiming to address some of these barriers to psychological care, we have developed MotivATE, a Web-based, motivation enhancement-focused program that specifically seeks to improve patient engagement at the initial assessment appointment, that is, at the point that a person is referred to an eating disorder service. This paper describes the development of this program.

Methods

We developed the MotivATE program using intervention mapping, which recognizes three phases of program development: needs assessment, program development, and evaluation [12]. As recommended by Bartholomew et al [12], our development team included developers (researchers at the university; SM, KA, KW, JD, ST, and PT), implementers (consultants working within adult eating disorder services; CN and JA), and prospective program participants (people with lived experience of having and recovering from an eating disorder; JG and HH). We also used a person-based approach to develop MotivATE to ensure that the user experience was at the heart of each stage of intervention development [13]. As highlighted in the introduction, there are a number of personal barriers to engagement with specialist services for people with eating disorders; therefore, it was essential that we had a deep understanding of their experience and needs to increase the likelihood that the intervention would be relevant, acceptable, and useful for our target group.

Needs Assessment

The aims of the needs assessment were to understand the problem of nonattendance at adult eating disorder services and to consider both patients' personal barriers and service-level barriers that the program would need to address. In line with the person-based approach, our first step was to review our own qualitative research with people who described themselves as not wanting to receive treatment for an eating disorder [4] and those who described themselves as in recovery [14,15], as these cases were the source of the idea for the program. Thus, we considered this work alongside other published work relating to patients' experiences of having an eating disorder and attending treatment. To understand the impact of nonattendance at specialist eating disorder services, we also conducted a telephone-based service provision survey with four lead consultants for outpatient services in the UK. The survey questions consisted of a mix of close-ended and open-ended questions and asked about the number of referrals, the number of patients who did not attend an assessment appointment, and the processes used to try to engage patients. The survey study received university ethics approval, and each service gave verbal consent to use of its data.

Program Development and Evaluation

Bartholomew et al [12] outline five steps of program development, and we detail these below, along with a description of the methods used to implement the steps.

1. Creating a Matrix of Proximal Program Objectives

The needs assessment, team discussions, and consultations with eating disorder-focused charities enabled us to determine (a) the objectives of the program, (b) the behaviors that potential users needed to engage in, (c) the factors (or determinants) influencing these behaviors, and (d) the target population (and any subgroups) who would use the program.

2. Selecting Theory-Based Intervention Methods and Practical Strategies

We reviewed the current theory related to increasing motivation to change, including the current evidence relating to eating disorders, and then considered practical strategies for implementing this theory. As per the person-based approach, this enabled us to develop guiding principles for the design of the program [13].

3. Designing and Organizing a Program

The team designed the structure and content of the intervention during team meetings, and we used open-source LifeGuide software to create the MotivATE platform [16]. We started with a booklet already devised by CN and JG that aimed to help people think about the recovery process, as this was already well received by existing service users. This booklet was based on motivational activities commonly used to improve motivation to change. We adapted it to (a) address some of the barriers to engagement identified in the needs assessment stage and incorporate the language and style of a person-based approach, (b) incorporate new knowledge gained from revisiting motivational theory, (c) better address the program aims (ie, to be specifically about attending an assessment appointment, rather than about beginning therapy), and (d) enhance usability via a Web-based platform (increasing interactivity with videos, quizzes, and click-throughs) and enable tailoring based on the person's stage of change. We also adapted the content based on our evaluation of the program (see below).

People with experience of an eating disorder then qualitatively evaluated our initial prototype of the program via think-aloud interviews to understand beliefs about the relevance, acceptability, and usability of the program [17]. We recruited participants from the university and a local eating disorder-focused charity via advertisements asking for people with experience of an eating disorder to evaluate a web program aimed at preparing people for their assessment, resulting in an opportunity sample of 12 participants (5 with binge eating disorder (4 female, 1 male), 4 with anorexia nervosa (1 male, 3 female), 2 with bulimia nervosa (both female), and 1 with an eating disorder not otherwise specified (female)). The think-aloud interviews followed an unstructured approach and asked participants to verbalize their thoughts as they occurred. Participants were asked to think back to when they were referred to an eating disorder service and to think aloud as they used the program. The researcher could then observe in-the-moment reactions to the program and used prompts (such as "What are you thinking about now?" or "Can you please explain why you chose to click on that option?") to encourage participants' verbalization and to understand their experience of the program. We subsequently used participant feedback to modify the program to make it more acceptable and relevant for program users.

4. Specifying Adoption and Implementation Plans

This phase involved making plans for the delivery of the program: two team members demonstrated the program to staff at a local eating disorder service that was typical of outpatient services across the UK and invited feedback about implementation.

5. Generating Program Evaluation Plans

The final stage of the intervention mapping described by Bartholomew et al [12] is to generate plans to evaluate the program.

Results

Needs Assessment

Literature Review

The idea to develop a program to address attendance at psychological services for eating disorders originated from previous qualitative research conducted by the authors [4,14-15]. Qualitative studies examined people who wished to maintain their eating disorder [4] and those who wished to recover [14,15] to understand their lived experience of having an eating disorder and attending treatment. The results from both types of studies identified the extreme ambivalence that people with eating disorders experience: people with eating disorders can perceive their eating disorder to be a coping mechanism, and at the same time recognise its consequence on their health, their family, and their future lives. Other qualitative research has also identified this ambivalence [18-21]. Ambivalence is a "natural phase in the process of change," but it can cause patients to get stuck in a phase of inaction, and therefore negatively impact treatment engagement [22]. People with eating disorders also experience barriers to recovery, including low self-efficacy and (often inaccurate) preconceived expectations of what treatment could entail [4,14,20]. Leavey et al [21] conducted qualitative interviews with 13 people with eating disorders who did not attend an assessment appointment. Underlying participants' experiences was an ambivalence about change that ultimately stopped them from attending their appointment. Participants also reported feelings of mistrust of health professionals, dissonance between their own and professional views of the disorder, fear of abandonment, comorbid mental health issues, previous negative experiences with services, misguided expectations, stigma about mental health services, and long waiting times as barriers to attendance. Although initiatives exist to improve service attendance in general health care (eg, appointment reminders or the use of opt-in systems where a person is invited to make an appointment), they can deter people who are already known to be more difficult to engage [23-25]. Given the ambivalence that many people with eating disorders experience, an intervention to improve service attendance needs to enhance autonomous motivation to change through active behavioral change techniques. Here, we chose a Web-based approach, as it would be less resource intensive for the service and more acceptable to patients who would not need to approach the service directly.

Service Provision Survey

Waller et al [9] reported a nonattendance rate of 16.4% in 2 South London services; we wanted to determine to what extent this was an issue in services across the UK. We sent email invitations to 9 services, and 4 (1 from the South of England, 2 from Central England, and 1 from the North) took part. Reasons for nonparticipation included a lack of time and/or a lack of useful audit data. Table 1 presents the results from the survey. Of those who were suitable for an assessment appointment, between 10% and 32% did not attend. Similar to published research [24,25], these results suggest that the use of opt-in systems to try to improve engagement may actually increase the number that do not attend.

Table 1. Results of the service provision survey relating to nonattendance rates and the assessment appointment process for 2013.

	Service 1	Service 2	Service 3	Service 4
Description of assessment appointment process	Contact by telephone, then send appointment letter with date and time	Send appointment letter with date and time	Opt-in process via letter. Patient to contact service within 2 weeks	Opt-in process via letter. Patient to contact service within 2 weeks
Resources provided before assessment	Map to service	Outcome measures packet	Some monitoring or dietician advice if advised by clinician	Outcome measures packet, information about service, map to service, questions about demographics
Average length of wait (referral to assessment)	14 days	2.5 months	Not reported	34 days
n suitable for outpatient assessment (in the year 2013)	172	135	153	352
n did not opt in[a] (% of suitable referrals)	N/A	N/A	24 (16)	86 (24)
n suitable outpatient referrals who did not attend appointment (% of suitable referrals)	33 (19)	14 (10)	25 (16)	16 (5)
Total who did not attend first assessment appointment (%)	33 (19)	14 (10)	49 (32)	102 (29)

[a]The number that did not schedule an appointment when invited to

Program Development and Evaluation

Creating a Matrix of Proximal Program Objectives

The main objective of the program is to "increase attendance at an eating disorder service". In contrast to the opt-in process detailed above, which simply asks patients to make an appointment at a convenient time, the MotivATE approach aims to increase attendance rates by fostering personal intrinsic motivation and increased self-efficacy to attend while addressing negative beliefs and expectations about the service. The target population for the program was all adults who have been referred to an outpatient eating disorder service for an assessment appointment. People in the UK are usually referred to an eating disorder service by their general practitioner, although there are other routes to treatment, depending on the structure of the local service model. Some services allow referral by any health or social care professional, and others welcome the person to refer himself or herself. Clinicians at the service review the referral letter to determine the next steps, guided by the urgency of referral, risks, etc. When the person is suitable for outpatient treatment (eg, there are no immediate risks requiring a higher level of care), the service will contact the person to invite him or her for an assessment appointment (eg, to assess eating disorder behaviors and symptoms and the need and motivations for treatment and to collaboratively develop a treatment plan). The wait times for the assessment appointment are different across the UK, ranging from 4 weeks to 6 months. It is when inviting the person for assessment that we intend to include the invitation to use MotivATE.

People who have been referred to the service may be in one of three of the five stages of change [26]. First, patients may be in the precontemplation stage of change; that is, they may not believe that they have an eating disorder and are not intending to change. Second, many are likely to be in the contemplation stage; they may be aware of the pros and cons of change but highly ambivalent about doing so. Third, those in the preparation stage may have plans to change within the next month but may not have high enough confidence (or self-efficacy) to do so. The last two stages of change include the action stage (those who have been making changes in the last 6 months) and the maintenance stage (those who have made a change and are working to prevent relapse). People in these two stages would not be target users of the program, as they are likely to be already engaging with a treatment program. Table 2 provides details of how theses stages of change could impact program requirements.

Table 2. Subgroups of potential program users.

Subgroup	Distinction	Implications for performance objectives	Example of performance objectives
Precontemplation	Not considering changing eating disorder and/or may not believe they have an eating disorder	Least likely to attend an assessment; require education about eating disorders and stories from others to start recognizing own problematic behaviors	Starting to recognize eating disorder experience and becoming educated about the cons of the disorder
Contemplation	Extremely ambivalent group; may be swaying between attending and not attending	Ambivalence is a salient determinant	Weighing pros and cons of change and addressing ambivalence
Preparation	Accept a need for change but may not have high enough confidence to do so	Low self-efficacy is an important determinant	Feel more confident about ability to change, think about assessment and what to expect, and prepare to attend

Table 3. Program objectives for MotivATE.

Performance objective	Determinants			
	Ambivalence about change	Self-efficacy	Recognition of need to change	Expectations about assessment
Attend assessment appointment	Recognize ambivalence but attend to learn more	Feel confident and in control of assessment appointment	Recognize possible need to change and attend to learn more	Have realistic expectations of what is involved at the assessment appointment

The needs assessment and the identification of the target group enabled us to ascertain four main determinants that the program needed to address: (1) patient ambivalence about change, (2) low patient self-efficacy, (3) recognition of the need to change, and (4) expectations about assessment. This resulted in the final matrix of proximal program objectives outlined in Table 3.

Selecting Theory-Based Intervention Methods and Practical Strategies

The main objective of the program is to increase motivation to attend an assessment appointment. Motivational therapies are advocated in the treatment of eating disorders [27] and are effective at improving motivation to change [28-30]. These interventions are based on or closely adapted from the principles of motivational interviewing [22,31,32] and involve addressing and working through ambivalence and initiating "change talk" from patients, encouraging them to make choices that fit with their own goals and values. Specifically, psychoeducation, examining the pros and cons of symptoms, experimental strategies, and exploring personal values are four methods proposed to help ambivalent eating disorder patients move through the stages of change [33]. A service traditionally delivers these methods face to face once a person has engaged with the service, but there is growing evidence for Web-based delivery [34,35] and for offering intervention prior to engagement among those with eating disorders [36].

We also drew on self-determination theory (SDT) for the intervention, which is in keeping with the person-based approach. SDT recognizes that human behavior centers on three innate needs: autonomy, competence, and relatedness [37]. People need to feel in control and autonomous to be able to internalize behavioral change and perceive it as important to their own values and goals. Choice is particularly important to patients with eating disorders, who may fear that control will be taken away from them during treatment [18,38]. It may also have a direct impact on service engagement. Indeed, when people with eating disorders referred for inpatient treatment had full choice (even including whether they would stay at all), they were less likely to drop out of treatment [39]. Competence refers to the person's self-efficacy or confidence to perform the behavioral change. Relatedness refers to the person's ability to relate to others and foster supportive relationships. As in motivational interviewing, the clinician's role, per SDT, is to provide supportive autonomy by encouraging patients to take the lead in making a change and to help them to internalize recognition of change as an important goal for themselves [40]. In MotivATE, we relied on video and written accounts of people's experiences and success stories of attending an assessment appointment (also known as narrative communication [41]) to enhance a sense of relatedness and to address the four determinants of the program (increase recognition of the need to change, increase self-efficacy, address expectations, and address ambivalence). For example, people could recognize their own situation in the stories (increase recognition), and reading success stories from others can increase self-efficacy and the intention to change [42].

The program objectives highlighted in the previous stage and the examination of theory and practical strategies allowed us to develop guiding principles, outlined by the person-based approach, for the program (Table 4).

Table 4. Guiding principles for MotivATE.

Intervention design objectives	Key feature(s)
To be delivered before any formal contact with the service and to address expectations about assessment (ie, address the question of "What will they *do* to me?")	Provide a digital intervention with education about service and assessment through interactive quizzes and stories about others' experiences
To address and acknowledge ambivalence and to enhance or maintain motivation to attend	Build autonomous motivation, address patients' mixed feelings about change and link change to their own personal goals and values, tailor program to stages of change, provide psychoeducation about eating disorders, and highlight choice that person can make during program and when they attend assessment
To increase self-efficacy and to help patients to make their own decisions	Develop intervention user's competence through user stories

Table 5. The content of the MotivATE program.

Module	Aim	Content
1. What happens at the first appointment?	Address expectations about the assessment appointment	Provides an interactive quiz to explore common misconceptions about assessment, information about the assessment appointment, and stories and videos about others' experiences.
2. How motivated are you?	Introduce the idea of change	Introduces people to the stages-of-change model with stories of others' experiences. Person can choose his or her stage of change.
3. Arming yourself with information	Help people to recognize problematic behaviors (precontemplation) and address ambivalence	Provides information about the pros and cons of eating disorders. Those who have selected the contemplation or preparation stage of change can complete their own tables of pros and cons and complete exercises designed to address ambivalence.
4. Preparing for your assessment	Improve confidence to attend	Includes a video of a clinician welcoming people to the assessment, and users can make plans to attend their appointment.

Designing and Organizing a Program

We aimed to present a professional-looking, gender- and age-neutral program. The color scheme is blue and white, and images are based on nature, with the intention of depicting positive well-being (see Figure 1). No images of people or food are included, as we do not want the program to negatively influence people or to cause them to compare their body shape or eating behaviors to those of others. Talking-head videos of real people are included throughout the intervention, depicting men and women with different eating disorders, under the assumption that their stories will resonate with program users. The university and service logos are included on each page to convey professionalism and credibility, and it is clear from the start that people with eating disorders, researchers, and clinicians designed the intervention.

The final MotivATE program consists of four 15-minute Web-based modules (see Table 5 for details about the content). The modules are brief to accommodate program users' potentially limited concentration levels. We wanted to design the program to give users as much choice as possible. Program users can work through the modules in any order (though a specific order is recommended) and can complete the modules all at once or as desired and when they had time. The choice of language reflects the person-based approach (see [12]), and an autonomy-supportive tone is used (eg, "you may find..." and "people have told us they feel worried about their assessment"). It is nonprescriptive and does not assume users' experiences but does acknowledge users' ambivalence (eg, "perhaps you are a little worried about letting go and have mixed feelings").

People with experience of an eating disorder evaluated early versions of MotivATE. The results of the evaluations fit into four overarching themes.

Figure 1. Home page of the MotivATE website.

Theme 1: Positive Perspectives on MotivATE

General comments about the MotivATE website were positive. Participants liked the esthetics of the site, describing it as "bright", "cheerful", and "calming". They liked the blue color scheme and neutral images.

> *It's quite a neutral image as well. I don't think it'd be very nice if there was like images of people or anything like that so I quite like it...I think they're right, neutral pictures, that's always a great idea.* [Kate, binge eating disorder]

Participants consistently referred to the information and stories on the site as "positive" and "reassuring". They felt that the information and stories were relevant to them; they related well to the people in the stories, and this seemed to improve self-efficacy and helped them to recognize areas for change.

> *That's very good, too, as you need proof. You desperately need to see someone or hear of someone who really has got better, and these are all things that are building confidence, aren't they?* [Lily, anorexia nervosa]

Theme 2: The Need to Tailor the Program to Different Motivational Needs

Some participants worried that the information could be inappropriate or unhelpful for those in the precontemplation stage of change. Sam, who did not believe "there was anything wrong" at the time of his assessment, gave good insight into how he would have felt at the time of referral:

> *After [I was] diagnosed and before [I was] assessed, not sure I would have felt any of these things...But as I was through my recovery, then yes, I probably said all of these things....* [Sam, anorexia nervosa]

Sam described how reading stories of others' experiences helped him to recognize similar thinking patterns and behaviors in himself. Once he started to realize that he had an eating disorder, he sought as much information as he could. These insights helped us to tailor the stories better, and we added more psychoeducation for those in the precontemplation stage of change.

Theme 3: Addressing Fears About Recovery

Thinking further ahead than the assessment appointment could be "daunting and scary" (Evie, Bulimia Nervosa), and it was clear from talking to participants that the website should not be overtly about "recovery"; instead, it should "sow the seed" (Sam) and focus on how to prepare for the assessment

appointment. Early versions of the program also discussed the concepts of recovery and psychological treatment, but based on the following feedback, the final program only considered the first step of the assessment appointment:

> *I freaked a little bit then. Thinking about change in the future. I'm going to move onto something else (chooses quiz to distract from message on page) because that's what I would do.* [Sally, eating disorder not otherwise specified]

Theme 4: Eating Disorder-Specific Aspects of Designing a Web-Based Program

Some participants (particularly those with a history of anorexia nervosa) believed that some modules were too long, and we therefore decided to shorten the modules to no longer than 10 minutes, focusing on essential information. Participants also commented on the terminology. For example, we referred to question *scales* and motivational *exercises*, but these have connotations related to body weight, so we removed these references.

We used the results from the think-aloud interviews to modify the program, and further consultations with participants as well as consultations with charity directors and others with experience of eating disorders confirmed that the program was acceptable to users.

Specifying Adoption and Implementation Plans

We demonstrated the MotivATE program to clinical and administrative staff at one eating disorder service before we asked for feedback about implementing MotivATE in their practice. Two key points arose: (1) it should not impact existing service resources and staff time, and (2) the modules needed to be short enough to optimize engagement of patients. MotivATE would be a free, stand-alone program that would not require training for service staff or patients. Invitation to MotivATE would occur via the same materials as the standard invitation to attend an assessment and would therefore not impact staff time and resources. We are planning a process evaluation with program users and service staff to further explore implementation.

Evaluation

We have already evaluated the acceptability and usability of the intervention as part of the program development described here. A randomized controlled trial (RCT) is also currently underway to evaluate the impact of the MotivATE program on improving attendance at an eating disorder service (Trial Registration: NCT02777944).

Discussion

This paper described the development of a pretreatment Web-based program designed to support adults with eating disorders as they prepare for an assessment appointment at a specialist outpatient eating disorder service. We have yet to establish the program's value for and impact on service attendance rates, although the RCT will enable us to determine this. Nonetheless, we believe the program will improve attendance at assessment appointments based on comments from service users and service staff.

The combined approach of using intervention mapping and a person-based approach worked well, as it allowed us to structure our development process in a logical manner by identifying areas of need, setting out key objectives from the outset, and highlighting key theory and strategies that could be used while always ensuring that each of these components would work for the target user. Our person-based approach is a key strength of the development process. Specifically, this program needs to be acceptable, motivating, and empowering for users who already find it difficult to engage with services. Interviews with service users and service staff also revealed important shortcomings of the first version of the intervention, developed based on existing literature and theory, which we have been able to address and tailor more to service user needs (ie, shorter sessions, more psychoeducation for those in an earlier stage of change, and more focus on assessment rather than the full recovery process). The use of existing qualitative literature and theory was also fundamental to our intervention design since they not only ensured an evidence-based approach to program development, but they also enabled the inclusion of a variety of processes designed to increase motivation, and allowed us to consider the characteristics of populations that can be difficult to engage. Our needs assessment has also demonstrated the potential usefulness of the MotivATE program across services in the UK, although one weakness of our service provision survey is that for practical reasons (resources and time demands making it difficult for services to engage), we included only four services. Nonetheless, the study still provides a more generalized view than existing studies, which have focused only on one area of the UK [9].

One difficulty in the design phase was the production of a Web-based intervention that utilized the principles of motivational interviewing and SDT, which rely heavily on face-to-face interaction. Use of a person-based language style, which enabled us to provide autonomy support [13], and optional interactive tasks, which allowed people to engage in motivation-to-change techniques, overcame this difficulty. Again, by working with participants to qualitatively evaluate the modules, we could adapt the language to ensure that it was motivating for them. Nonetheless, a weakness of the program is that we have not yet assessed whether the intervention improves motivation to change in individuals, and this is a plan for a future study.

Despite positive feedback regarding the acceptability of the MotivATE program, a key unknown is whether people will register for and engage with it, particularly as Web-based interventions are known to have low rates of engagement [43]. Our RCT will give us some details about this, but further research is required to understand uptake of and engagement with Web-based interventions, particularly in populations already known to be difficult to engage by face-to-face intervention. It seems that consideration of user engagement should form part of the intervention design [44] and could be implemented within the intervention mapping process. A developing area of interest regarding uptake is the study of how peripheral cues, such as esthetic appeal, may improve website

stickiness [45]; however, this concept is yet to be applied to the design of Web-based health behavioral change interventions, and further research is needed.

To our knowledge, the MotivATE program is the first intervention designed for delivery to eating disorder patients prior to formal contact with an eating disorder service with the aim of enhancing engagement with face-to-face services. If the program is effective, it could act as a template for the design of similar pretreatment Web-based programs for other patient groups in which ambivalent attitudes and/or a lack of engagement with services may be an issue.

Acknowledgments

We would like to thank the services that spent time providing audit data for our service provision survey and all those who shared their experiences in the program. We would also like to thank Fern Griffiths for helping to collect the service provision data.

Conflicts of Interest

None declared.

References

1. Beat. The costs of eating disorders: Social, health and economic impacts. 2015. URL: https://www.b-eat.co.uk/assets/000/000/302/The_costs_of_eating_disorders_Final_original.pdf?1424694814 [accessed 2017-07-20] [WebCite Cache ID 6s5keEp80]
2. NHS Information Centre for Health and Social Care. Adult Psychiatric Morbidity in England, 2007: Results of a Household Survey. 2009. URL: http://content.digital.nhs.uk/catalogue/PUB02931/adul-psyc-morb-res-hou-sur-eng-2007-rep.pdf [accessed 2017-07-20] [WebCite Cache ID 6s5kzXgu1]
3. American PA. Diagnostic and statistical manual of mental disorders (5th ed). Washington DC: Author; 2013.
4. Williams S, Reid M. Understanding the experience of ambivalence in anorexia nervosa: The maintainer's perspective. Psychol Health 2010 Jun;25(5):551-567. [doi: 10.1080/08870440802617629] [Medline: 20204933]
5. Arcelus J, Mitchell AJ, Wales J, Nielsen S. Mortality rates in patients with anorexia nervosa and other eating disorders. A meta-analysis of 36 studies. Arch Gen Psychiatry 2011 Jul;68(7):724-731. [doi: 10.1001/archgenpsychiatry.2011.74] [Medline: 21727255]
6. Le Grange D, Loeb KL. Early identification and treatment of eating disorders: prodrome to syndrome. Early Interv Psychiatry 2007 Feb;1(1):27-39. [doi: 10.1111/j.1751-7893.2007.00007.x] [Medline: 21352106]
7. Treasure J, Russell G. The case for early intervention in anorexia nervosa: theoretical exploration of maintaining factors. Br J Psychiatry 2011 Jul;199(1):5-7 [FREE Full text] [doi: 10.1192/bjp.bp.110.087585] [Medline: 21719874]
8. Hart LM, Granillo MT, Jorm AF, Paxton SJ. Unmet need for treatment in the eating disorders: a systematic review of eating disorder specific treatment seeking among community cases. Clin Psychol Rev 2011 Jul;31(5):727-735. [doi: 10.1016/j.cpr.2011.03.004] [Medline: 21501580]
9. Waller G, Schmidt U, Treasure J, Murray K, Aleyna J, Emanuelli F, et al. Problems across care pathways in specialist adult eating disorder services. Psychiatric Bulletin 2009 Jan 01;33(1):26-29. [doi: 10.1192/pb.bp.107.018325]
10. Bell L. What predicts failure to engage in or drop out from treatment for bulimia nervosa and what implications does this have for treatment? Clin. Psychol. Psychother 2001 Nov;8(6):424-435. [doi: 10.1002/cpp.288]
11. Innes NT, Clough BA, Casey LM. Assessing treatment barriers in eating disorders: A systematic review. Eat Disord 2017;25(1):1-21. [doi: 10.1080/10640266.2016.1207455] [Medline: 27485375]
12. Bartholomew LK, Parcel GS, Kok G. Intervention mapping: a process for developing theory- and evidence-based health education programs. Health Educ Behav 1998 Oct;25(5):545-563. [Medline: 9768376]
13. Yardley L, Morrison L, Bradbury K, Muller I. The person-based approach to intervention development: application to digital health-related behavior change interventions. J Med Internet Res 2015;17(1):e30 [FREE Full text] [doi: 10.2196/jmir.4055] [Medline: 25639757]
14. Newell C. Unpublished thesis. 2007. Recovery in anorexia nervosa: the struggle to develop a new identity URL: http://ethos.bl.uk/OrderDetails.do?uin=uk.bl.ethos.488710 [accessed 2017-07-20] [WebCite Cache ID 6s5lYZVau]
15. Williams S, Reid M. 'It's like there are two people in my head': a phenomenological exploration of anorexia nervosa and its relationship to the self. Psychol Health 2012;27(7):798-815. [doi: 10.1080/08870446.2011.595488] [Medline: 21736500]
16. Williams S, Yardley L, Wills GB. A qualitative case study of LifeGuide: users' experiences of software for developing Internet-based behaviour change interventions. Health Informatics J 2013 Mar;19(1):61-75. [doi: 10.1177/1460458212458915] [Medline: 23486826]
17. Yardley L, Morrison LG, Andreou P, Joseph J, Little P. Understanding reactions to an internet-delivered health-care intervention: accommodating user preferences for information provision. BMC Med Inform Decis Mak 2010;10:52 [FREE Full text] [doi: 10.1186/1472-6947-10-52] [Medline: 20849599]
18. Reid M, Burr J, Williams S, Hammersley R. Eating disorders patients' views on their disorders and on an outpatient service: a qualitative study. J Health Psychol 2008 Oct;13(7):956-960. [doi: 10.1177/1359105308095070] [Medline: 18809647]

19. Cockell S, Geller J, Linden W. Decisional balance in anorexia nervosa: capitalizing on ambivalence. Eur. Eat. Disorders Rev 2003 Mar;11(2):75-89. [doi: 10.1002/erv.493]
20. Espíndola CR, Blay SL. Anorexia nervosa treatment from the patient perspective: a metasynthesis of qualitative studies. Ann Clin Psychiatry 2009;21(1):38-48. [Medline: 19239831]
21. Leavey G, Vallianatou C, Johnson-Sabine E, Rae S, Gunputh V. Psychosocial barriers to engagement with an eating disorder service: a qualitative analysis of failure to attend. Eat Disord 2011;19(5):425-440. [doi: 10.1080/10640266.2011.609096] [Medline: 21932972]
22. Miller WR, Rollnick S. Motivational Interviewing: Preparing people for change (2nd ed). London: The Guildford Press; 2002.
23. Schauman O, Aschan LE, Arias N, Beards S, Clement S. Interventions to increase initial appointment attendance in mental health services: a systematic review. Psychiatr Serv 2013 Dec 01;64(12):1249-1258. [doi: 10.1176/appi.ps.201200540] [Medline: 24036532]
24. Houghton S, Saxon D, Smallwood A. Effects of opt-in letters in a National Health Service psychotherapy service. The Psychiatrist 2010 Nov 30;34(12):507-510. [doi: 10.1192/pb.bp.109.027581]
25. Hawker D. Increasing initial attendance at mental health out-patient clinics: opt-in systems and other interventions. Psychiatric Bulletin 2007 May 01;31(5):179-182. [doi: 10.1192/pb.bp.105.007377]
26. Velicer WF, Prochaska JO, Fava JL, Norman GJ, Redding CA. Smoking Cessation and Stress Management: Applications of the Transtheoretical Model of Behavior Change. Homeostasis 1998;38(5-6):216-233.
27. National Collaborating Centre for Mental Health. Eating disorders: core interventions in the treatment and management of anorexia nervosa, bulimia nervosa and related eating disorders. 2004. URL: http://www.rcpsych.ac.uk/PDF/NICE%20Eating%20Disorders.pdf [accessed 2017-07-20] [WebCite Cache ID 6s5midNy0]
28. Treasure JL, Katzman M, Schmidt U, Troop N, Todd G, de SP. Engagement and outcome in the treatment of bulimia nervosa: first phase of a sequential design comparing motivation enhancement therapy and cognitive behavioural therapy. Behav Res Ther 1999 May;37(5):405-418. [Medline: 10228313]
29. Cassin SE, von RKM, Heng K, Brar J, Wojtowicz AE. Adapted motivational interviewing for women with binge eating disorder: a randomized controlled trial. Psychol Addict Behav 2008 Sep;22(3):417-425. [doi: 10.1037/0893-164X.22.3.417] [Medline: 18778135]
30. Gowers SG, Smyth B. The impact of a motivational assessment interview on initial response to treatment in adolescent anorexia nervosa. Eur. Eat. Disorders Rev 2004 Feb 18;12(2):87-93. [doi: 10.1002/erv.555]
31. Schmidt U, Treasure J. Clinician?s guide to getting better bit(e) by bit(e). In: Clinician's guide to Getting better bit(e) by bit(e): a survival kit for sufferers of bulimia nervosa and binge eating disorders. Hove, East Sussex, UK: Psychology Press; 1997.
32. Treasure J, Schmidt U. Ready, willing and able to change: motivational aspects of the assessment and treatment of eating disorders. Eur. Eat. Disorders Rev 2001 Jan;9(1):4-18. [doi: 10.1002/erv.390]
33. Vitousek K, Watson S, Wilson GT. Enhancing motivation for change in treatment-resistant eating disorders. Clin Psychol Rev 1998 Jun;18(4):391-420. [Medline: 9638355]
34. Hötzel K, von BR, Schmidt U, Rieger E, Kosfelder J, Hechler T, et al. An Internet-based program to enhance motivation to change in females with symptoms of an eating disorder: a randomized controlled trial. Psychol Med 2014 Jul;44(9):1947-1963. [doi: 10.1017/S0033291713002481] [Medline: 24128818]
35. Leung SF, Ma J, Russell J. Enhancing motivation to change in eating disorders with an online self-help program. Int J Ment Health Nurs 2013 Aug;22(4):329-339. [doi: 10.1111/j.1447-0349.2012.00870.x] [Medline: 22882349]
36. Weiss CV, Mills JS, Westra HA, Carter JC. A preliminary study of motivational interviewing as a prelude to intensive treatment for an eating disorder. J Eat Disord 2013;1:34 [FREE Full text] [doi: 10.1186/2050-2974-1-34] [Medline: 24999413]
37. Deci EL, Ryan RM. Self-determination theory in health care and its relations to motivational interviewing: a few comments. Int J Behav Nutr Phys Act 2012;9:24 [FREE Full text] [doi: 10.1186/1479-5868-9-24] [Medline: 22385839]
38. Nordbø RHS, Gulliksen KS, Espeset EMS, Skårderud F, Geller J, Holte A. Expanding the concept of motivation to change: the content of patients' wish to recover from anorexia nervosa. Int J Eat Disord 2008 Nov;41(7):635-642. [doi: 10.1002/eat.20547] [Medline: 18528876]
39. Nordbø RHS, Gulliksen KS, Espeset EMS, Skårderud F, Geller J, Holte A. Expanding the concept of motivation to change: the content of patients' wish to recover from anorexia nervosa. Int J Eat Disord 2008 Nov;41(7):635-642. [doi: 10.1002/eat.20547] [Medline: 18528876]
40. Vansteenkiste M, Soenens B, Vandereycken W. Motivation to change in eating disorder patients: a conceptual clarification on the basis of self-determination theory. Int J Eat Disord 2005 Apr;37(3):207-219. [doi: 10.1002/eat.20099] [Medline: 15822077]
41. Hinyard LJ, Kreuter MW. Using narrative communication as a tool for health behavior change: a conceptual, theoretical, and empirical overview. Health Educ Behav 2007 Oct;34(5):777-792. [doi: 10.1177/1090198106291963] [Medline: 17200094]

42. Ranjit N, Menendez T, Creamer M, Hussaini A, Potratz C, Hoelscher D. Narrative Communication as a Strategy to Improve Diet and Activity in Low-Income Families: The Use of Role Model Stories. American Journal of Health Education 2015 Mar 04;46(2):99-108. [doi: 10.1080/19325037.2014.999962]
43. Kelders SM, Kok RN, Ossebaard HC, Van GJEWC. Persuasive system design does matter: a systematic review of adherence to web-based interventions. J Med Internet Res 2012;14(6):e152 [FREE Full text] [doi: 10.2196/jmir.2104] [Medline: 23151820]
44. Ritterband LM, Tate DF. The science of internet interventions. Introduction. Ann Behav Med 2009 Aug;38(1):1-3. [doi: 10.1007/s12160-009-9132-5] [Medline: 19816750]
45. Short CE, Rebar AL, Plotnikoff RC, Vandelanotte C. Designing engaging online behaviour change interventions: A proposed model of user engagement. European Health Psychologist 2015;17(1):32.

Abbreviations

RCT: randomized controlled trial
SDT: self-determination theory

Edited by G Eysenbach; submitted 02.02.17; peer-reviewed by S Bauer, L Morrison; comments to author 26.02.17; revised version received 12.06.17; accepted 13.06.17; published 26.07.17.

Please cite as:
Muir S, Newell C, Griffiths J, Walker K, Hooper H, Thomas S, Thomas PW, Arcelus J, Day J, Appleton KM
MotivATE: A Pretreatment Web-Based Program to Improve Attendance at UK Outpatient Services Among Adults With Eating Disorders
JMIR Res Protoc 2017;6(7):e146
URL: http://www.researchprotocols.org/2017/7/e146/
doi:10.2196/resprot.7440
PMID:28747295

Protocol

Brazilian Samba Protocol for Individuals With Parkinson's Disease: A Clinical Non-Randomized Study

Ana Cristina Tillmann[1*], MSc; Alexandro Andrade[2*], MSc, PhD; Alessandra Swarowsky[2*], MSc, PhD; Adriana Coutinho De Azevedo Guimarães[2*], MSc, PhD

[1]Health Sciences Centre (CEFID), Research Laboratory in Leisure and Physical Activity (LAPLAF), University of Santa Catarina State, Florianópolis, Brazil

[2]Health Sciences Centre (CEFID), University of Santa Catarina State, Florianopolis, Brazil

[*]all authors contributed equally

Corresponding Author:
Ana Cristina Tillmann, MSc
Health Sciences Centre (CEFID)
Research Laboratory in Leisure and Physical Activity (LAPLAF)
University of Santa Catarina State
R. Pascoal Simone, 358
Florianópolis, 88080-350
Brazil
Phone: 55 48999248566
Email: actillmann@gmail.com

Abstract

Background: In the 10 most populated countries in the world, Parkinson's disease (PD) affects more than 5 million individuals. Despite optimal treatment options already developed for the disease, concomitant involvement of other areas of health care plays an important role in complementing the treatment. From this perspective, dancing can be viewed as a non-drug alternative that can reduce falls by improving some motor skills, such as mobility, balance, gait, and posture, and can also improve the overall quality of life. Brazilian samba promotes improvement in motor and non-motor symptoms in individuals with PD, providing a new treatment option for this population.

Objective: The main objective of this quasi-experimental study is to provide a 12-week samba protocol (2x/week) for individuals with PD and to compare its effects with the group without intervention. The hypothesis is that the Brazilian samba protocol will promote improvement in primary (motor) and secondary (non-motor) outcomes in individuals with PD.

Methods: The sample will be selected at random from individuals diagnosed with PD in the city of Florianopolis (SC, Brazil). Sample size calculation was performed with the G*Power 3.1.9.2 software, with 0.447 effect size, at 5% significance level, power of 0.9, and test and sample loss of 20%. This yielded 60 individuals divided between the intervention and control groups. The questionnaires will be filled out before and after the dance intervention. The data collection for the control group will be held simultaneously to the intervention group. The classes will last for 1 hour, twice a week in the evening for 12 weeks, and all classes will be divided into warm-up, main part, and relaxation. Two-way analysis of variance with repeated measures and Sidak post-hoc comparison test will be used for a comparative analysis of the final results of the control group with the experimental group and of the within-group changes between pre- and postintervention period.

Results: We expect to complete follow-up in September 2017.

Conclusions: The major inspiration for this study was to encourage the creation of new rehabilitation programs that do not emphasize doctor involvement. This is a unique protocol for PD and we believe it can be an important tool to alleviate the motor and non-motor symptoms of individuals with PD. Dance is a simple activity depending on little equipment and few financial resources, facilitating its implementation and improving the cost-benefit relationship. In addition, activities that have a cultural aspect for the population in question, and which are pleasant, enable the participants to commit long term. This can enhance patient's compliance with the therapy, which is often a problem for many rehabilitation programs.

(JMIR Res Protoc 2017;6(7):e129) doi:10.2196/resprot.6489

KEYWORDS

Parkinson's disease; protocol; balance; quality of life; therapy

Introduction

In the 10 most populated countries in the world, Parkinson's disease (PD) affects more than 5 million individuals and the projection is that by 2030 more than 9.3 million people will have been diagnosed [1]. Given its epidemiological importance, the disease can be considered a public health problem, manifestations of which encompass social, family, economic, and even legal problems [2], and involve high costs to the health system. Individuals with chronic diseases, such as PD, deal with physical discomforts on a daily basis arising from deficits and motor symptoms [3-6] and as autonomic, sensory, and behavioral disorders from non-motor symptoms. These can result in a severe reduction of independence [7] and quality of life in this population [8].

From this perspective, dancing can be viewed as a non-drug alternative for both symptomatologies: (1) improving some motor skills (eg, mobility, balance, gait, posture, fall reduction), and (2) improving some non-motor symptoms (eg, fatigue and depression). The benefit is an overall improvement in quality of life [9-11]. For this population, dance is perhaps the most "complete" of all interventions, mainly because the stimulation of different cerebral areas is so important for patients with PD.

Recently, Sharp et al [12] conducted a systematic review, which sought to analyze the effectiveness of dance as an intervention for PD. They found improvement in motor scores on Unified Parkinson's Disease Rating Scale (UPDRS), balance, and gait speed in subjects who underwent dance therapy compared to the group that did not receive any intervention. Similarly, there was an improvement in quality of life when dance intervention was compared to exercise interventions [12]. In another systematic review, dance demonstrated maintenance of muscle strength and improvements in support and balance, aerobic power, full range of body movements, resulting in positive lifestyle changes in individuals with PD [13].

Among the surveys already performed with dance and patients with PD, tango is the most commonly applied ballroom dance form in studies involving PD [12]. According to Earhart [14], the practice of this particular rhythm could facilitate the activation of brain areas that normally are less active in PD. Tango movements, following a well-defined and precise rhythm, were associated with increased activation of neural areas not normally active in patients with PD [15] and with stimulation of cortical activation by increasing motor skills [16]. These results indicate that the characteristics of this rhythm may increase the demand for conscious awareness of movement in patients with PD, thus facilitating mobility [14].

Widespread in Latin America, especially in Brazil, the samba is a dance that evolved similar to tango. It was influenced by African rhythms and became popular in Europe at the same time, which explains the similarity in the execution of steps in the two rhythms [17]. Samba has a two-four time rhythm and has similar passages and diversity of execution as tango. Movement can be performed with higher or lower speed without necessarily being out of the musical time [18]. Samba marking characteristics and basic step, with stops in the movements and shifts forward and back, are similar to tango markings [19].

In addition, samba has many lively rhythms and makes use of percussion instruments, stimulating its dancers, facilitating awareness, and marking the rhythm. There are numerous styles of samba, like the slower bossa nova, or the faster gafieiras sambas [20]. This rhythm has already been used in the area of rehabilitation, with patients recovering from heart disease. It was shown that participants adapted well to the samba protocol, and it was feasible as possible exercise during cardiac rehabilitation [18].

Although the tango world is widespread, use of other dance styles could lead to more accessible and attractive interventions, when adapted to culture of the population. Furthermore, it may facilitate diversity of music [21] and application protocols. However, there is still a lack of evidence of the effectiveness of rhythms other than tango in PD. Thus, the main objective of this non-randomized study is to provide a 12-week samba protocol (2x/week) for individuals with PD and to compare its effects with the group without intervention. We hypothesize that the Brazilian samba protocol will promote improvement in primary (motor) and secondary (non-motor) outcomes in individuals with PD, providing a new treatment option for this population.

Methods

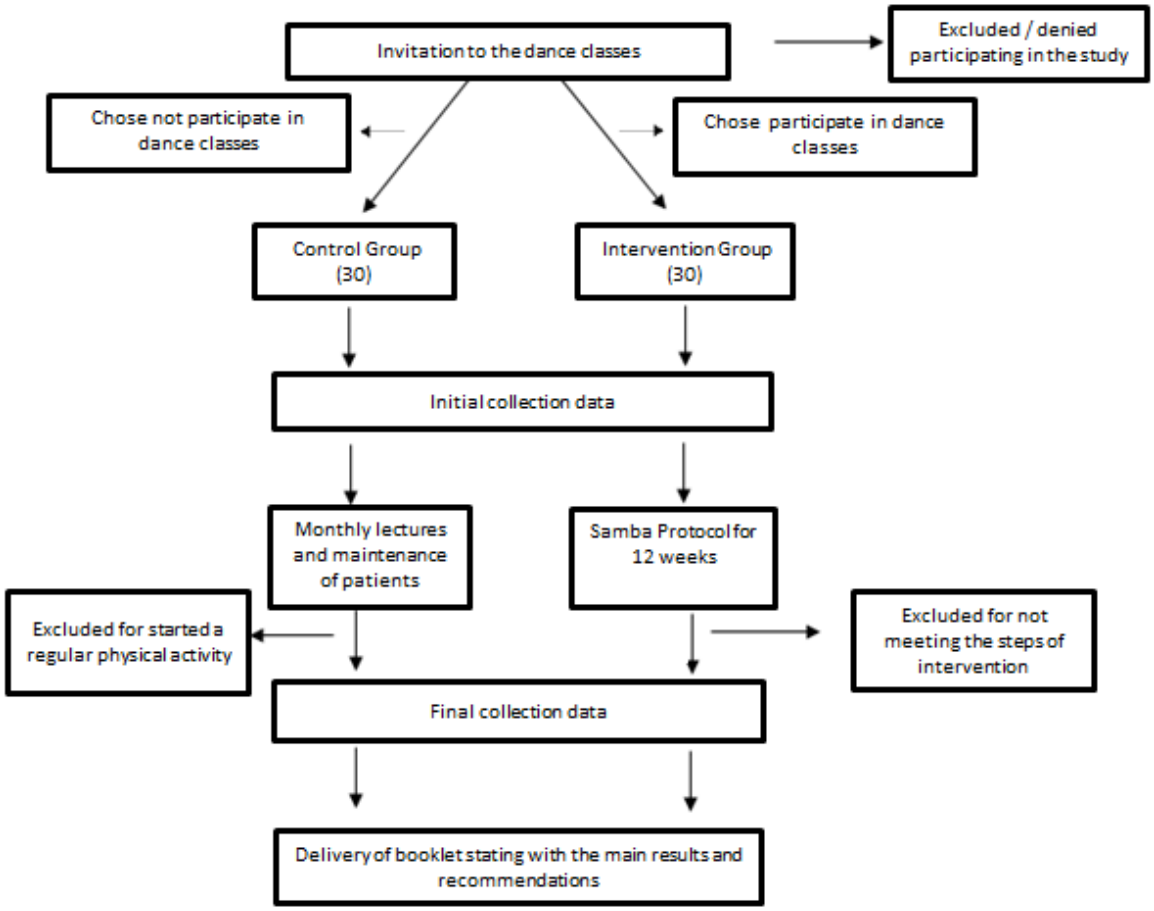
Study Type

This clinical non-randomized study comprises 12 weeks of intervention and monitoring of a control group (Figure 1).

Participants

The sample will be selected at random from individuals diagnosed with PD in the city of Florianopolis (SC, Brazil). They will be recruited from a telephone list of individuals who take part in the Parkinson Association Santa Catarina. Half of those (n=30, intervention group) will be take part in activities in the Rhythm and Movement Extension Program at the Health Sciences and Sports Centre at the State University of Santa Catarina in the Santa Catarina Rehabilitation Center (CCR).

Figure 1. Flowchart showing the process of participant selection and steps in the study protocol.



Inclusion criteria consist of individuals of both sexes; aged ≥50 years; with a clinical diagnosis of PD, according to the criteria of the London Brain Bank [22]; on stable doses of medication; who attend one or two times weekly, a physiotherapy section and who have not participated in any dance classes for at least 3 months. Exclusion criteria consist of people who are taking part in combined practice of any physical activity program and/or exercise; fail to complete all stages of the study (intervention); are decompensated clinically; do not meet the cut-off points on the Mini-Mental State Examination, in accordance with the criteria established by Bertolucci et al [23] for the Brazilian population (13=illiterate, 18=medium level of education, 26=high school); and with physical disability affecting daily or social life activities, due to a condition other than PD.

In order to avoid confusion bias before the intervention, participants will be excluded from either of the groups, if they have participated in systematic physical activity, for at least 3 months prior to the start of the study.

Outcome Measures

According to interventions already undertaken with distinctive dance forms [9,21,24-27], it is believed that the samba classes can generate positive results in both motor symptoms and non-motor symptoms. The expectation is that the activity will have a greater effect on the primary outcomes such as motor exploration and balance, and a minor effect on non-motor symptoms such as depression and fatigue. We also decided to include an assessment for sleep disorders, as this outcome is still not observed in dance studies. To maintain uniformity in the results of future studies, we chose the more popular assessment tools for each variables, as well as the number of outcomes. Table 1 lists the variables to be evaluated, as well as the instruments used to measure them.

Ethical Approval

The project was approved by the Research Ethics Committee in Human Beings, University of Santa Catarina State under the protocol 1.268.353.

Table 1. Variables and instruments used for assessment of the outcomes in individuals with PD.

Variables	Definition	Instruments
Symptomatology		
General condition of the patient with PD	Light disability, Moderate disability, High disability	HY[a]-Degree of Disability Scale
Evaluation of PD	Progression of the disease	UPDRS[b]
Motor/Non-motor Symptoms		
Balance	Restricted to the wheelchair; Needs during walking; Independent walking	BBS[c]
Sleep quality		PDSS[d]
Depressive symptoms	Minimal, mild, moderate, severe	BDI[e]
Fatigue		FSS[f]
Quality of life		PDQ-39[g]

[a]HY: Hoehn and Yahr.

[b]Unified Parkinson's Disease Rating Scale.

[c]BBS: Berg Balance Scale.

[d]PDSS: Parkinson's Disease Sleep Scale.

[e]BDI: Beck Depression Inventory.

[f]FSS: Fatigue Severity Scale.

[g]PDQ-39: Parkinson's Disease Questionnaire.

Data Collection

Experimental Group

The classes will be held at the CCR while participants are taking their medication. They will be invited to participate in the study voluntarily and to take part in the dance classes. The potential participants will be provided with an explanation of the study procedures (assessment prior to data collection, dance classes, and assessment after data collection) and the importance of attending the classes for health benefits. After the participants sign the informed consent forms, we will start collecting data. The questionnaires will be filled out before the dance intervention in a quiet place to facilitate subjects' understanding of the questions, during a 2-week period preceding the application of the protocol. After the initial assessment, the dance classes will start twice a week and last 1 hour each time, according to the study protocol. At the end of the 12-week course, a second assessment will be held, in the same manner as the first one.

Control Group

The data collection for the control group will be held simultaneously to the intervention group of the period. The researcher will schedule a visit to the patient's home or other preferred place, where they will clarify the goals of the study, emphasize the importance of keeping to normal daily activities, and request that the patient avoids starting a physical activity during these 12 weeks. The subjects in the control group will also be advised that not performing physical activity for 12 weeks is against the guidance for prevention of disease and maintenance of health, and therefore, it is only a guideline.

The participants in the control group will be invited to monthly lectures that address the maintenance of health, prevention of falls, and psychological care. They will be asked, in person, about their general health and performance of daily activities. During the interview after the 12 weeks of data collection, any subjects who state that they have started a regular physical activity of any type will be excluded from the control group. At the end of the study, all participants (control and intervention) will receive a booklet stating, in a clear and objective way, the main results for both the group and individually (including the activities started during the period and the option to be excluded from the databank). Since the dance classes will continue after the end of the study, all participants will be invited to take part in them.

Intervention: Brazilian Samba Protocol

The dance protocol will consist of dance classes, which will be conducted in a spacious room with appropriate facilities for a dance class for individuals with PD (floor without deformities, chairs for resting, and stereo with moderate volume to allow everyone to clearly hear the music). The classes will last for 1 hour, twice a week in the evening, for 12 weeks. The rhythm chosen for the classes is the Brazilian samba (two-four rhythm), as it was identified that its high resemblance to tango in the strong marking and the basic forward-backward steps can help development of balance and muscle tone of individuals. Furthermore, as a known national rhythm, appreciated by most of the population, it should facilitate obtaining participants' compliance with the protocol. All classes will be divided into warm-up, main part, and relaxation. The activities will start with typical, 10-minute warm-up for ballroom dances suggested by Hackney and Earhart [9], including light walking to the rhythm of pre-selected music (samba), focusing on the breath, followed by light exercise of upper limb movement (rotation, abduction, and adduction), while always working on the musicality and rhythm, as well as postural alignment. During

the main part of the lesson, the participants will follow the teacher/researcher instructions. The teacher will first demonstrate the step to be taught in that class, and the participants will initially execute it without a partner. Next, they will be paired up and perform the requested activity. The main part of the lesson will last 35 minutes, and partners will change every 7 minutes. This is aimed at facilitating practice with the largest possible number of pairings to develop motor skills and balance and to improve the adaptation to change process. During the lessons, activities will be divided into (1) following the commands of the teacher, or (2) dancing freely. The steps to be taught are described in Table 2. The sequences of classes and selected songs, including the steps, are shown in Multimedia Appendix 1.

Table 2. Description of the steps to be taught.

Steps	Feature execution
Presentation of Rhythm	During the class, traversing movements with songs of different speeds will be executed, to familiarize students with the rhythm.
Basics Steps	One step forward, two steps in place, and a step back.
Ginga[a]	With one foot forward and one foot back, the students shift their weight between the front and back legs without moving.
Working with Rhythm	Adapting previously learned movements and steps to songs of different rhythms and speeds.
"X"[a]	The pair forms an X, to perform the basic step forward. The gentleman goes on the side of the lady.
Cruzado[a]	Starting in the position of X, the pair faces each other and returns to the X position.
Bate e Volta[a]	Starting in the starting position, the lady and gentleman move away from each other and return to the starting position.
Steps Sequence	Students repeat the learned steps in predefined sequence, first pausing after each step, until they will are able to perform them with music.
Samba no pé[a]	Steps taken individually focusing on shifts at different rhythms.
Giro da Dama[a]	Starting with the backwards basic step, the gentleman leads the lady to make the turn, the lady holds the rotation moving forward, and the gentleman accompanies her movement walking forward at her side.
Review of Steps	At random, a review with all learned steps will be performed to enhance learning and improve step implementation.
Prom	During the free dancing session, music of different speeds and rhythms will be included. Students will be dancing together, and the pairs will be encouraged to swap with every song to practice the already-learned steps.

[a]The steps names were maintained in their original language.

The songs were divided, according to the beats per minute (bpm), into three movements: slow (40-72 bpm), medium (72-120 bpm), and fast (120-208 bpm) [18]. The beats analysis was performed with BPM Detector Pro.

At the end of every class, calm exercises will be performed for 5 minutes to promote relaxation after activity, involving massage, stretching, or a slow walk with quiet music in the background.

Statistical Analysis and Sample Size

Sample size was based on primary outcomes and calculation performed with the G*Power 3.1.9.2 software [28], assuming a moderate effect of Brazilian samba on motor signals (UPDRS III), according to Cohen [29] with 0.447 effect size. We chose a more cautious effect size because there is still no evidence of Brazilian samba in DP rehabilitation. However, due to the effects already found in similar interventions (ref=-0.62/-0.55) [30] as described in the meta-analysis by Lutzke et al, a significant effect is expected regarding to motor symptoms. We used alpha=.05 and power of 0.9, applied in two groups (experimental group and control group) analyzing the results through a two-way analysis of variance (ANOVA) with repeated measures and Sidak post-hoc comparison test for a comparative analysis into and between groups. Significance level will be set at 5%. Anticipating 25 individuals in each group, but foreseeing a sample loss of around 20% [31,32], we have chosen to include 30 individuals per group, ending with a total of 60 subjects.

After the intervention, the data will be transferred to SPSS v. 20.0. First, descriptive statistics will be performed (mean, standard deviation, and percentage). Two-way ANOVA with repeated measures and Sidak post-hoc comparison test will be used for a comparative analysis of the results of the control group with the experimental group and of the within-group changes between pre- and postintervention period. Significance level will be set at 5%.

Discussion

Principal Findings

The major inspiration for this study was to encourage the creation of new rehabilitation programs that do not emphasize doctor involvement. A further goal was to provide an environment where patients, caregivers, and teachers can interact in a friendly and relaxed manner, while stimulating and encouraging social relations, important for maintaining of the well-being of patients [21].

Dance, already used as a rehabilitation tool with other diseases [33,34], has properties that address important aspects of PD [12,13]: music stimulates affective memory and the rhythm

engages different neural regions [35]. Dance replaces treatments or exercises that sometimes discourage patients. In addition, because it embraces natural movements to the human being [36], dance stimulates control and motor actions, which are of great value to individuals with PD [10-13].

The positive results already found in similar studies lead us to believe in the potential of this intervention for these individuals. The protocol's main characteristics are based on four pillars: gradual progression, stimulation of adaptability, constant revision, and provision of a lively environment during the activities. The first two pillars mainly involve motor symptoms such as gait control and balance, while the last two pillars stimulate non-motor symptoms such as cognitive stimulation and memory, providing an enjoyable activity leading to a reduction in fatigue and depressive symptoms, in addition to stimulating social interaction.

The gradual progression of difficulty of the exercises will facilitate learning and give students the motivation to learn new steps. Introduction of new steps every 2 weeks (except when the turns are taught) is extremely important in PD because the motor skills essential to daily activities often require adaptability to changing environments and the ability to deal with unpredictable fluctuations in the disease. Therefore, expanding the motor skills repertoire must be constant [9].

Further, stimulating memory function is no less important than stimulating adaptability. The process of constantly reviewing the steps already learned will promote the exercise of cognitive abilities, instigating memory formation, and activation of neural areas that normally have a reduced activity in PD [15,37]. The basic samba steps, characterized by steps forward and back and performed rhythmically, can stimulate cortical activation, as has been observed in tango, increasing the attention and concentration, especially in regards to mobility [14].

Conclusions

This is a unique protocol for individuals with PD, which can be an important tool to alleviate motor and non-motor symptoms. Currently, validated study protocols for this population are geared mostly to exercises for specific motor tasks [38,39], ways to run long-term monitoring and management of the patients [40,41], or even different types of dance [42]. Dance is a simple activity depending on little equipment and few financial resources, facilitating its implementation and improving the cost-benefit relationship. In addition, activities that have a cultural aspect for the population in question, and which are pleasant, enable the participants to commit long term. This can enhance patient's compliance with therapy, which is often a problem for many rehabilitation programs [14].

While these benefits are important on the international scene, they present great value in countries similar to Brazil, which faces challenges in funding disease treatment and has limited investments for research in rehabilitation.

Multimedia Appendix 1

Brazilian samba protocol for 12 weeks to PD patients.

[PNG File, 237KB - resprot_v6i7e129_app1.png]

References

1. Dorsey ER, Constantinescu R, Thompson JP, Biglan KM, Holloway RG, Kieburtz K, et al. Projected number of people with Parkinson disease in the most populous nations, 2005 through 2030. Neurology 2007 Jan 30;68(5):384-386. [doi: 10.1212/01.wnl.0000247740.47667.03] [Medline: 17082464]
2. Corvol JC. Addictions comportementales dans la maladie deParkinson. Bull Acad Natl Med 2014;198(7):1297-1308 [FREE Full text] [doi: 10.1016/j.praneu.2011.02.005]
3. Eggers C, Kahraman D, Fink GR, Schmidt M, Timmermann L. Akinetic-rigid and tremor-dominant Parkinson's disease patients show different patterns of FP-CIT single photon emission computed tomography. Mov Disord 2011 Feb 15;26(3):416-423. [doi: 10.1002/mds.23468] [Medline: 21264942]
4. Lewis MM, Du G, Sen S, Kawaguchi A, Truong Y, Lee S, et al. Differential involvement of striato- and cerebello-thalamo-cortical pathways in tremor- and akinetic/rigid-predominant Parkinson's disease. Neuroscience 2011 Mar 17;177:230-239 [FREE Full text] [doi: 10.1016/j.neuroscience.2010.12.060] [Medline: 21211551]
5. Helmich RC, Hallett M, Deuschl G, Toni I, Bloem BR. Cerebral causes and consequences of parkinsonian resting tremor: a tale of two circuits? Brain 2012 Nov;135(Pt 11):3206-3226 [FREE Full text] [doi: 10.1093/brain/aws023] [Medline: 22382359]
6. Lee HK, Altmann LJP, McFarland N, Hass CJ. The relationship between balance confidence and control in individuals with Parkinson's disease. Parkinsonism Relat Disord 2016 May;26:24-28. [doi: 10.1016/j.parkreldis.2016.02.015] [Medline: 26949065]
7. Prakash KM, Nadkarni NV, Lye W, Yong M, Tan E. The impact of non-motor symptoms on the quality of life of Parkinson's disease patients: a longitudinal study. Eur J Neurol 2016 May;23(5):854-860. [doi: 10.1111/ene.12950] [Medline: 26806538]
8. A'Campo LEI, Spliethoff-Kamminga NGA, Roos RAC. An evaluation of the patient education programme for Parkinson's disease in clinical practice. Int J Clin Pract 2011 Nov;65(11):1173-1179. [doi: 10.1111/j.1742-1241.2011.02765.x] [Medline: 21951713]

9. Hackney ME, Earhart GM. Recommendations for Implementing Tango Classes for Persons with Parkinson Disease. Am J Dance Ther 2010 Mar 16;32(1):41-52. [doi: 10.1007/s10465-010-9086-y]
10. Rios RS, Anang J, Fereshtehnejad S, Pelletier A, Postuma R. Tango for treatment of motor and non-motor manifestations in Parkinson's disease: a randomized control study. Complement Ther Med 2015 Apr;23(2):175-184. [doi: 10.1016/j.ctim.2015.01.015] [Medline: 25847555]
11. Westheimer O, McRae C, Henchcliffe C, Fesharaki A, Glazman S, Ene H, et al. Dance for PD: a preliminary investigation of effects on motor function and quality of life among persons with Parkinson's disease (PD). J Neural Transm (Vienna) 2015 Sep;122(9):1263-1270. [doi: 10.1007/s00702-015-1380-x] [Medline: 25836752]
12. Sharp K, Hewitt J. Dance as an intervention for people with Parkinson's disease: a systematic review and meta-analysis. Neurosci Biobehav Rev 2014 Nov;47:445-456. [doi: 10.1016/j.neubiorev.2014.09.009] [Medline: 25268548]
13. Shanahan J, Morris ME, Bhriain ON, Saunders J, Clifford AM. Dance for people with Parkinson disease: what is the evidence telling us? Arch Phys Med Rehabil 2015 Jan;96(1):141-153. [doi: 10.1016/j.apmr.2014.08.017] [Medline: 25223491]
14. Earhart GM. Dance as therapy for individuals with Parkinson disease. Eur J Phys Rehabil Med 2009 Jun;45(2):231-238 [FREE Full text] [Medline: 19532110]
15. Brown S, Martinez MJ, Parsons LM. The neural basis of human dance. Cereb Cortex 2006 Aug;16(8):1157-1167. [doi: 10.1093/cercor/bhj057] [Medline: 16221923]
16. Sacco K, Cauda F, Cerliani L, Mate D, Duca S, Geminiani GC. Motor imagery of walking following training in locomotor attention. The effect of “the tango lesson”. Neuroimage 2006 Sep;32(3):1441-1449. [doi: 10.1016/j.neuroimage.2006.05.018] [Medline: 16861008]
17. Ried B. In: Ried B, editor. Fundamentos da dança de salão. Londrina: Midiograf; 2004:205.
18. Braga H, Gonzáles A, Sties S, Carvalho G, Netto A, Campos O, et al. The brasilian samba protocol for cardiac rehabilitation. Rev Bras Med Esporte 2015;21(5):395-399. [doi: 10.1590/1517-869220152105136354]
19. Perna M. Samba de Gafieira - a História da Dança de Salão Brasileira. Rio de Janeiro: Marco Antonio Perna; 2005:230.
20. Jost M. A construção/invenção do samba: Mediações e interações estratégicas. Rev Inst Estud Bras 2015;62:112-125. [doi: 10.11606/issn.2316-901X.v0i62p112-125]
21. McNeely ME, Mai MM, Duncan RP, Earhart GM. Differential Effects of Tango Versus Dance for PD in Parkinson Disease. Front Aging Neurosci 2015;7:239 [FREE Full text] [doi: 10.3389/fnagi.2015.00239] [Medline: 26733865]
22. Hughes AJ, Daniel SE, Kilford L, Lees AJ. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. J Neurol Neurosurg Psychiatry 1992 Mar;55(3):181-184 [FREE Full text] [Medline: 1564476]
23. Bertolucci P, Brucki S, Campacci S, Juliano Y. The Mini-Mental State Examination in an outpatient population: influence of literacy. Arq Neuro-Psiquiatr 1994;52(1):01-07. [doi: 10.1590/S0004-282X1994000100001]
24. Hackney ME, Kantorovich S, Levin R, Earhart GM. Effects of tango on functional mobility in Parkinson's disease: a preliminary study. J Neurol Phys Ther 2007 Dec;31(4):173-179. [doi: 10.1097/NPT.0b013e31815ce78b] [Medline: 18172414]
25. Hackney ME, Earhart GM. Short duration, intensive tango dancing for Parkinson disease: an uncontrolled pilot study. Complement Ther Med 2009 Aug;17(4):203-207 [FREE Full text] [doi: 10.1016/j.ctim.2008.10.005] [Medline: 19632547]
26. McGill A, Houston S, Lee RY. Dance for Parkinson's: a new framework for research on its physical, mental, emotional, and social benefits. Complement Ther Med 2014 Jun;22(3):426-432. [doi: 10.1016/j.ctim.2014.03.005] [Medline: 24906580]
27. Hashimoto H, Takabatake S, Miyaguchi H, Nakanishi H, Naitou Y. Effects of dance on motor functions, cognitive functions, and mental symptoms of Parkinson's disease: a quasi-randomized pilot trial. Complement Ther Med 2015 Apr;23(2):210-219. [doi: 10.1016/j.ctim.2015.01.010] [Medline: 25847558]
28. Faul F, Erdfelder E, Buchner A, Lang A. Statistical power analyses using G*Power 3.1: tests for correlation and regression analyses. Behav Res Methods 2009 Nov;41(4):1149-1160. [doi: 10.3758/BRM.41.4.1149] [Medline: 19897823]
29. Cohen J. Statistical power analysis for the behavioral sciences (2nd ed.). Hillsdale, NJ: Lawrence Erlbaum Associates; 1988:474.
30. Lötzke D, Ostermann T, Büssing A. Argentine tango in Parkinson disease--a systematic review and meta-analysis. BMC Neurol 2015 Nov 05;15:226 [FREE Full text] [doi: 10.1186/s12883-015-0484-0] [Medline: 26542475]
31. McKay JL, Ting LH, Hackney ME. Balance, Body Motion, and Muscle Activity After High-Volume Short-Term Dance-Based Rehabilitation in Persons With Parkinson Disease: A Pilot Study. J Neurol Phys Ther 2016 Oct;40(4):257-268. [doi: 10.1097/NPT.0000000000000150] [Medline: 27576092]
32. Earhart GM, Duncan RP, Huang JL, Perlmutter JS, Pickett KA. Comparing interventions and exploring neural mechanisms of exercise in Parkinson disease: a study protocol for a randomized controlled trial. BMC Neurol 2015 Feb 05;15:9 [FREE Full text] [doi: 10.1186/s12883-015-0261-0] [Medline: 25652002]
33. Kiepe M, Stöckigt B, Keil T. Effects of dance therapy and ballroom dances on physical and mental illnesses: A systematic review. The Arts in Psychotherapy 2012 Nov;39(5):404-411. [doi: 10.1016/j.aip.2012.06.001]
34. Pisu M, Demark-Wahnefried W, Kenzik KM, Oster RA, Lin CP, Manne S, et al. A dance intervention for cancer survivors and their partners (RHYTHM). J Cancer Surviv 2017 Jun;11(3):350-359. [doi: 10.1007/s11764-016-0593-9] [Medline: 28070770]

35. Barrett FS, Janata P. Neural responses to nostalgia-evoking music modeled by elements of dynamic musical structure and individual differences in affective traits. Neuropsychologia 2016 Oct;91:234-246. [doi: 10.1016/j.neuropsychologia.2016.08.012] [Medline: 27526666]
36. Hwang PW, Braun KL. The Effectiveness of Dance Interventions to Improve Older Adults' Health: A Systematic Literature Review. Altern Ther Health Med 2015;21(5):64-70. [Medline: 26393993]
37. McKee KE, Hackney ME. The effects of adapted tango on spatial cognition and disease severity in Parkinson's disease. J Mot Behav 2013;45(6):519-529 [FREE Full text] [doi: 10.1080/00222895.2013.834288] [Medline: 24116748]
38. Brauer SG, Woollacott MH, Lamont R, Clewett S, O'Sullivan J, Silburn P, et al. Single and dual task gait training in people with Parkinson's disease: a protocol for a randomised controlled trial. BMC Neurol 2011 Jul 27;11:90 [FREE Full text] [doi: 10.1186/1471-2377-11-90] [Medline: 21791117]
39. Capato TT, Tornai J, Ávila P, Barbosa ER, Piemonte ME. Randomized controlled trial protocol: balance training with rhythmical cues to improve and maintain balance control in Parkinson's disease. BMC Neurol 2015 Sep 07;15:162 [FREE Full text] [doi: 10.1186/s12883-015-0418-x] [Medline: 26347052]
40. Nilsson MH, Iwarsson S. Home and health in people ageing with Parkinson's disease: study protocol for a prospective longitudinal cohort survey study. BMC Neurol 2013 Oct 09;13:142 [FREE Full text] [doi: 10.1186/1471-2377-13-142] [Medline: 24107116]
41. Dorsey ER, Achey MA, Beck CA, Beran DB, Biglan KM, Boyd CM, et al. National Randomized Controlled Trial of Virtual House Calls for People with Parkinson's Disease: Interest and Barriers. Telemed J E Health 2016 Jul;22(7):590-598. [doi: 10.1089/tmj.2015.0191] [Medline: 26886406]
42. Ashburn A, Roberts L, Pickering R, Roberts H, Wiles R, Kunkel D, et al. A Design to Investigate the Feasibility and Effects of Partnered Ballroom Dancing on People With Parkinson Disease: Randomized Controlled Trial Protocol. JMIR Res Protoc 2014;3(3):e34. [doi: 10.2196/resprot.3184]

Abbreviations

BBS: Berg Balance Scale
BDI: Beck Depression Inventory
Bpm: beats per minute
CCR: Health Sciences and Sports Centers at State University of Santa Catarina in Santa Catarina Rehabilitation Center
FSS: Fatigue Severity Scale
HY: Hoehn and Yahr
PD: Parkinson’s disease
PDQ-39: Parkinson’s Disease Questionnaire
PDSS: Parkinson’s Disease Sleep Scale
UPDRS: Unified Parkinson’s Disease Rating Scale

Edited by G Eysenbach; submitted 01.09.16; peer-reviewed by M Morris, I Reuter; comments to author 04.10.16; revised version received 24.10.16; accepted 28.03.17; published 04.07.17.

Please cite as:
Tillmann AC, Andrade A, Swarowsky A, Guimarães ACDA
Brazilian Samba Protocol for Individuals With Parkinson’s Disease: A Clinical Non-Randomized Study
JMIR Res Protoc 2017;6(7):e129
URL: http://www.researchprotocols.org/2017/7/e129/
doi:10.2196/resprot.6489
PMID:28676466

Protocol

Treatment of Peritoneal Dissemination in Stomach Cancer Patients With Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy (HIPEC): Rationale and Design of the PERISCOPE Study

Rosa T van der Kaaij[1*], MD; Hidde JW Braam[2*], MD, PhD; Henk Boot[3], MD, PhD; Maartje Los[4], MD, PhD; Annemieke Cats[3], MD, PhD; Cecile Grootscholten[5], MD, PhD; Jan HM Schellens[6], MD, PhD; Arend GJ Aalbers[1], MD; Alwin DR Huitema[7,8], PhD; Catherijne AJ Knibbe[9], PhD; Djamila Boerma[2], MD, PhD; Marinus J Wiezer[2], MD, PhD; Bert van Ramshorst[2], MD, PhD; Johanna W van Sandick[1], MD, PhD

[1]The Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital, Department of Surgical Oncology, Amsterdam, Netherlands

[2]St. Antonius Hospital, Department of Surgery, Nieuwegein, Netherlands

[3]The Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital, Department of Gastroenterology, Amsterdam, Netherlands

[4]St. Antonius Hospital, Department of Medical Oncology, Nieuwegein, Netherlands

[5]The Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital, Department of Medical Oncology, Amsterdam, Netherlands

[6]The Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital, Department of Clinical Pharmacology, Amsterdam, Netherlands

[7]The Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital, Department of Pharmacy and Pharmacology, Amsterdam, Netherlands

[8]University Medical Center Utrecht, Department of Clinical Pharmacy, Utrecht, Netherlands

[9]St. Antonius Hospital, Department of Pharmacology, Nieuwegein, Netherlands

[*]these authors contributed equally

Corresponding Author:
Rosa T van der Kaaij, MD
The Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital
Department of Surgical Oncology
Plesmanlaan 121
Amsterdam, 1066 CX
Netherlands
Phone: 31 0205129111
Fax: 31 0205122459
Email: r.vd.kaaij@nki.nl

Abstract

Background: Patients with gastric cancer and peritoneal carcinomatosis have a very poor prognosis; median survival is 3 to 4 months. Palliative systemic chemotherapy is currently the only treatment available in the Netherlands. Intraoperative hyperthermic intraperitoneal chemotherapy (HIPEC) has an established role in the treatment of peritoneal carcinomatosis originating from colorectal cancer, appendiceal cancer, and pseudomyxoma peritonei; its role in gastric cancer is uncertain. Currently, there is no consensus on the choice of chemotherapeutic agents used in HIPEC for gastric cancer.

Objective: The main objectives of this study are (1) to investigate the safety, tolerability, and feasibility of gastrectomy combined with cytoreductive surgery and HIPEC after systemic chemotherapy, as a primary treatment option for patients with advanced gastric cancer with tumor positive peritoneal cytology and/or limited peritoneal carcinomatosis; and (2) to determine the maximum tolerated dose (MTD) of intraperitoneal docetaxel in combination with a fixed dose of intraperitoneal oxaliplatin.

Methods: The PERISCOPE study is a multicenter, open label, phase I-II dose-escalation study. The MTD of docetaxel will be studied using a 3+3 design. Patients with locally advanced (cT3-cT4) gastric adenocarcinoma are eligible for inclusion if the primary gastric tumor is considered resectable, tumor positive peritoneal cytology and/or limited peritoneal carcinomatosis is confirmed by diagnostic laparoscopy/ laparotomy, and prior systemic chemotherapy was without disease progression. At laparotomy, cytoreductive surgery (complete removal of all macroscopically visible tumor deposits) and a total or partial gastrectomy with a D2 lymph node dissection is performed. An open HIPEC technique is used with 460mg/m2 hyperthermic oxaliplatin for 30

minutes (41°C to 42°C) followed by normothermic docetaxel for 90 minutes (37°C) in a dose that will be escalated per 3 patients (0, 50, 75, 100, 125, 150 mg/m2). The primary endpoint is treatment related toxicity.

Results: Patient accrual is ongoing and the first results are expected in 2017.

Conclusions: The PERISCOPE study will determine the safety, tolerability, and feasibility of gastrectomy combined with cytoreduction and HIPEC using oxaliplatin in combination with docetaxel after systemic chemotherapy as primary treatment option for gastric cancer patients with tumor positive peritoneal cytology and/or limited peritoneal carcinomatosis. This study will provide pharmacokinetic data on the intraperitoneal administration of oxaliplatin and docetaxel, including the MTD of intraperitoneal-administered docetaxel. These data are a prerequisite for the safe conduct of future HIPEC studies in patients with gastric cancer.

Trial Registration: Netherlands Trial Registration (NTR): NTR4250; http://www.trialregister.nl/trialreg/admin/rctview.asp?TC=4250 (Archived by WebCite at http://www.webcitation.org/6rWJONgkt)

(JMIR Res Protoc 2017;6(7):e136) doi:10.2196/resprot.7790

KEYWORDS

gastric cancer; peritoneal carcinomatosis; gastrectomy; cytoreduction; HIPEC; hyperthermic intraperitoneal chemotherapy; oxaliplatin; docetaxel

Introduction

Patients with advanced gastric cancer have a poor prognosis. The 5-year survival rate is around 30%, even after potentially curative treatment [1-3]. In approximately 15% of patients the peritoneum is synchronously affected at diagnosis [4]. Patients with gastric cancer and peritoneal carcinomatosis have a very poor prognosis with a median survival of about 3 to 4 months without treatment [5]. It has been proposed that extended resection consisting of cytoreductive surgery (ie, complete removal of all macroscopically visible tumor deposits) and gastrectomy, combined with intraperitoneal chemotherapy, could improve survival in patients with peritoneal carcinomatosis from gastric cancer [6]. The limited permeability of the peritoneal plasma barrier allows the delivery of high concentrations of chemotherapeutic drugs directly into the peritoneal cavity without the danger of high plasma concentrations and subsequent systemic toxicity [7].

Intraoperative hyperthermic intraperitoneal chemotherapy (HIPEC) has an established role in the treatment of peritoneal carcinomatosis originating from colorectal cancer, appendiceal cancer, and pseudomyxoma peritonei [7,8]; however, the role of HIPEC in the treatment of gastric cancer with peritoneal carcinomatosis is uncertain. A systematic review showed that good quality evidence is limited as many studies included heterogeneous patient populations and differed in type, timing, method, and duration of drug delivery [9]. Better-designed studies showed longer survival of patients receiving intraperitoneal chemotherapy and cytoreductive surgery than those treated with surgery alone. Currently, various intraperitoneal chemotherapeutic drugs are used in gastric cancer but the best and the most suitable regimen is unknown [10]. An important issue which needs to be addressed is the choice of intraperitoneal chemotherapy and the most effective dose.

This study aims to evaluate the safety, tolerability, and feasibility of gastrectomy combined with cytoreductive surgery and HIPEC with oxaliplatin and docetaxel after systemic chemotherapy, as primary treatment for gastric cancer patients with tumor positive peritoneal cytology and/or limited peritoneal carcinomatosis.

Methods

Objectives

Primary Objective

The primary objective of this study is to investigate the safety, tolerability, and feasibility of gastrectomy combined with cytoreductive surgery and HIPEC after systemic chemotherapy, as a primary treatment option for advanced gastric cancer with tumor positive peritoneal cytology and/or limited peritoneal carcinomatosis.

Secondary Objectives

The secondary objectives are (1) to determine the maximum tolerated dose (MTD) of intraperitoneal docetaxel that can be given in combination with a fixed dose of oxaliplatin in patients with gastric cancer undergoing a gastrectomy combined with cytoreductive surgery and HIPEC after systemic chemotherapy; (2) to investigate the pharmacokinetics of intraoperative intraperitoneal-administered oxaliplatin and docetaxel; and (3) to determine the 2-year disease-free and overall survival of patients with advanced gastric cancer with tumor positive peritoneal cytology and/or limited peritoneal carcinomatosis, treated with gastrectomy, cytoreductive surgery and HIPEC.

Study Population

Patients, 18 years or older, with biopsy proven surgically resectable (cT3-cT4, any N) gastric adenocarcinoma with tumor positive peritoneal cytology and/or limited peritoneal carcinomatosis are eligible for participation. Patients have to be treated with systemic chemotherapy, preferably 3 to 4 courses, with the last course ending within 8 weeks prior to inclusion. Accepted neoadjuvant chemotherapy regimens generally consist of a platinum drug combined with a fluoropyrimidine. In addition, an anthracycline or taxane may have been added according to local protocol. Examples of accepted chemotherapy regimens are (1) docetaxel with oxaliplatin and capecitabine (DOC); (2) docetaxel with cisplatin and 5-fluorouracil (5-FU; DCF); (3) epirucibin with cisplatin and capecitabine (ECC); and (4) epirucibin with oxaliplatin and

capecitabine (EOC). Progressive disease under systemic chemotherapy precludes inclusion. Patients with metachronous peritoneal carcinomatosis, distant metastases, or recurrent gastric cancer will not be eligible for the current study. An overview of the inclusion and exclusion criteria is shown in Textbox 1 [11].

Textbox 1. Inclusion and exclusion criteria for the PERISCOPE study.

Criteria

- Inclusion criteria
  - Age 18 years or older
  - World Health Organization (WHO) performance status 0 to 2
  - American Society of Anesthesiologists classification I to III
  - Biopsy proven adenocarcinoma of the stomach (also tumors at the esophagogastric junction with the bulk located in the stomach for which the intended surgical treatment is a gastric resection, not a resection of the esophagus and cardia)
  - T3-T4 tumor according to the 7th edition of the tumor, node, metastasis (TNM) classification system [11]
  - Tumor positive peritoneal cytology and/or peritoneal carcinomatosis limited to the upper abdominal cavity (above the transverse colon) and/or at the most at one location in the lower abdominal cavity (eg, Douglas' pouch, ovarian metastasis, Sister Mary Joseph nodule) confirmed by diagnostic laparoscopy or laparotomy
  - Treated with neoadjuvant systemic chemotherapy (last course ending within 8 before inclusion)
  - Adequate bone marrow, hepatic, and renal function. Acceptable laboratory values at inclusion:
    - Absolute neutrophil count greater than or equal to 1.5 x 10^9/L
    - Platelet count greater than or equal to 100 x 10^9/L
    - Serum bilirubin less than or equal to 1.5 times the upper limit of normal (ULN) and alanine transaminase and aspartate transaminase less than or equal to 2.5 times ULN
    - Creatinine clearance greater than or equal to 50 ml/min (measured or calculated by Cockcroft-Gault formula)
  - Negative pregnancy test (urine/serum) for female patients with childbearing potential
  - Life expectancy 3 months or greater
  - Able and willing to undergo blood sampling for pharmacokinetics
  - Written informed consent
- Exclusion criteria
  - Distant metastases (eg, liver, lung, para-aortic lymph nodes) or small bowel dissemination
  - Signs of local irresectability of the primary gastric tumor
  - Recurrent gastric cancer
  - Metachronous peritoneal carcinomatosis
  - Prior resection of the primary gastric tumor
  - Pregnancy, breast feeding, active pregnancy ambition, or unreliable contraceptive methods
  - Uncontrolled infectious disease or known infection with human immunodeficiency virus
  - Known history of hepatitis B or C with active viral replication
  - Recent myocardial infarction (less than 6 months) or unstable angina
  - Uncontrolled diabetes mellitus
  - Any medical condition that is considered to possibly, probably, or definitely interfere with study procedures (including adequate follow-up and compliance) and/or would jeopardize safe treatment
  - Known hypersensitivity for any of the applied chemotherapeutic agents and/or their solvents

Design

This is a multicenter, open label, phase I-II dose-escalation study. The MTD of docetaxel will be studied using a 3+3 design. The first 3 patients will be treated at the lowest docetaxel dose level (0 mg/m^{2}docetaxel), that is, with the fixed dose of oxaliplatin only (460 mg/m^2). If none of the patients in this dosage cohort experience a dose-limiting toxicity (DLT), the next 3 patients will be treated with a higher docetaxel dose.

Docetaxel dosages will be escalated per cohort of at least 3 patients (0, 50, 75, 100, 125, 150 mg/m^2). If at least 1 of the 3 patients in a dosage cohort experiences a DLT, a total of 6 patients will be treated at the same dose level. When dose-limiting toxicities occur in 2 or more patients in a cohort, no further dose escalation steps will be undertaken (see safety paragraph). The MTD of docetaxel is defined as the dose below the dose level that caused DLT in 2 or more patients in a cohort.

Sample Size

The sample size cannot be determined upfront since the number of patients will depend on the number of dose-escalation steps. It is expected that 20 to 30 patients will be included in the study.

Study Procedures

Patients with locally advanced (cT3-cT4, any N) gastric adenocarcinoma are eligible for inclusion if the primary gastric tumor is considered resectable, tumor positive peritoneal cytology and/or limited peritoneal carcinomatosis is confirmed by diagnostic laparoscopy/ laparotomy, there is no evidence for distant metastasis, and systemic chemotherapy was without disease progression. Following informed consent, patients will proceed to surgery no longer than 12 weeks after the last course of chemotherapy. The flowchart of this study is shown in Figure 1.

Laparotomy

At laparotomy, a thorough inspection of the peritoneal cavity is performed. Before manipulation, the presence and extent of peritoneal tumor deposits will be recorded according to the peritoneal cancer index and the simplified peritoneal cancer index (Figures 2 and 3) [12,13]. Gross peritoneal carcinomatosis (more than one location below the transverse colon and/or small bowel dissemination) is considered tumor progression and will preclude further study participation. Similarly, if a potentially curative gastric resection is not possible, the patient is further treated off study. In these instances, HIPEC is not performed and it will be up to the surgeon to decide on the best palliative surgical intervention (if possible).

Figure 1. Flowchart of the study design.

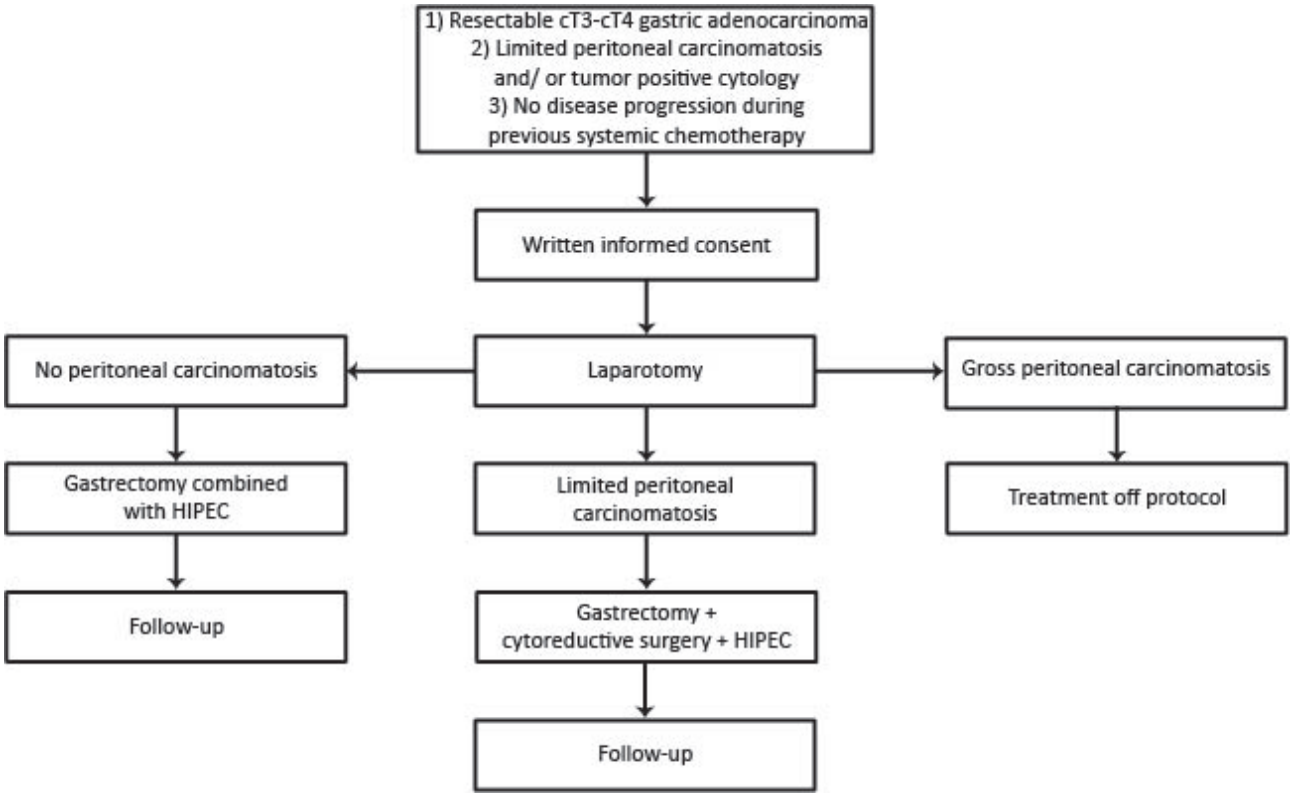


Figure 2. Peritoneal cancer index.

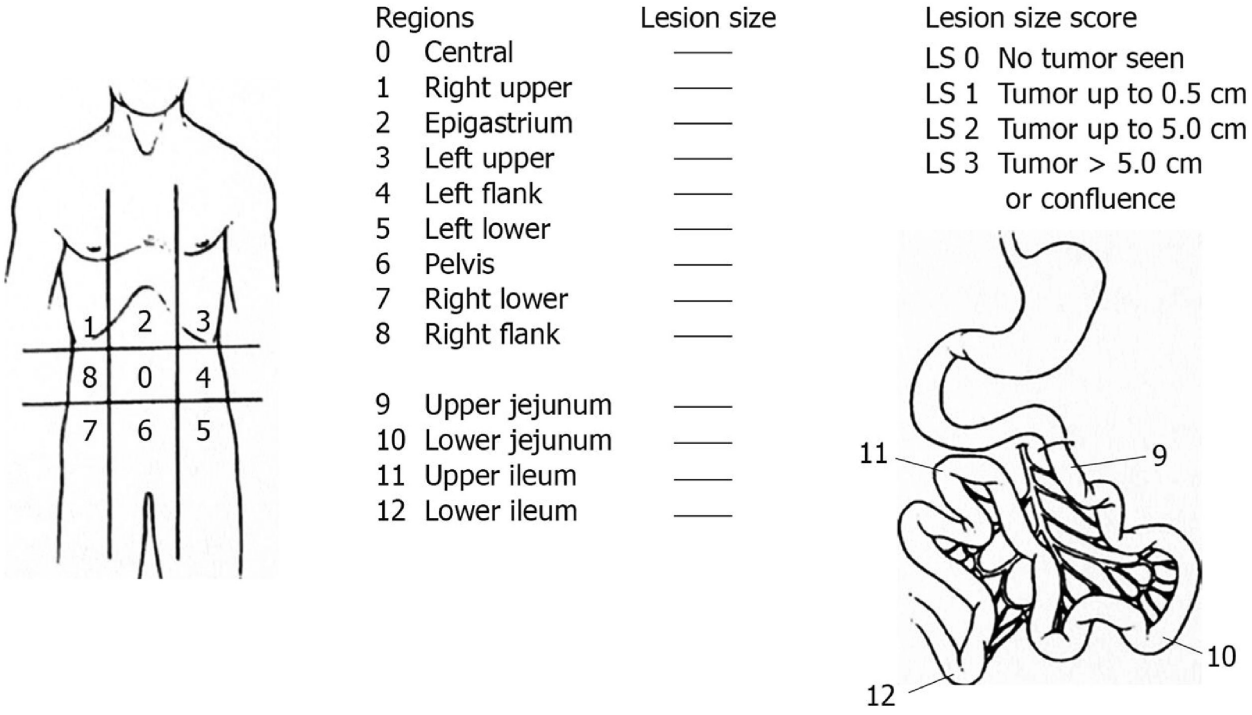


Figure 3. Simplified peritoneal cancer index.

Tumor size	None	<2cm	2-5cm	>5cm
Score	0	1	2	3
Pelvis				
Right lower abdomen				
Omentum/Transverse colon				
Small bowel/Mesentery				
Subhepatic space/ Stomach				
Right subphrenic space				
Left subphrenic space				

Gastrectomy, Cytoreductive Surgery, and Hyperthermic Intraperitoneal Chemotherapy

When a potentially curative resection of the primary tumor can be achieved, a total or partial gastrectomy with a D2 lymph node dissection is performed. In patients with limited peritoneal carcinomatosis, cytoreductive surgery will be performed with the objective to leave no macroscopic tumor behind. Peritonectomy is performed as described previously [14]. Reconstruction of the gastrointestinal continuity is postponed until the intraperitoneal chemoperfusion is completed.

HIPEC is performed using an open abdominal technique with 3 inflow and 2 outflow catheters under continuous circulation. The peritoneal cavity is perfused with 460 mg/m^{2}oxaliplatin at an intraperitoneal temperature of 41°C to 42°C. After 30 minutes, the perfusion fluid is drained from the abdomen and the peritoneal cavity is perfused with docetaxel for 90 minutes at 37°C. In successive patient cohorts, escalating docetaxel doses will be used (0, 50, 75, 100, 125, 150 mg/m^2). Gastrointestinal continuity is restored by either a Billroth II or Roux-en-Y reconstruction. A feeding jejunostomy catheter is inserted and will remain in situ until oral intake is adequate.

Pharmacokinetics

For pharmacokinetic analysis, plasma and perfusion samples will be obtained at the start, after 15 minutes, and at end of oxaliplatin perfusion, and at the start of docetaxel perfusion, after 45 minutes, and at the end of docetaxel perfusion.

Approximately 2 and 12 hours after the operation, plasma samples will be collected.

Adjuvant Treatment

Adjuvant treatment is not part of the standard study protocol but it will be discussed for all study patients in the multidisciplinary tumor board meeting. The decision will be made based upon the patient's individual intraoperative and pathological results, response to previous systemic therapy and experienced toxicity, as well as postoperative recovery.

Follow-Up

All patients will be seen at the outpatient clinic once every 3 months for the first year (including the first month after surgery), and every 6 months thereafter until 2 years after surgery. Survival status and disease recurrence/progression will be assessed until death. Follow-up will consist of physical examination, diagnostic investigations (blood tests, computed tomography scans), and hospital admission details (if applicable).

Safety

There will be at least a period of 2 weeks between the HIPEC procedures within 1 dose-level cohort. To allow adequate toxicity assessment, dose-escalation cannot take place until 4 weeks have elapsed since the last patient's HIPEC procedure in a previous dose level. When the treatment of 3 patients in 1 dose level is completed, the study team will discuss the toxicity and morbidity of the patients in the cohort and will decide in consensus whether dose-escalation can be performed or whether the endpoint of the study has been reached. Toxicity will be graded using the National Cancer Institute (NCI) Common Toxicity Criteria version 4.0. In this study, dose-limiting toxicities include the following events within 30 days after the HIPEC procedure: (1) thrombocytopenia with platelets less than 25.000 $x10^6$/L of any duration; (2) grade 4 neutropenia during 7 days or more; (3) grade 3 or 4 febrile neutropenia; (5) grade 3 or higher non-hematological toxicities (excluding grade 3 diarrhea, nausea, vomiting, fatigue, or lethargy); and (6) any other (non)-hematological toxicity, which is regarded as dose-limiting by the investigators.

Early Stopping Rules

If DLT is observed in more than 1 patient who is treated at the lowest dose level, the current study protocol is considered unsafe and the study will be terminated. At the following dose levels, no further dose escalation steps will be undertaken if DLT occurs in 2 or more patients. In addition, the study team can decide that continuation is undesirable or unethical for other reasons than mentioned in the protocol and thus terminate the study.

Analysis

Study outcome parameters will be analyzed using descriptive statistical methods. For the calculation of pharmacokinetic parameters, non-compartmental methods will be used. Disease-free and overall survival analyses will be performed by the Kaplan-Meier method for all patients. In these analyses, survival will be measured from the date of start of systemic chemotherapy to the date of disease recurrence and/or death.

Ethical Considerations

The study protocol has been approved by the medical ethical committee of the Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital. The study will be performed in accordance with the declaration of Helsinki. The protocol of this study is registered at the Netherlands Trial Registration (NTR) with code NTR4250, and in the Dutch Central Committee on Research Involving Human Subjects (NL42799.031.13). After explanation of the study objectives and procedures (both verbally and in writing), written informed consent will be acquired from all patients.

Results

Patient recruitment started in January 2014. At first, systemic chemotherapy was part of the study procedure (ie, patients were included prior to chemotherapy). This turned out to hamper patient accrual because most patients were referred after or during systemic chemotherapy given in another hospital. In June 2015, an amendment was submitted in which systemic chemotherapy was abandoned as study treatment (the current protocol). To date, 17 patients underwent the intervention under study (ie, gastrectomy combined with cytoreductive surgery and HIPEC). The results of this study are expected in 2017.

Discussion

Study Rationale

The PERISCOPE study aims to determine the safety, tolerability, and feasibility of gastrectomy combined with cytoreductive surgery and HIPEC using oxaliplatin in combination with docetaxel after systemic chemotherapy, as a primary treatment option for patients with advanced gastric cancer with tumor positive peritoneal cytology and/or limited peritoneal carcinomatosis. Previous studies of intraperitoneal chemotherapy in gastric cancer patients suggest that intraperitoneal chemotherapy may be beneficial in selected patients [9,15-17]. However, many of these studies are of limited quality as they were based on heterogeneous patient populations including either patients at risk, being treated prophylactically, or patients with manifested peritonitis treated with therapeutic intent. Most studies use different (neo)adjuvant and intraperitoneal chemotherapy regimens, and many of these studies have been performed in Asian countries which raises the question whether the results can be extrapolated to other ethnic populations.

Well-designed prospective randomized trials are warranted with clearly defined inclusion criteria, distinct neoadjuvant and adjuvant treatment protocols, and with uniform surgical and HIPEC treatment. Prior to such trials, pharmacokinetic studies are mandatory to identify the most optimal chemotherapeutic regimen to be compared to the best available standard treatment. An important issue in intraperitoneal chemotherapy in gastric cancer, therefore, is the choice and dosing of the chemotherapeutic agent. The present PERISCOPE study was designed as the first Western dose escalation trial of intraperitoneal docetaxel in patients with gastric cancer.

Choice of Intraperitoneal Drugs

Several regimens of intraoperative hyperthermic chemoperfusion in gastric cancer have been explored or are still under investigation [9]. Mitomycin and cisplatin are the most frequently used chemotherapeutic agents, originating from the widespread usage of these drugs in ovarian and colorectal HIPEC. We performed an extensive literature review on the selection of intraperitoneal chemotherapeutic drugs for the use in patients with gastric cancer [10]. Theoretically, a combination of drugs results in more effective treatment. Based on a pioneer study by Elias et al, oxaliplatin is increasingly used as a drug for intraperitoneal chemotherapy with promising results [18]. Oxaliplatin was preferred over cisplatin, as oxaliplatin is not nephrotoxic and appears to have a more favorable pharmacokinetic profile. Following the study by Elias et al, the current dosage of intraperitoneal oxaliplatin is known and widely applied, which provides a valuable starting point for further exploration of combinations of intraperitoneal chemotherapeutic drugs. The taxanes docetaxel and paclitaxel, both seem like promising drugs for intraperitoneal chemotherapy as their systemic uptake is limited, permitting the use of high local concentrations. As the tumor and cell penetration appears to be significantly higher in docetaxel compared to paclitaxel following intraperitoneal administration, we selected docetaxel as the taxane [19]. In addition, severe anaphylactic hypersensitivity reactions have been described of paclitaxel's solvent Cremophor EL [20]. A combination of oxaliplatin and docetaxel may result in a promising chemotherapeutic regimen. However, no dose-finding study has been performed on intraperitoneal docetaxel administration. Furthermore, the intraperitoneal administration of the combination of oxaliplatin and docetaxel has not yet been investigated in Western patients.

Patient Selection

In patients with limited peritoneal carcinomatosis and/or tumor positive peritoneal cytology, cytoreductive surgery combined with HIPEC might improve the overall and disease free survival based on current literature. Therefore, this study was considered ethically justified for this patient group. In patients with limited peritoneal dissemination, a complete cytoreduction (ie, complete removal of all macroscopically visible tumor deposits) can be achieved. Complete cytoreduction is one of the key factors associated with improved survival following HIPEC treatment [21,22]. Patients with extensive disease, unresectable tumors, or distant metastases are excluded as the prognosis of these patients is extremely poor. These patients qualify for palliative treatment, or best supportive care only, and are not eligible for an extensive treatment of which the associated complications do not outweigh the potential benefits.

Patients with tumor positive cytology of the peritoneal fluid without macroscopic peritoneal carcinomatosis have a median survival of 15 months and a 5-year survival rate of 0%.[23] As many as 15% of patients without visible metastatic disease will have tumor positive peritoneal cytology, and this proportion will increase to 30% to 50% in patients with serosa-infiltrating tumors or lymph node metastases [24-26]. In these high risk patients, HIPEC is expected to decrease the risk of peritoneal dissemination. Therefore, this group of patients was also included in the study.

Systemic Chemotherapy

Perioperative treatment has demonstrated an improved progression-free and overall survival in patients with resectable adenocarcinoma of the stomach [1]. Commonly applied regimes include epirubicin with cisplatin and continuous 5-FU (ECF), ECC, and DCF. Similarly, these regimens are used in the palliative setting for metastatic gastric cancer. All 3 regimens have fairly good response rates of 35% to 50%, but the median survival will only be prolonged by a few months and does not surpass 12 months [27]. At present, neoadjuvant chemotherapy is considered standard treatment prior to surgery with curative intent for gastric cancer. In the current study, it was decided that patients prior to inclusion have to be treated with preferably 3 to 4 courses of systemic chemotherapy. All regimens, consisting of a platinum drug combined with a fluoropyrimidine, or those with an additional anthracycline or taxane (according to the local protocol), are accepted. Patients showing progression under systemic chemotherapy were excluded for the study.

Conclusions

The PERISCOPE study will determine the safety, tolerability, and feasibility of gastrectomy combined with cytoreductive surgery and HIPEC using oxaliplatin in combination with docetaxel after systemic chemotherapy as a primary treatment option for patients with advanced gastric cancer with tumor positive peritoneal cytology and/or limited peritoneal carcinomatosis. The study will provide pharmacokinetic data on the intraperitoneal administration of both oxaliplatin and docetaxel. The acquired study results are a prerequisite for the safe conduct of future studies on HIPEC in patients with gastric cancer, either in the prophylactic or therapeutic setting. The ultimate goal of this ongoing project is to establish a new treatment standard for advanced gastric cancer patients by providing significant survival benefit with acceptable treatment related morbidity.

Conflicts of Interest

None declared.

Authors' Contributions

BvS and JvS share senior authorship. All authors made substantial contributions to conception and design of the study. All authors have been involved in revising the manuscript critically and all authors read and approved the final manuscript.

References

1. Cunningham D, Allum WH, Stenning SP, Thompson JN, Van de Velde CJ, Nicolson M, et al. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. N Engl J Med 2006 Jul 06;355(1):11-20. [doi: 10.1056/NEJMoa055531] [Medline: 16822992]
2. Smalley SR, Benedetti JK, Haller DG, Hundahl SA, Estes NC, Ajani JA, et al. Updated analysis of SWOG-directed intergroup study 0116: a phase III trial of adjuvant radiochemotherapy versus observation after curative gastric cancer resection. J Clin Oncol 2012 Jul 01;30(19):2327-2333 [FREE Full text] [doi: 10.1200/JCO.2011.36.7136] [Medline: 22585691]
3. Dassen AE, Dikken JL, Bosscha K, Wouters MW, Cats A, van de Velde CJ, et al. Gastric cancer: decreasing incidence but stable survival in the Netherlands. Acta Oncol 2014 Jan;53(1):138-142. [doi: 10.3109/0284186X.2013.789139] [Medline: 23829603]
4. Thomassen I, van Gestel YR, van Ramshorst B, Luyer MD, Bosscha K, Nienhuijs SW, et al. Peritoneal carcinomatosis of gastric origin: a population-based study on incidence, survival and risk factors. Int J Cancer 2014 Feb 01;134(3):622-628 [FREE Full text] [doi: 10.1002/ijc.28373] [Medline: 23832847]
5. Sadeghi B, Arvieux C, Glehen O, Beaujard AC, Rivoire M, Baulieux J, et al. Peritoneal carcinomatosis from non-gynecologic malignancies: results of the EVOCAPE 1 multicentric prospective study. Cancer 2000 Jan 15;88(2):358-363. [Medline: 10640968]
6. Yonemura Y, Endou Y, Shinbo M, Sasaki T, Hirano M, Mizumoto A, et al. Safety and efficacy of bidirectional chemotherapy for treatment of patients with peritoneal dissemination from gastric cancer: selection for cytoreductive surgery. J Surg Oncol 2009 Sep 15;100(4):311-316. [doi: 10.1002/jso.21324] [Medline: 19697437]
7. Sugarbaker PH. New standard of care for appendiceal epithelial neoplasms and pseudomyxoma peritonei syndrome? Lancet Oncol 2006 Jan;7(1):69-76. [doi: 10.1016/S1470-2045(05)70539-8] [Medline: 16389186]
8. Verwaal VJ, Bruin S, Boot H, van Slooten G, van Tinteren H. 8-year follow-up of randomized trial: cytoreduction and hyperthermic intraperitoneal chemotherapy versus systemic chemotherapy in patients with peritoneal carcinomatosis of colorectal cancer. Ann Surg Oncol 2008 Sep;15(9):2426-2432. [doi: 10.1245/s10434-008-9966-2] [Medline: 18521686]
9. Matharu G, Tucker O, Alderson D. Systematic review of intraperitoneal chemotherapy for gastric cancer. Br J Surg 2011 Sep;98(9):1225-1235. [doi: 10.1002/bjs.7586] [Medline: 21644239]
10. Braam HJ, Schellens JH, Boot H, van Sandick JW, Knibbe CA, Boerma D, et al. Selection of chemotherapy for hyperthermic intraperitoneal use in gastric cancer. Crit Rev Oncol Hematol 2015 Sep;95(3):282-296. [doi: 10.1016/j.critrevonc.2015.04.004] [Medline: 25921419]
11. Edge SB, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti A, editors. AJCC Cancer Staging Manual, 7th Edition. New York, NY: Springer; 2011.
12. Jacquet P, Sugarbaker PH. Clinical research methodologies in diagnosis and staging of patients with peritoneal carcinomatosis. Cancer Treat Res 1996;82:359-374. [Medline: 8849962]
13. Verwaal VJ, van Tinteren H, van Ruth S, Zoetmulder FA. Predicting the survival of patients with peritoneal carcinomatosis of colorectal origin treated by aggressive cytoreduction and hyperthermic intraperitoneal chemotherapy. Br J Surg 2004 Jun;91(6):739-746. [doi: 10.1002/bjs.4516] [Medline: 15164445]
14. Sugarbaker PH. Peritonectomy procedures. Ann Surg 1995 Jan;221(1):29-42. [Medline: 7826158]
15. Coccolini F, Cotte E, Glehen O, Lotti M, Poiasina E, Catena F, et al. Intraperitoneal chemotherapy in advanced gastric cancer. Meta-analysis of randomized trials. Eur J Surg Oncol 2014 Jan;40(1):12-26. [doi: 10.1016/j.ejso.2013.10.019] [Medline: 24290371]
16. Mi DH, Li Z, Yang KH, Cao N, Lethaby A, Tian JH, et al. Surgery combined with intraoperative hyperthermic intraperitoneal chemotherapy (IHIC) for gastric cancer: a systematic review and meta-analysis of randomised controlled trials. Int J Hyperthermia 2013;29(2):156-167. [doi: 10.3109/02656736.2013.768359] [Medline: 23418917]
17. Gill RS, Al-Adra DP, Nagendran J, Campbell S, Shi X, Haase E, et al. Treatment of gastric cancer with peritoneal carcinomatosis by cytoreductive surgery and HIPEC: a systematic review of survival, mortality, and morbidity. J Surg Oncol 2011 Nov 01;104(6):692-698. [doi: 10.1002/jso.22017] [Medline: 21713780]
18. Elias D, Bonnay M, Puizillou JM, Antoun S, Demirdjian S, El OA, et al. Heated intra-operative intraperitoneal oxaliplatin after complete resection of peritoneal carcinomatosis: pharmacokinetics and tissue distribution. Ann Oncol 2002 Feb;13(2):267-272. [Medline: 11886004]
19. Miyamoto K, Shimada T, Sawamoto K, Sai Y, Yonemura Y. Disposition kinetics of taxanes in peritoneal dissemination. Gastroenterol Res Pract 2012;2012:963403 [FREE Full text] [doi: 10.1155/2012/963403] [Medline: 22666236]
20. Gelderblom H, Verweij J, Nooter K, Sparreboom A. Cremophor EL: the drawbacks and advantages of vehicle selection for drug formulation. Eur J Cancer 2001 Sep;37(13):1590-1598. [Medline: 11527683]
21. Sugarbaker PH, Ryan DP. Cytoreductive surgery plus hyperthermic perioperative chemotherapy to treat peritoneal metastases from colorectal cancer: standard of care or an experimental approach? Lancet Oncol 2012 Aug;13(8):e362-e369. [doi: 10.1016/S1470-2045(12)70210-3] [Medline: 22846841]
22. Levine EA, Stewart JH4, Shen P, Russell GB, Loggie BL, Votanopoulos KI. Intraperitoneal chemotherapy for peritoneal surface malignancy: experience with 1,000 patients. J Am Coll Surg 2014 Apr;218(4):573-585 [FREE Full text] [doi: 10.1016/j.jamcollsurg.2013.12.013] [Medline: 24491244]

23. Bentrem D, Wilton A, Mazumdar M, Brennan M, Coit D. The value of peritoneal cytology as a preoperative predictor in patients with gastric carcinoma undergoing a curative resection. Ann Surg Oncol 2005 May;12(5):347-353. [doi: 10.1245/ASO.2005.03.065] [Medline: 15915368]
24. Wong J, Kelly KJ, Mittra A, Gonen M, Allen P, Fong Y, et al. RT-PCR increases detection of submicroscopic peritoneal metastases in gastric cancer and has prognostic significance. J Gastrointest Surg 2012 May;16(5):889-96; discussion 896. [doi: 10.1007/s11605-012-1845-2] [Medline: 22362071]
25. Bonenkamp JJ, Songun I, Hermans J, van de Velde CJ. Prognostic value of positive cytology findings from abdominal washings in patients with gastric cancer. Br J Surg 1996 May;83(5):672-674. [Medline: 8689216]
26. Lee SD, Ryu KW, Eom BW, Lee JH, Kook MC, Kim YW. Prognostic significance of peritoneal washing cytology in patients with gastric cancer. Br J Surg 2012 Mar;99(3):397-403. [doi: 10.1002/bjs.7812] [Medline: 22101572]
27. Wagner AD, Unverzagt S, Grothe W, Kleber G, Grothey A, Haerting J, et al. Chemotherapy for advanced gastric cancer. Cochrane Database Syst Rev 2010 Mar 17(3):CD004064. [doi: 10.1002/14651858.CD004064.pub3] [Medline: 20238327]

Abbreviations

5-FU: 5'fluorouracil
DCF: docetaxel with cisplatin and 5-fluorouracil
DLT: dose limiting toxicity
ECC: epirucibin with cisplatin and capecitabine
HIPEC: hyperthermic intraperitoneal chemotherapy
MTD: maximum tolerated dose
ULN: upper limit of normal

Edited by G Eysenbach; submitted 31.03.17; peer-reviewed by B Ansa; accepted 30.05.17; published 13.07.17.

Please cite as:
van der Kaaij RT, Braam HJW, Boot H, Los M, Cats A, Grootscholten C, Schellens JHM, Aalbers AGJ, Huitema ADR, Knibbe CAJ, Boerma D, Wiezer MJ, van Ramshorst B, van Sandick JW
Treatment of Peritoneal Dissemination in Stomach Cancer Patients With Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy (HIPEC): Rationale and Design of the PERISCOPE Study
JMIR Res Protoc 2017;6(7):e136
URL: http://www.researchprotocols.org/2017/7/e136/
doi:10.2196/resprot.7790
PMID:28705789

Protocol

Data Preparation for West Nile Virus Agent-Based Modelling: Protocol for Processing Bird Population Estimates and Incorporating ArcMap in AnyLogic

Hamid Reza Nasrinpour[1], MSc; Alexander A Reimer[1], BSc; Marcia R Friesen[1], PhD; Robert D McLeod[1], PhD

University of Manitoba, Electrical and Computer Engineering Department, Winnipeg, MB, Canada

Corresponding Author:
Hamid Reza Nasrinpour, MSc
University of Manitoba
Electrical and Computer Engineering Department
E1-450 EITC, University of Manitoba
Winnipeg, MB, R3T 5V6
Canada
Phone: 1 204 474 7360
Fax: 1 204 474 7312
Email: Hamid.Nasrinpour@UManitoba.CA

Abstract

Background: West Nile Virus (WNV) was first isolated in 1937. Since the 1950s, many outbreaks have occurred in various countries. The first appearance of infected birds in Manitoba, Canada was in 2002.

Objective: This paper describes the data preparation phase of setting up a geographic information system (GIS) simulation environment for WNV Agent-Based Modelling in Manitoba.

Methods: The main technology used in this protocol is based on AnyLogic and ArcGIS software. A diverse variety of topics and techniques regarding the data collection phase are presented, as modelling WNV has many disparate attributes, including landscape and weather impacts on mosquito population dynamics and birds' roosting locations, population count, and movement patterns.

Results: Different maps were combined to create a grid land cover map of Manitoba, Canada in a shapefile format compatible with AnyLogic, in order to modulate mosquito parameters. A significant amount of data regarding 152 bird species, along with their population estimates and locations in Manitoba, were gathered and assembled. Municipality shapefile maps were converted to built-in AnyLogic GIS regions for better compatibility with census data and initial placement of human agents. Accessing shapefiles and their databases in AnyLogic are also discussed.

Conclusions: AnyLogic simulation software in combination with Esri ArcGIS provides a powerful toolbox for developers and modellers to simulate almost any GIS-based environment or process. This research should be useful to others working on a variety of mosquito-borne diseases (eg, Zika, dengue, and chikungunya) by demonstrating the importance of data relating to Manitoba and/or introducing procedures to compile such data.

(JMIR Res Protoc 2017;6(7):e138) doi:10.2196/resprot.6213

KEYWORDS

AnyLogic; shapefiles; ArcMap; West Nile Virus; land cover; bird roosts; bird home range; Manitoba

Introduction

This paper examines data inputs into an agent-based model (ABM) and simulation of West Nile Virus (WNV) using the AnyLogic software [1], with a specific focus on data collection and compatibility, and preparation or processing techniques. Mosquitoes of certain genera carry and transmit WNV to other animals including humans. Under certain weather and habitat conditions, adult female mosquitoes take a blood meal from their hosts to obtain necessary nutrition to lay their eggs. During the next stages of the mosquito life-cycle, eggs hatch into larvae, and then begin molting their skins until they change into pupae that develop into adult mosquitoes [2]. The main means of transmission and spread of WNV is through birds [3]. An infected mosquito can infect a (healthy) bird by feeding on it. An infected bird can, in turn, infect a (healthy) mosquito that

bites the bird. In this transmission cycle, birds act as amplifying hosts since the virus is amplified in their bloodstream, and it could be transmitted to the next group of feeding mosquitoes. Conversely, various kinds of mammals (including humans) act as incidental or dead-end hosts that cannot pass the virus to another host or feeding mosquitoes. The process is shown in Figure 1.

Many scientific studies have examined the transmission dynamic modelling of WNV. Various approaches to model WNV transmission risk or spread are reviewed in Chevalier et al [4]. Most notably, differential equation (DE) models have been utilized to model disease transmission dynamics. Thomas and Urena formulated a difference equation for WNV evolution in a mosquito-bird-human community with a focus on mitigation via pesticide [5]. Wonham et al developed a single-season susceptible-infectious-removed DE model for WNV transmission in a bird-mosquito population [6]. Bowman et al proposed a single-season DE model of WNV transmission dynamics in a mosquito-bird-human population [7]. In this context, ABMs could be deployed to incorporate biodiversity of birds and mosquitoes as completely as possible, along with their interactions with humans. To date, the use of ABMs in the WNV literature has been rather scant, even though it has been extensively employed in many different health care applications [8-13]. In the WNV literature, an ABM was proposed by Li et al [14] for an area of 165 km^2in Cook County, Illinois, which was modelled as a raster map. Three possible bird species of black-capped chickadee, blue jay, and American crow were considered within this ABM. Another ABM with no human component was proposed by Bouden et al [15] for southern Quebec, Canada. Two bird-biting species of *Culex pipiens* and *Culex restuans*, and two general groups of birds (ie, American crows and the remainder, competent species) were considered within this ABM. In their respective ABM, birds are grouped into roost agents whose moving behavior is modelled with particle systems proposed by Reeves [16], wherein birds' flight speed and home range are crucial model parameters.

Although AnyLogic is a powerful multi-paradigm modelling framework, there are few user group resources or forums available for its users. To the best of our knowledge, there is only one active user community in LinkedIn for the AnyLogic modelling software. In addition to more traditional simulation, AnyLogic also has relatively recent support for geographic information system (GIS) simulation and modelling. Within GIS, Esri shapefiles are the most commonly used [17-21]. The shapefile format includes vector data representing location, shape, and attributes of geographic features such as lakes, mountains, buildings, and roads.

However, it can be quite difficult to format shapefiles in a way that a modeler could easily apply or use within the AnyLogic framework for GIS-based simulations. This paper explains (in a tutorial-based style) the procedures used to prepare the data required to develop an ABM of WNV spread in Southern Manitoba, Canada. The region of interest is an area of approximately 148,812 km^2that is partially covered by grasslands (Canadian Prairies), where the primary WNV vector is *Culex tarsalis*.

The value of ABMs is being established through a growing literature base in various fields, but the modelling approach itself is still considered a relative newcomer in relation to mathematical models and more established simulation models of social and human agent systems. ABM is recognized as a computational model that permits a distinctive approach to complementary empirical research [22,23]. In ABMs, dynamic social systems are modelled as a collection of highly stochastic agents (in many cases, primarily humans), their individual profiles or characteristics, their individual behaviors, and interactions between agents and between agents and the environment. Agents are purposeful and autonomous entities able to assess their situation, make decisions, and compete or co-operate with one another on the basis of a set of rules. The conceptual depth of an ABM is derived from its ability to model behavior that may be counterintuitive and/or to discern a complex behavioral whole that is greater than the sum of its parts. ABM provides a natural description of a system that can be calibrated and validated by representative expert agents and is flexible enough to be tuned to high degrees of sensitivity in agent behaviors and interactions. ABMs are particularly well suited to dissipative irreversible system modelling in which agent behavior is complex, nonlinear, stochastic, and may exhibit memory or path-dependence [24,25]. However, the full potential of ABMs remains unrealized as the methods to exploit massive amounts of data are still emerging. The key challenges of an ABM approach applied to socio-ecological systems are improving agent decision and adaption models, improving validation and verification, and improving spatial representation and levels of abstraction [26]. Furthermore, the key challenges for the ABM approach to advance and realize its potential include validating agent behaviors and emergent phenomena, better agent behavioral models, improved simulation analytics, and improving hybrid and large-scale ABMs [27-29].

As noted, WNV is carried and transmitted by mosquito vectors. Birds and humans are among the hosts for the infection. A WNV model requires, at a minimum, data on these three agent types. The mosquito-related data include (but are not limited to) weather for population dynamics, landscape features for habitat preferences, and twilight times and daylight duration for setting peak periods of mosquito agents' biting activities. A conceptual ABM may model the area as a grid, in which each cell has different properties regarding mosquito population dynamics. Such data would be used to tune or modulate the mosquito parameters of each cell according to weather, landscape, and daylight conditions, ultimately governing mosquito behaviors and interactions. The bird-related data that are collected include nesting/roosting locations, population estimates of each species, home range areas, breeding season months, communal or solitary living habits, and typical flight speeds. A conceptual ABM may distribute and initialize the bird agents of different species based on the population estimates and roosting locations. The movement patterns of birds may be determined based on the home range, flight speed, and living habits of each species. For instance, in each time-step, birds could pick a random flight speed in a certain range and fly up to a certain maximum distance. The algorithms used for movement simulation may be different depending on whether the species are solitary, and whether they are mating at a particular time of the year. The

human-related data necessary to incorporate realistic human movement patterns include census counts, street networks, and coordinates of cellular telephone towers providing service for a number of anonymized mobile users, where mobile phones act as proxies for their users. A conceptual ABM may initially distribute human agents over the map based on the census data. Human agents may then move inside the street network according to cellular phone towers or trajectories provided by the data, with cellphones serving as proxies for individuals. The high-level architecture of such an ABM is illustrated in Figure 2. This paper describes and presents the methodology and results for collecting, assembling, and reformatting some of these data for each agent type of a conceptual ABM of WNV propagation.

Figure 1. Mosquito life cycle and West Nile Virus transmission cycle diagram.

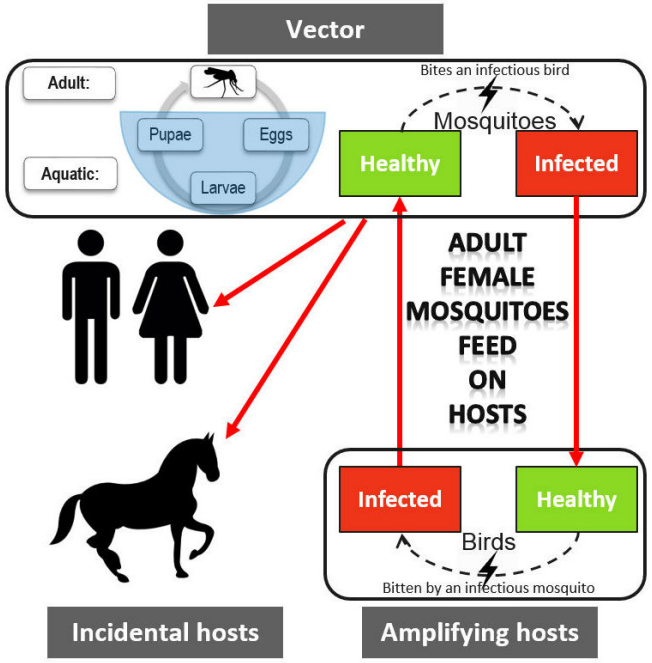
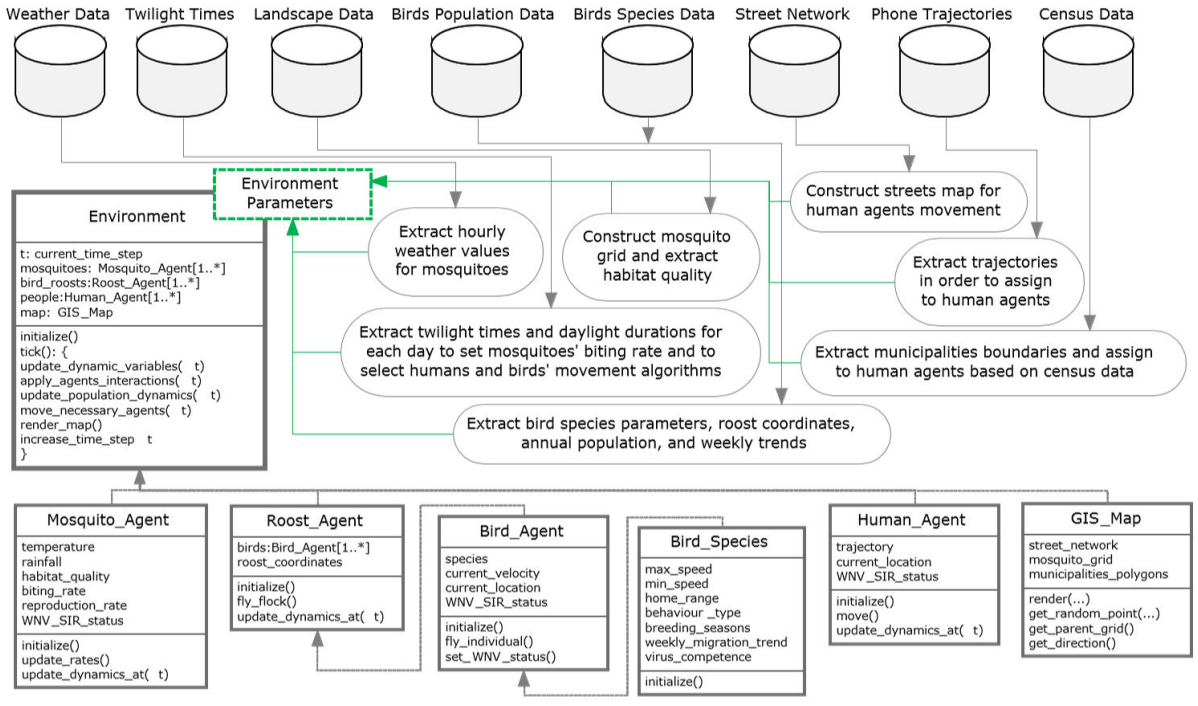


Figure 2. High-level architecture of the ongoing agent-based model.



Methods

The validity and relevance of any ABM relies on incorporating as much real and meaningful data as possible to characterize the environment and the agents. This section examines the collection and processing techniques of data most relevant for an ABM associated with WNV. This information includes agent data related to mosquitoes, birds, and humans. Similar data processing would be required for other mosquito-transmitted diseases.

The applied techniques are described in some detail, in order to assist others using AnyLogic in combination Esri ArcGIS, which combine to provide a powerful toolbox to modelers, particularly those working on geo-simulations. The details provided here would significantly reduce frustration for other modelers who are beginning to utilize the software, as there is a high level of subtlety in the mechanism/interface of both suites of software. The techniques also illustrate a primary challenge in ABM: specifically, combining different and often disparate datasets.

Mosquito Data

Weather

Preparing weather data is a simple process, and does not need to be discussed in detail; this is primarily due to the familiarity everyone has with weather, as well as readily available data. For this work, one weather station per municipality was considered. The weather data (including precipitation and temperature) for the years 2002-2014 were downloaded from Canada National Climate Data and Information Archive and BioSim databases [30] whenever possible. For the municipalities in which there was no weather station, and for filling in any missing data in the real data, BioSim was used to provide simulated weather data. As an input point for the BioSim built-in simulator [30], whenever possible the coordinates of an existing weather station were used. Otherwise, a location provided by Wikipedia and confirmed on Google maps was used as the coordinates of a municipality. These data were combined with the gathered hourly and daily data. Wherever simulated data were used (in 114 out of 118 municipalities included), the data were flagged for future reference.

Landscape

A common approach to describe landscape features is to classify different regions of land into various categories based on ground cover, ground features, and land use. As such, this land feature is called either *land cover* or *land use* classification. These categories or classes may include an urban area, rural area, grassland, agricultural cropland, various forest types, sands, roads, and water. When the classes are defined, remote sensing satellite images (from the Manitoba Remote Sensing Centre in our case) are usually used to classify each region.

This data and other geospatial data are typically available in the shapefile format. The GIS library and components available in AnyLogic have the ability to work with shapefiles. As such, one way to add land-based habitat characteristics for mosquitoes in a WNV model in any GIS-integrated software (such as AnyLogic) is through shapefiles. A square grid shapefile of Southern Manitoba was chosen, where each cell represented a 5 x 5 km^2mosquito site. Within each cell, the area of each land cover class can be calculated and recorded in the shapefile database file (DBF). The shapefile can then be loaded in AnyLogic. For any given coordinate in the map, one could retrieve the covering mosquito cell and its associated information in the shapefile database. Here, the procedure to create such a shapefile using the Esri ArcMap (part of the ArcGIS software package) is explained in detail. It is noted that the changes in land cover over the span of simulation years are negligible.

First, the land cover data for each region of Manitoba was downloaded from the Manitoba Initiative Data Warehouse [31] in the shapefile format. The class of land cover for each feature (polygon) in the data was identified with a *GridCode* number in the shapefile DBF. The coordinate system of these shapefiles is the Universal Transverse Mercator (UTM), which is a projected coordinate system that enables the ArcMap to calculate geometric properties of a polygon feature such as area or perimeter. For this reason, the coordinate system was kept unchanged at this time.

All shapefiles were then added together to make a single general map of land cover using the *append* command in the geo-processing toolbox of ArcMap. Next, the geometry of the new map was repaired using the *features* toolset under the data management toolbox, which is part of the geo-processing toolbox. Repairing the geometry was necessary to fix some common geometry problems (eg, empty parts or duplicate vertices). The outcome was a map (or shapefile) with standard geometric specifications, as shown in Figure 3.

At this stage, the 5 x 5 km^2mosquito grid had to be built to incorporate the land cover data from the previously prepared shapefile. An overlay grid of southern Manitoba (ie, region of interest) with an accuracy of 5 km x 5 km was created using the *Fishnet* command in the geo-processing toolbox of ArcMap. The output of this procedure was a rectangle-shaped map containing many square cells, as shown in Figure 4. It is noted that the coordinate system of this grid was the UTM, the same as that of the data source and data frame of all the layers in the ArcMap project.

Subsequently, the land cover shapefile from the previous step had to be attached to the mosquito grid. To do so, the *identity* command in the geo-processing toolbox was applied to find the geometric intersection of the grid and land cover map by setting the grid as the *identity feature*, and the land cover map as the *input feature*. As a result, the land cover map (or portions thereof) that overlapped the grid obtained the attributes of the grid, which were basically the square cell identifications (IDs). This means for every single pair of a square cell and a land cover polygon with some overlapping area, a new polygon feature is created in the new map (or shapefile). Figure 5 illustrates an example of this operation. The new map is called the *land cover grid*. For all entries (polygon features) with a known square cell ID in the land cover grid, the land cover *GridCode* is also known. For the next step, the geometric area of each of these entries is required. Therefore, a new field called

Area_Sq_M was added to the shapefile database using the *attribute table* in the ArcMap. The area of each feature in square meters was then calculated and stored in this field using the *calculate geometry* feature in the *attribute table*.

There are ways to find the proportional area of each land cover class for each square cell using ArcMap. Once these metadata are calculated, they can be stored in the shapefile DBF format, and can be accessed in a classical FoxPro database query. However, there are two techniques that a developer should consider. First, the filename plus its extension must be less than eight characters. Second, there is only one table per DBF, so the table name in a Structured Query Language (SQL) *select* command is the same as the filename, and the database address in the connection string only includes the location without the filename. A sample Java code is provided in Multimedia Appendix 1, illustrating how to connect to a shapefile DBF using a Miscrosoft (MS) Access dBase driver connection string.

Given the limitation of shapefile databases, a decision was made to clone the shapefile database into an MS access database, and apply necessary queries and adjustments there. As such, the land grid shapefile database was exported into a text file, and the text file was imported into an MS Access dBase. Using a small C# application, the proportional area of each land cover class within each square cell was then calculated and stored in an MS Access table where the primary key was the square cell ID. This means that for any given mosquito cell, if the cell ID is known, a simple SQL query could reveal the exact information regarding the land cover within the cell. The AnyLogic GIS library is helpful in these instances. Once a shapefile is loaded into a GIS map component of AnyLogic, for any given pair of latitude and longitude, the ID (or any other attribute) of the shapefile feature at the same point is accessible using the *findPoliticalArea* function. In our case, AnyLogic was set to return the square cell ID for the polygon feature over a given coordinate. The cell ID can, in turn, be used to query land cover information of the area.

The last step is to prepare the mosquito grid shapefile to be loaded into AnyLogic. For this, the mosquito grid must be clipped to reduce the number of unnecessary cells in which no information about the land cover is present. First, a mask of all the cells with useful information is created to clip out the remaining cells. The mask creation procedure is as follows: (1) the *dissolve* command from the geo-processing tool is applied by setting the land cover grid (including the grid and land cover data) as the input, and (2) the "Create multipart feature" option is unchecked; no field is added to the *dissolve* or *statistics* fields.

This would give a single polygon for the whole map of the land cover grid, which could be used as the boundary of the region of interest. At this stage, a hole was noticed in the single boundary (mask) polygon which was due to missing data in the land cover map. As such, a filling donut holes procedure was necessary: (1) the *editor toolbar* was added to the ArcMap toolbar, then an edit session was started by selecting the *editor toolbar*; (2) the mask in the *create features* bar was selected as the active layer, then a template as the *construction tool* from the box below it was selected; (3) a rectangle or a polygon over the donut hole was drawn, then edits were saved and the edit session ended; and (4) once again the shapefile was dissolved to merge all polygons in this shapefile together. At this stage, the mask without any holes was ready, as shown in Figure 6.

To exclude the unnecessary mosquito cells, either the *clip* or *intersection* command must be applied on the mask and the mosquito grid. It is noted that while the *intersect* method saves a copy of feature ID (FID) fields of both shapefiles in the new shapefile, the *clip* method keeps no record of FIDs. Therefore, if one uses the *clip* method, the FID of each cell of the grid (ie, mosquito cell ID) should be copied into a new field beforehand.

Finally, the coordinate system must be projected from UTM to World Geodetic System 1984 so that it is consistent with AnyLogic. One more vital technique is that the shapefile must have at least two fields (other than the default FID and Shape) so that it can be loaded within AnyLogic, in particular for use with the *findPoliticalArea* function.

Figure 3. Manitoba Land Cover map (shapefile) generated by combing data from all regions. Blue color represents water body or wetlands; green represents different forest types; orange represents agricultural or forage cropland.

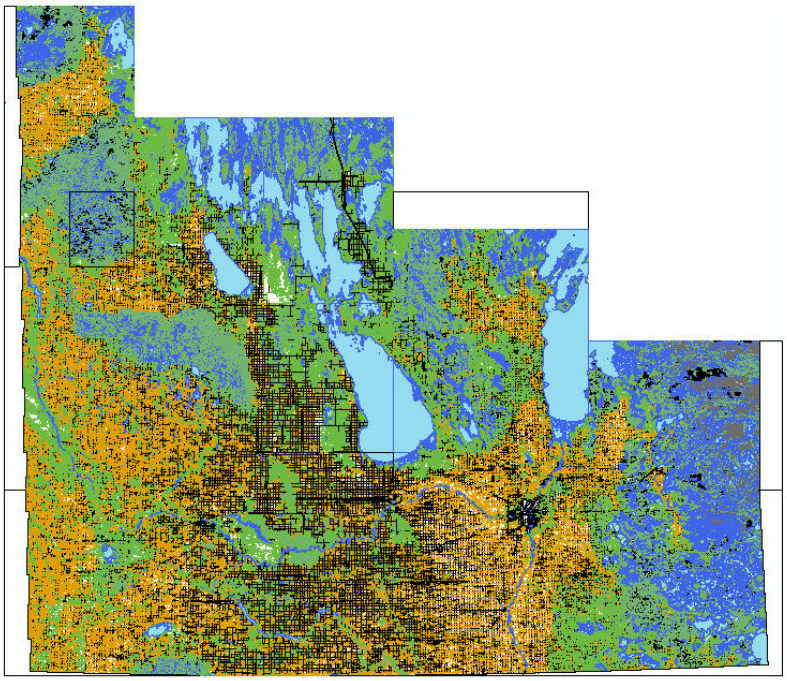


Figure 4. Mosquito grid beneath the map of municipal boundaries. The municipalities are shown (in color) for a better visual clarity of where the mosquito grids are located.

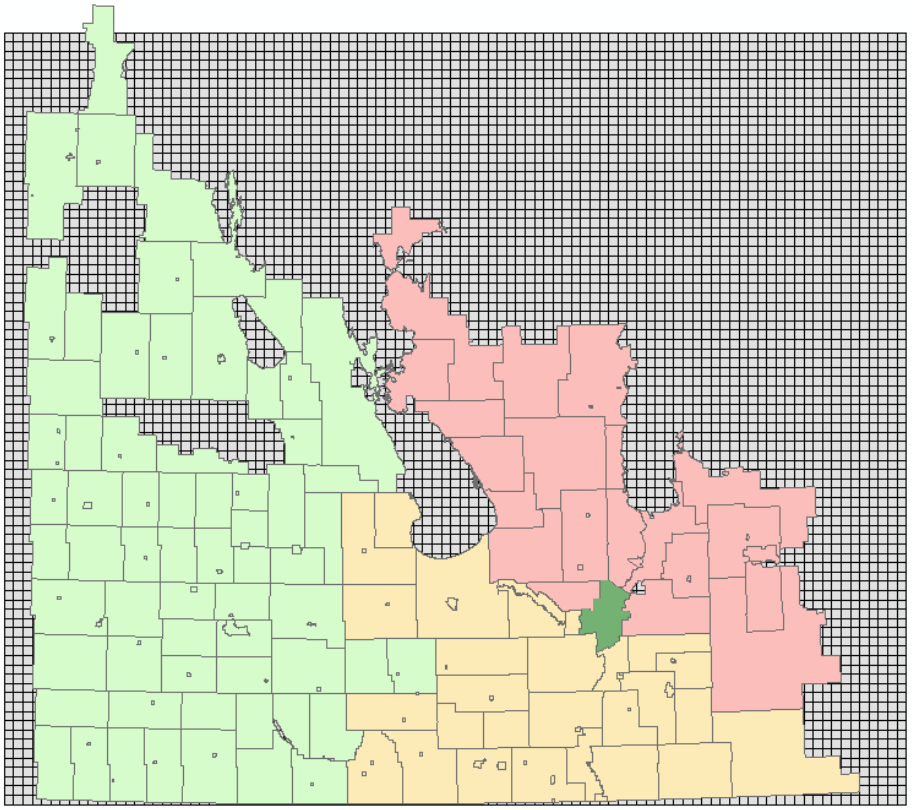


Figure 5. The result of the "identity" command by setting mosquito grid as the "identity feature" and municipal boundaries as the "input feature".

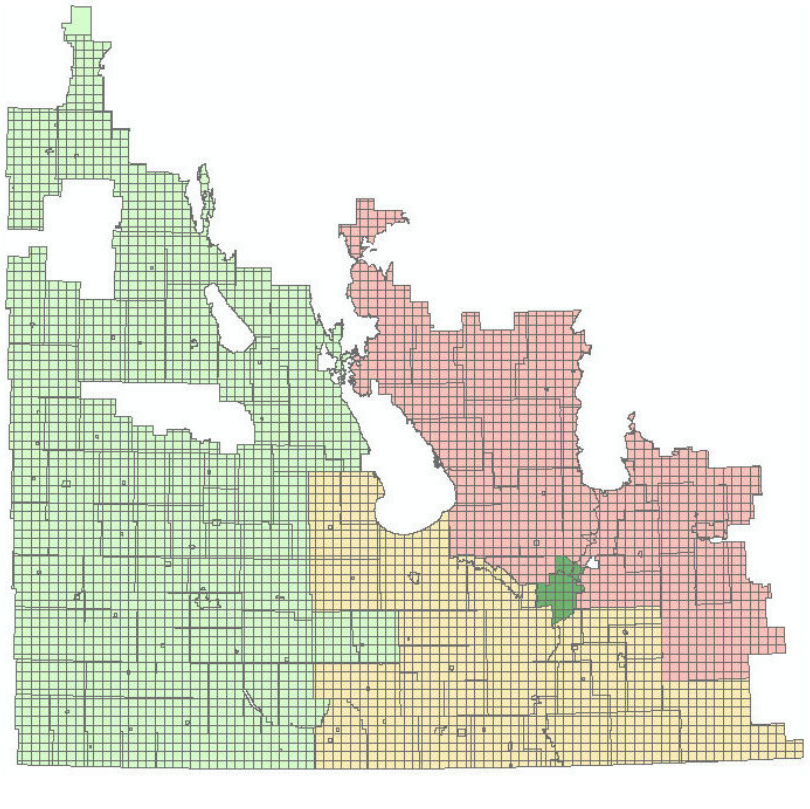
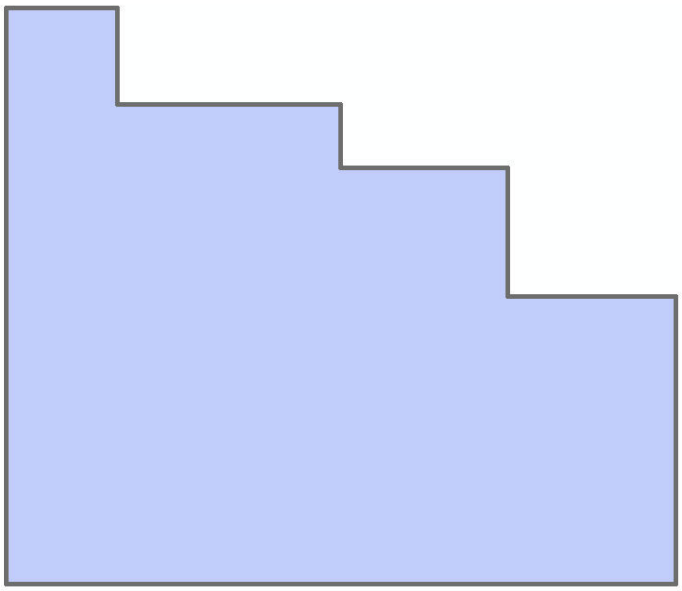


Figure 6. The boundary mask of land cover grid. The area indicates locations where the land cover data are known.



Bird Data

Population Estimate

Many different data sources had to be combined to produce the bird population database. Since detailed population maps were not readily available for most species, a process had to be developed to estimate the population of individual species within relatively small areas. Two approaches were developed to create these estimates. The first was a “top-down” approach, which relied heavily on population estimates for large regions and relative abundance maps for local distributions. The second method could be considered a “bottom-up” approach. This approach used localized point count surveys and species-specific correction factors to estimate population. Using these two separate approaches, it was possible to establish population estimates that were suitable for our models. As with many ABM

approaches attempting to use as realistic and meaningful data as possible, best guess estimations were required. As more accurate data becomes available, the veracity of the estimates improves.

Partners In Flight Approach

The first "top-down" approach used the United States Geological Survey (USGS) abundance maps, which were created by USGS from their 50 roadside stops breeding bird surveys that were conducted at peak breeding season (June for most species) [32]. The files were downloaded from the website in the form of shapefiles [32]. Each cell in these maps contained a relative abundance value representing the average number of birds observed by the survey in that area. The data from these surveys had been extrapolated and processed so that a map of the entire United States and Southern Canada was available (see Figure 7).

These abundance maps were then combined with a 10 x 10 km^2grid, provided by the Manitoba Breeding Bird Atlas (MBBA) [33]. This was done to make the data compatible with the breeding location data from the MBBA. The grid was downloaded as a Keyhole Markup Language Zipped file from the MBBA website, and combined with the abundance map shapefiles using a Python script in the Esri ArcMap.

Each 10 km x 10 km square received the relative abundance value of the abundance map cell that covered it. If a square was covered by parts of two or more cells, the relative abundance value was taken as the weighted mean between all cells values, with more weight being given to those cells that covered the majority of the 10 km x 10 km square. If the square was not completely covered by the abundance map cells, the parts that were not covered were considered to be covered by a cell with a relative abundance value of zero. This value assumed that the species in question did not live beyond the edges of the abundance map. In many places, this will have been a valid assumption, but at the edges of the USGS study area, this may have caused an underestimation of abundance. In this regard, the relative abundance data was combined with the MBBA 10 km x 10 km squares as shown in Figure 8.

Next, the relative abundances were combined with the Partners in Flight (PIF) population estimates for regions in Manitoba [34]. Each PIF population estimate was an estimated population of a certain species for an individual Bird Conservation Region (BCR) in Manitoba. The study area contained three BCR regions, and the PIF gave population estimates for each of the three regions for all species (see Figure 9 [35]). The population was distributed between the squares in each region to create real population estimates for each square. A greater population was given to squares with a higher relative abundance. Some squares were not exactly 10 km x 10 km, so a greater population was also given to the larger squares. The equation for the estimated real population of each square is provided in Figure 15.

To achieve an idea of how the population changed over the course of a year (mostly due to migration), the population estimates of each square were combined with weekly abundance estimates of bird species in Manitoba, made available by the Manitoba Naturalist Society [36]. The population estimate was assumed to be the population at the time of maximum abundance in June when the USGS point counts were conducted. From this value, the rest of the data were scaled accordingly. In this way, the single population estimate was extrapolated over the year.

Finally, the squares were filtered by whether or not the bird species bred in that area. Using the breeding status data provided by the MBBA, it was possible to remove each square that did not contain a nesting or roosting area within it. Considering the requirements of the WNV ABM, no differentiation was made between roosting and breeding areas.

An assumption was made that by filtering out squares after dividing population estimates, the number of birds in each square was underestimated. However, efforts to divide the population after filtering by breeding status led to negligibly different results (<0.5%), since most squares where a species was found contained breeding, so this effect could be ignored.

Figure 7. An example of the USGS abundance map. The darker areas denote areas of high species abundance.

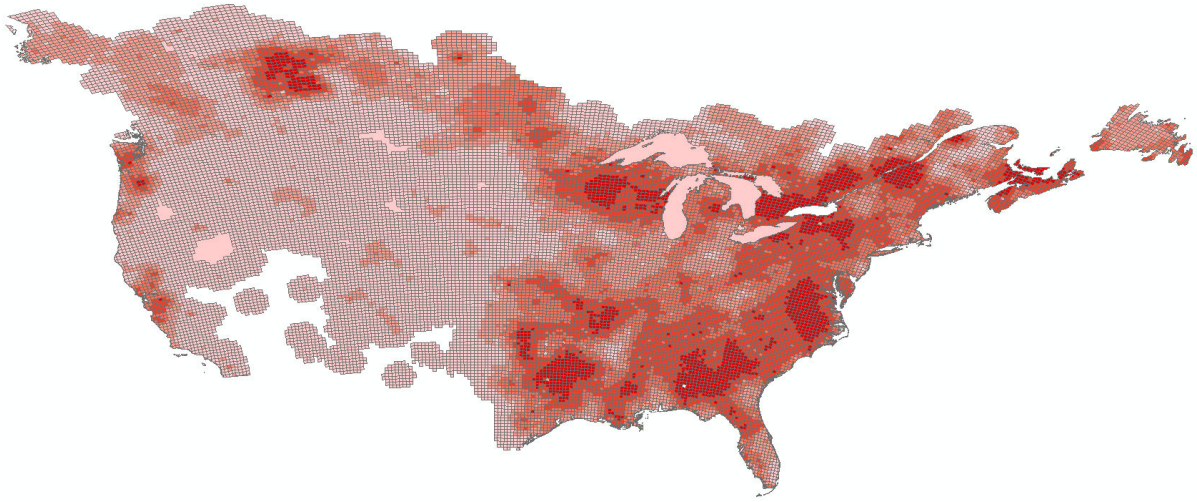


Figure 8. United States Geological Survey abundance data for Manitoba quantized into a 10 km by 10 km grid.

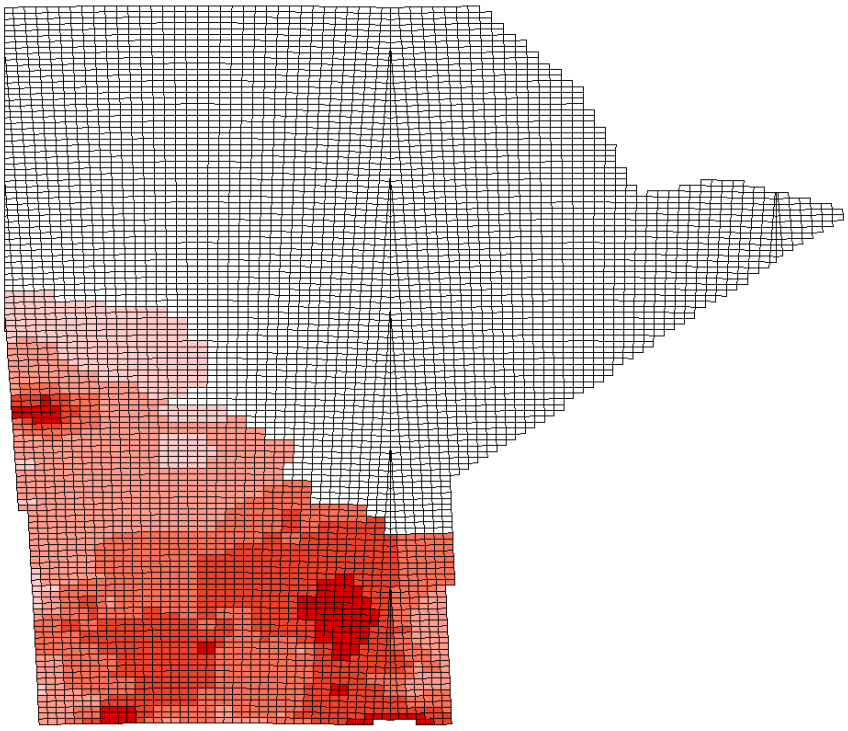
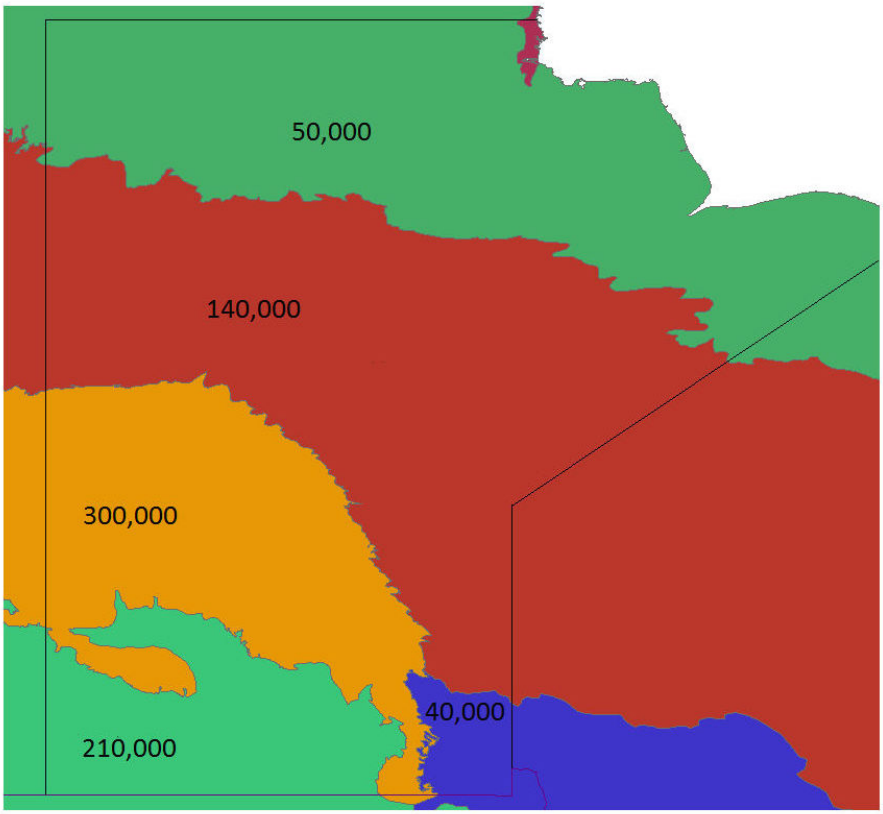


Figure 9. Bird Conservation Regions in Manitoba, with example population estimates for each region. Population estimates did not include birds in the same Bird Conservation Region outside of Manitoba.



Boreal Avian Modelling Approach

The population was also estimated using a second process, the "bottom-up" approach. Using this approach, we began with point count data that was provided by the MBBA. This data was only for squares where breeding was suspected, and gave a larger sample size than the USGS abundance maps had within Manitoba. The MBBA point counts were conducted by a participant standing in several predetermined locations inside each 10 km x 10 km square who recorded the number of birds that they observed or heard within 5 minutes. This system did not record all birds in the area, but it did give a relative index into how many birds were in the area. To convert the point count data into a real population estimate for the square, correction factors needed to be applied.

Correction factors were obtained from the Boreal Avian Modelling (BAM) project [37]. Although BAM takes many different and complex correction factors into consideration as they create their own population estimates, only two are considered here: the effective detection radius (EDR) and singing rate. The EDR is defined as the distance from the point of observation where as many birds were detected beyond this radius as were undetected within this radius [37]. This factor took into consideration the fact that a bird further away would be less likely to be detected, and that certain species would be harder to detect at further distances. Thus, when the point count data were considered, it was reasonable to assume that the point count numbers correlated to the number of birds within the EDR.

The singing rate was given as the rate at which a bird sang out per minute, or similarly the proportion of a bird population that sang at least once in one minute. Since most point counts depend on hearing the sound of a bird more than seeing it to identify the species, the singing rate gives a useful approximation of how many birds remain quiet and thus undetected during the point count. By multiplying the singing rate by the number of minutes spent in observation, one can find the proportion of birds that sang out and had a chance of being identified in the point count. If the point count was long enough, this proportion would rise above 100% as birds began to sing more than once. However, the observer for each point count was trained to count individual birds, not individual bird songs, so multiple bird songs by the same bird could be discarded [38]. Therefore, the singing rate-time product was capped at 100%. The population estimate for each square was calculated as shown in Figure 16.

After calculating population estimates for each square, the population was again modulated to show annual changes. This was done in the same fashion as the first "top-down" approach using the annual abundance data. In this way, both approaches were used to create usable population estimates for the model.

Species Data

Other data that were collected and inferred from a diverse variety of sources regarding each species are reported in Multimedia Appendix 1. These data include home range area, breeding season months, communal or solitary living habits, and typical flight speeds.

The spring/summer home range of all birds was considered to be a circular area. As such, the average radius in meters was calculated and reported in Multimedia Appendix 1. The home range of a given species depends heavily on the habitat and food abundance conditions. The top priority was to collect the data from Manitoba. If possible, reported mean home ranges for the landscapes neighboring the province were considered. When there were no data for similar landscapes, the mean of the home ranges (as reported in different sources and weighted by the sample sizes) was used. It was also desirable to avoid underestimating the average home range, as the ongoing ABM required the ceiling of an average home range to be set as the maximum flight distance for birds.

Breeding timing and living habit data were primarily collected from the Birds of North America online database [39]. The breeding season range goes up to, but does not include, the end month. Living habits were categorized into three groups: solitary roosting behavior, year-round communal roosting, and semiannual communal roosting. Semiannual communal roosting included species that roost individually or in pairs during the breeding season, and then form flocks for migration in the fall. In general, the roosting behaviors of birds are often difficult to categorize. These designations represent an estimate on which type of model each species' behavior may best fit in the specific ABM, and are not intended to reflect a universal definition of communal roosting.

Mean flight speed is reported in the format of meters per second in Multimedia Appendix 1. For many species, the data on flight speed were either very sparse or nonexistent. For such species, certain approximations had to be made, such as using the reported speed for a similar species of that genus or taking the average of reported speeds of the whole family. It was decided to find the typical flight speed at which birds fly/forage during a day; however, in most sources it was unclear what type of speed was measured. Values were generally either *minimum power speed* (*Vmp*) or *maximum range speed* (*Vmr*). If a certain species had both *Vmp* and *Vmr* available, the smaller *Vmp* would have been recorded as the flight speed of the species. Whenever there were only reports on the maximum flight speed, the minimum number in the given range of maximum flight speeds was used as the typical speed. It is notable that a bird's normal flight speed going from perch to perch is much less than the numbers reported in Multimedia Appendix 1. These values were treated as the ceiling of typical speed in the birds' movement component of the ongoing ABM, and the birds' minimum flight speed was set at two meters per second.

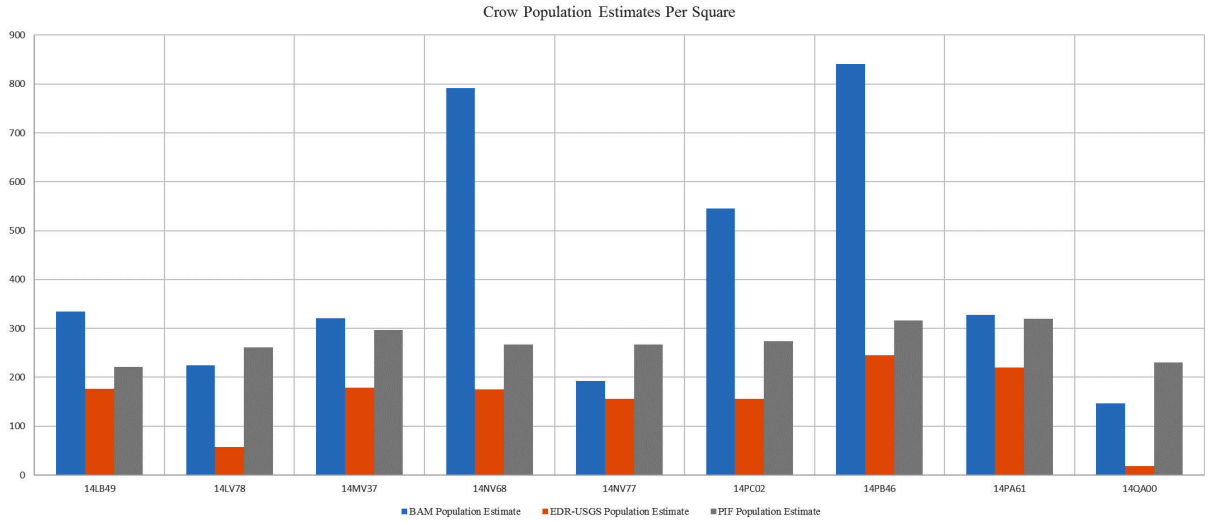
Human Data

The Open Street Map of the province was downloaded from GeoFabrik.de as a highly compressed Protocol-Buffer Binary Format file. The street map was then extracted from this binary file using the routing features of AnyLogic. A sample street map of Southern Manitoba including only trunk, primary, and secondary roads can be seen in Figure 10. The A* pathfinding algorithm was applied on this network for human agents' routing. Census data for each municipality of the province for initial location of human agents were downloaded from Statistics Canada. Municipal boundaries in Manitoba were downloaded

as a shapefile from the National Resources Canada website. The population of human agents then had to be distributed within these boundaries according to the census data for each municipality. AnyLogic has a *GISRegion* component, in which one can call the function *randomPointInside* to randomly choose a point inside the given region. Therefore, this function can be used to initialize the human agents' population inside each municipality. However, the shapefile polygon features, representing municipal boundaries, first had to be converted to AnyLogic *GISRegion(s)*. Up to AnyLogic version 7.2, the built-in converter was not fully functional to convert all the shapefile features to AnyLogic *GISRegion(s)*. A sample AnyLogic Java code for this nonintuitive conversion can be found in Multimedia Appendix 1. The code also gives hints to developers on how to extract all point coordinates of objects in a shapefile. It is notable that each shapefile has a different number of nested layers of objects. This may be the reason why the built-in converter does not work for all shapefiles.

For the purpose of this paper and brevity, human movement patterns, data collection, and processing methods are not discussed further, but these factors are integral to ongoing WNV agent-based modelling. In addition to the readily available census data mentioned above, other sources include those related to personal cellular devices, as well as technologies being developed for intelligent transportation systems. Earlier proofs of concept were demonstrated in prior work [13,40,41]. A further extension of this paper will discuss the preparation and manipulation of these data sources.

Figure 10. Comparison of crow population estimates between the Boreal Avian Modelling (BAM) and Partners In Flight (PIF) methods in some selected squares. EDR-USGS: Effective Detection Radius-United States Geological Survey.



Results

Mosquito Data

The final weather database had daily and hourly values of weather temperature and rainfall for 118 rural and urban municipalities in Manitoba from 2002 to 2014. This dataset could be used for any weather-dependent studies in the Southern Manitoba region. The final land cover database had information on 6067 square cells in Southern Manitoba. For each cell, the corresponding municipality and weather station, total area, coordinates, and area of different land cover classes present in the cell were known. The land cover classes used in this dataset include Agricultural Field, Deciduous Forest, Water Body, Range and Grassland, Mixed-Wood Forest, Wetland-Marsh, Wetland-Treed Bog, Treed Rock, Coniferous Forest, Fire-Burnt Area, Open Deciduous Forest/Shrub, Agricultural-Forage Crop, Cultural Features, Forest Cut Block, Sand and Gravel, Roads and Rail Lines, Wetland-Fen, and Lichen health. The land cover database can be used in geo-spatial studies in Southern Manitoba. Such studies are of particularly high importance for agricultural purposes. One limitation of the land cover database and the extraction procedure is that the land cover was assumed to be static. Generally, more work on land cover (and in particular on dynamic land cover changes) is ongoing. For instance, Murray-Rust et al proposed an open-frame ABM to capture changes in land cover [42]. As future work, the land cover extraction procedure could be automated using Python scripts in ArcGIS. Such an automated procedure makes the system adjustable in response to changes in land cover data. The land cover database, in conjunction with the weather database, could benefit studies that focus on the forecasting of mosquito-borne diseases in Sothern Manitoba.

Future work on weather data may focus on improving algorithms used for simulating missing data, particularly hourly rainfall values for a specific area, if hourly estimates are necessary. In this study, the BioSim software was applied for this purpose, which produced estimates of hourly rainfall values. Depending on the fidelity of the application, one may need to include more weather stations in Manitoba by going through the same procedures explained earlier.

Bird Data

The final bird database contained information on 152 different bird species. For each species, there were population estimates for each of the 2056 square cells, which were roughly 10 km x 10 km areas located in Southern Manitoba. Each of these population estimates was also used to create a weekly population

estimate for each square to represent weekly impacts of migration. Only squares in which some evidence of breeding had been found were included for each species, as these squares were assumed to also contain nocturnal roosts for the species [15]. This dataset could also be used by other researchers working on topics such as modelling birds' movements, bird interactions in various ABMs, and geo-simulations including birds.

Due to fundamental differences between the two population estimation approaches, their assumptions, and availability of data, the two estimates show a degree of disparity in some areas. The chart in Figure 11 shows a comparison of population estimates of American crow species for various locations (squares) in Manitoba. The BAM population estimates were calculated using the methodology previously discussed. The EDR-USGS estimates in Figure 11 were calculated in a similar manner, but used the USGS 50 stops data for point counts instead of the MBBA point counts. The PIF population estimates, as mentioned before, were calculated from the regional PIF estimates and abundance maps created from the USGS 50 stops data. The similarity between the EDR-USGS and PIF estimates in most of the squares reveals the importance of the availability of stops and point counts data. Notably, the difference between the two estimates in the other squares confirms the differences between the "top-down" and "bottom-up" approaches. Figure 12 shows the physical location of selected squares in Figure 11. To achieve an idea of how the two estimates compare against some historical data in Manitoba, an average density for a number of species was calculated from the average BAM and PIF estimates for the species across the province. In Figure 13 and Figure 14, these densities are compared against the Manitoban bird densities calculated for 1966-1994 by Downes and Collins [43] and reported in the work of Kirk et al [44] for two groups of species of short-distance and long-distance migrants. If a species winters mostly within Canada or North America, it is categorized as a short-distance migrant. If the birds mainly spend winters in Central or South America, they are considered long-distance migrants [44]. In general, for the long-distance migrants, the BAM densities have less disparity from the birds' densities provided by Downes and Collins [43], compared to the PIF. Conversely, for the short-distance migrants, the PIF densities are closer to the birds' densities provided by Downes and Collins [43].

Both bird population estimate approaches have several assumptions and shortcomings built in. The "top-down" approach used USGS abundance maps that were based on a very small sample size (<2% of the birds' project area, or approximately 4112 of 205,600 km^2), and these points had only been surveyed approximately once per year (50 stops per year). Additionally, the PIF regional population estimates, although useful for large-scale conservation efforts and approximations [34], are not made to be accurate at a small scale. Thus, the first approach contains rather sparse data that has been heavily processed and extrapolated to pertain to a large detailed area. The "bottom-up" approach sought to fix some of these problems, and was based on the MBBA point counts, which were available for all of the squares over several years. These squares were again not surveyed regularly over the span of a year (15 times over 5 years) but much more of the study area was covered by these point counts [38]. The correction factors used to convert point counts into population estimates were also (in part) designed by BAM to make up for the weaknesses in the PIF population estimates. However, the correction factors used here did not take every factor into account that could have influenced the point counts. The EDR (and possibly the singing rate) would have varied with different habitats and vegetation types, but the approach described here did not take this into account. The EDR has a large effect on the population estimate, and is consistently smaller than the radius used in the PIF estimates. As a result, the population estimates are likely to be higher than the PIF estimates. There is also likely a habitat bias against certain hard-to-reach habitats. The point counts were done by volunteers, and mostly beside roads, so the more remote locations were less likely to be surveyed. This factor may have caused an over- or under-representation, depending on the species and its preferred habitat. In addition to this problem, there is evidence that point counts done next to roads obtained biased results for some species. More work on correction factors, and population estimates in general, is ongoing and future studies and data should be able to improve on these processes.

Bird species data, including home range area, breeding season months, communal or solitary living habits, and typical flight speeds, are presented in Multimedia Appendix 1. As mentioned in the Methods section, as well as Multimedia Appendix 1, many of the reported species data are estimations of some kind. Therefore, many more field studies and work on bird species (although improving) are consistently required.

Figure 11. Southern Manitoba street network showing only trunk, primary, and secondary roads.

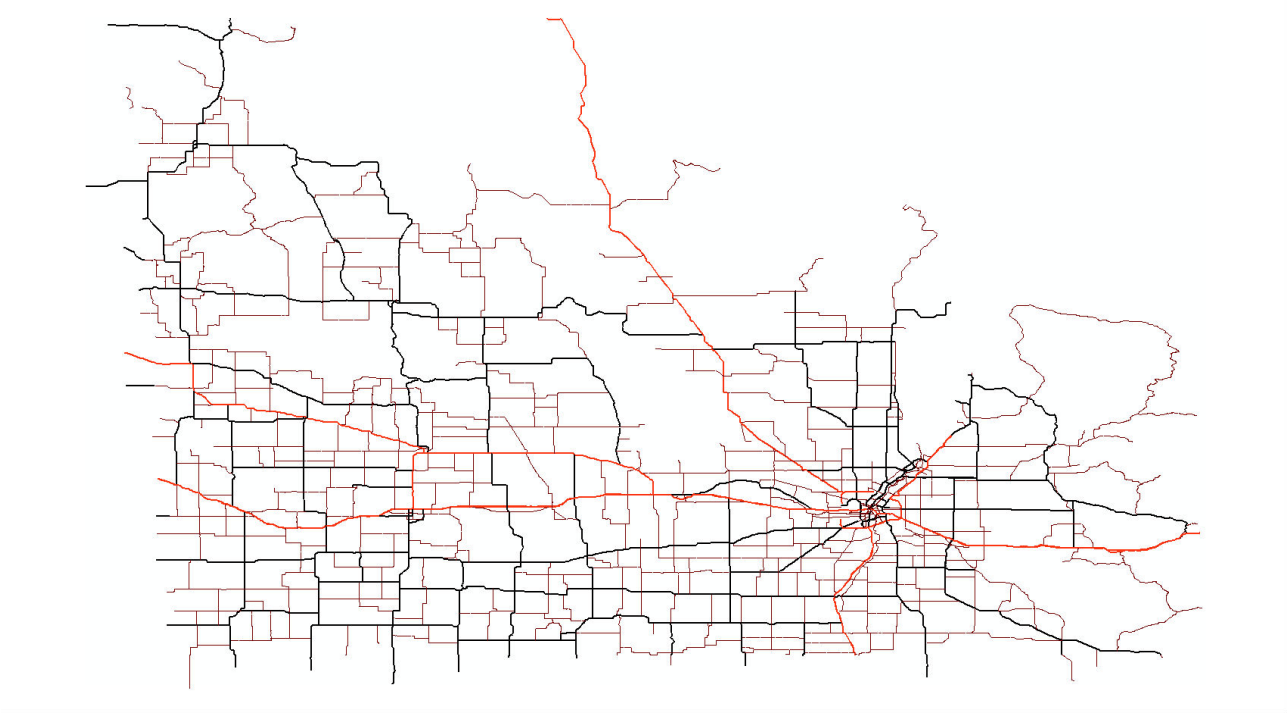


Figure 12. Physical location of some selected squares of bird roosts.

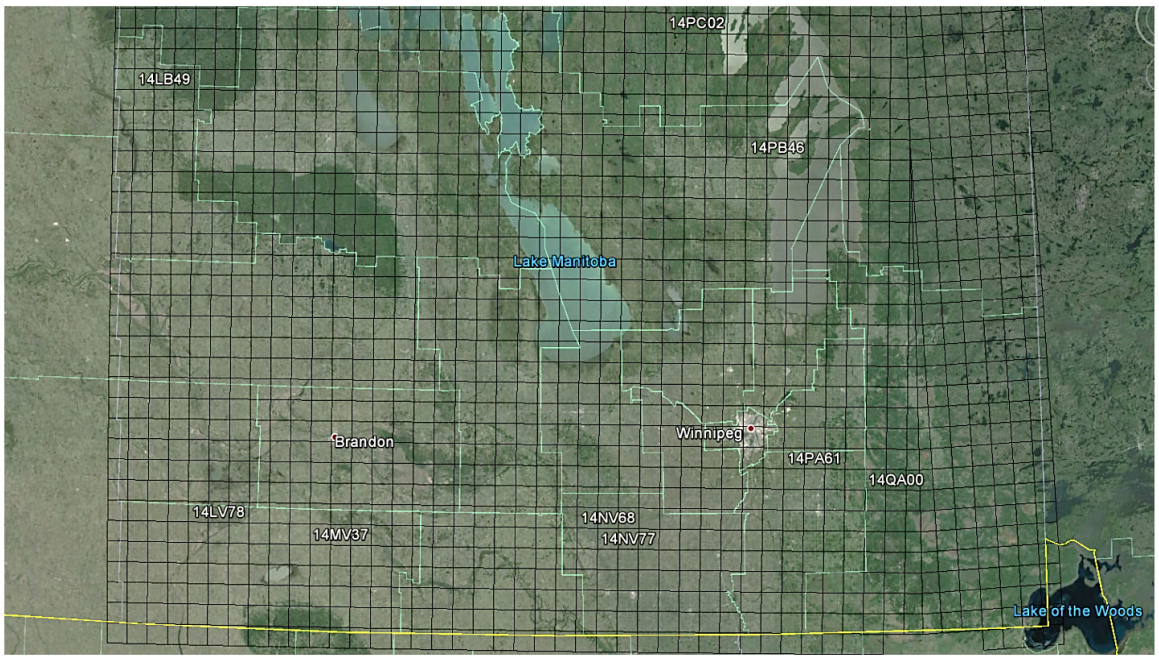


Figure 13. Comparison of the mean densities of Boreal Avian Modelling (BAM) and Partners In Flight (PIF) against densities in Downes and Collins for a number of long-distance migrant species.

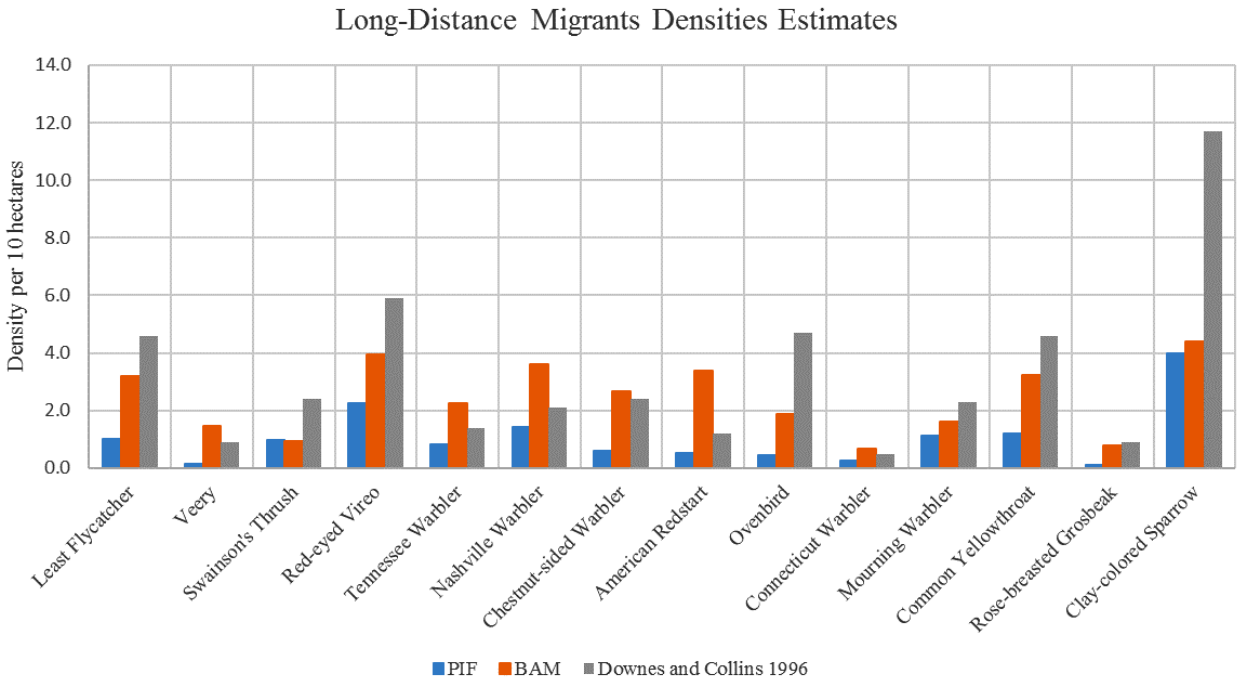


Figure 14. Comparison of the mean densities of Boreal Avian Modelling (BAM) and Partners In Flight (PIF) against densities in Downes and Collins for a number of short-distance migrant species.

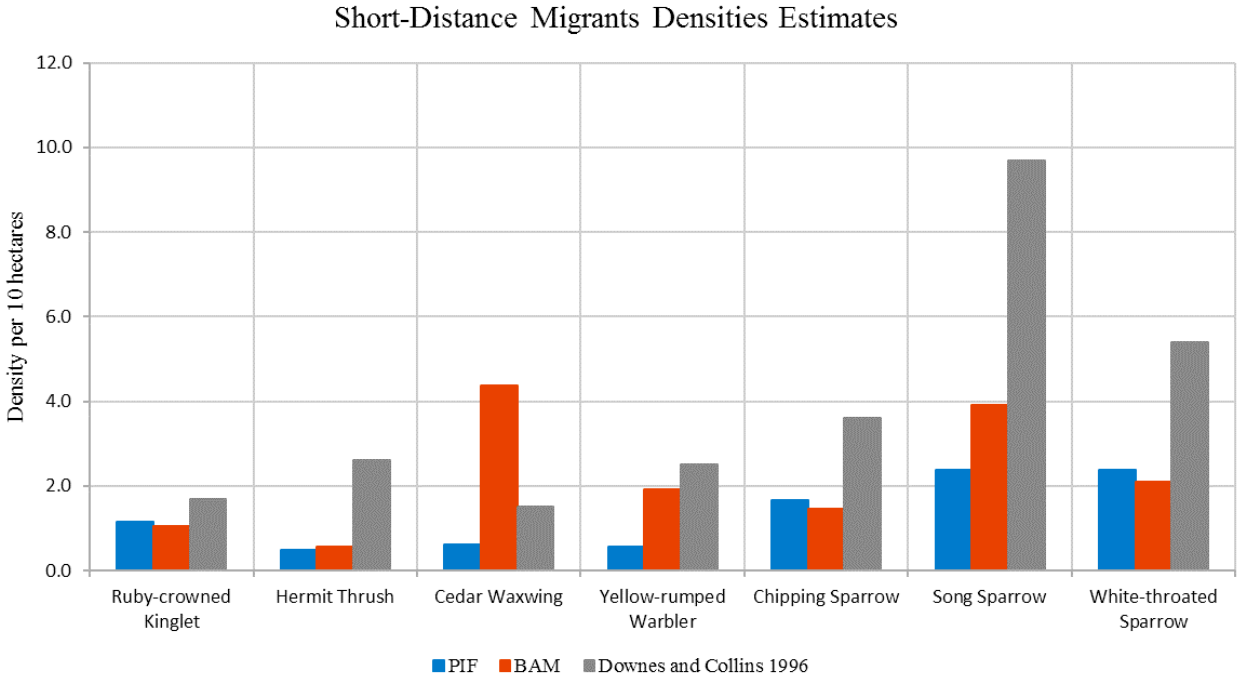


Figure 15. Equation to estimate real population of bird species using the Boreal Avian Modelling (BAM) approach.

$$Area\ of\ the\ square \times \left(\frac{Birds\ Observed}{Point\ Counts\ \times\ \pi(EDR)^2 \times (Singing\ rate\ \times Average\ time\ spent)}\right)$$

Figure 16. Equation to estimate real population of bird species using the Partners In Flight (PIF) approach.

$$Population\ of\ BCR \times \left(\frac{Relative\ Abundance(RA) of\ the\ square}{\sum RA\ of\ squares\ of\ the\ same\ species\ in\ the\ region} + \frac{Area\ of\ the\ square}{\sum Area\ of\ squares\ in\ the\ region} \right) / 2$$

Human Data

The procedures explained in this paper (for preparing the human data) have two outputs. The first output details a database of human census in municipalities of Manitoba with their boundary coordinates. These coordinates are saved as AnyLogic *GISRegion* objects on file. The second output involves the street network of the province in a compatible format with AnyLogic GIS components. A future extension of this paper will discuss issues regarding the extraction of trajectories for human agents according to cellular phone tower data.

Discussion

Conclusions

AnyLogic simulation software, in combination with Esri ArcGIS, provides a powerful toolbox for developers and modelers to simulate almost any GIS-based environment or process. In this paper, the application of interest was WNV propagation in the province of Manitoba. The land cover data of Manitoba was rasterized in an optimum sized shapefile compatible with AnyLogic. Some hints and techniques regarding working with shapefiles in AnyLogic were reviewed. A database of over 150 different bird species vulnerable to WNV, including their nesting locations, population estimates, home range radii, roosting behavior, and start and end of the breeding season, was collected. The street network for Manitoba, extracted from OpenStreetMap, was loaded into AnyLogic to be used in its pathfinding library. The procedures for collecting, combining, and reformatting all these data are explained in detail in a tutorial-based style to benefit other modelers working in similar areas.

Researchers are constantly exploiting new nontraditional sources of data for modelling different human diseases. For example, in a relatively recent study, Google search data have been used for modelling transmission dynamics of the Zika virus [45]. On the contrary, in this paper, more traditional data sources were gathered and prepared in a suitable way for agent-based modelling of WNV. However, the final proposed dataset could also be used to model mosquito population dynamics (eg, to evaluate control strategies). Some recent studies in this area can be found in the work of Ewing and Cobbold [46] and Marini et al [47]. Inevitably, modelling natural or environmental processes depends heavily on the availability of appropriate data; this is particularly true for verification and validation of models, as models and simulations would not gain significant attention unless they are shown to closely resemble reality. This resemblance can only occur with meaningful data; therefore, the importance of data cannot be overstated. The pertinent procedures and an overview of resultant data for WNV geo-modelling are presented in this paper.

Limitations

There are some limitations in our data mining and assembling procedures, each of which was discussed in the corresponding section. Notwithstanding, similar mining methods could be adopted by other researchers to compile such datasets according to their own specific needs for other geographic areas (eg, estimating population and location of birds in other provinces/states in North America). This research should be useful to others working on a variety of mosquito-borne diseases (eg, Zika, dengue, and chikungunya) by providing the data relating to Manitoba and/or a systematic path to follow for producing and processing such crucial data. Unlike WNV, these viruses generally only survive in humans. WNV has been able to permanently establish itself in the United States because it can survive in humans, horses, and birds, giving the virus a wider variety of hosts. However, the requirement for modelling human movement patterns, weather, and habitat is still equally important, as any WNV model is tightly correlated with these components.

Acknowledgments

The authors would like to thank Dr. Christian Artuso from the Manitoba Program Manager at Bird Studies Canada for his kind and thoughtful guidance on collecting birds' roosting location, abundance estimations, and species information. The authors gratefully acknowledge financial support from the Natural Sciences and Engineering Research Council of Canada Discovery Grants program, and the University of Manitoba for Graduate Enhancement of Tri-Council Stipends funding.

Conflicts of Interest

None declared.

Multimedia Appendix 1

Sample codes and birds species data.

[PDF File (Adobe PDF File), 165KB - resprot_v6i7e138_app1.pdf]

References

1. Borshchev A. The Big Book of Simulation Modeling: Multimethod Modeling with AnyLogic 6. Lisle, IL: AnyLogic North America; Jun 11, 2013.
2. American Mosquito Control Association. 2016. Mosquito Life Cycle URL: http://www.mosquito.org/life-cycle [accessed 2016-06-16] [WebCite Cache ID 6iJntDZde]
3. Reed K, Meece J, Henkel J, Shukla S. Birds, migration and emerging zoonoses: west nile virus, lyme disease, influenza A and enteropathogens. Clin Med Res 2003 Jan;1(1):5-12 [FREE Full text] [Medline: 15931279]
4. Chevalier V, Tran A, Durand B. Predictive modeling of West Nile virus transmission risk in the Mediterranean Basin: how far from landing? Int J Environ Res Public Health 2014 Jan;11(1):67-90 [FREE Full text] [doi: 10.3390/ijerph110100067] [Medline: 24362544]
5. Thomas D, Urena B. A model describing the evolution of West Nile-like encephalitis in New York City. Math Comput Model 2001 Oct;34(7-8):771-781. [doi: 10.1016/S0895-7177(01)00098-X]
6. Wonham MJ, de-Camino-Beck T, Lewis MA. An epidemiological model for West Nile virus: invasion analysis and control applications. Proc Biol Sci 2004 Mar 7;271(1538):501-507 [FREE Full text] [doi: 10.1098/rspb.2003.2608] [Medline: 15129960]
7. Bowman C, Gumel AB, van den Driessche P, Wu J, Zhu H. A mathematical model for assessing control strategies against West Nile virus. Bull Math Biol 2005 Sep;67(5):1107-1133. [doi: 10.1016/j.bulm.2005.01.002] [Medline: 15998497]
8. Silverman BG, Hanrahan N, Bharathy G, Gordon K, Johnson D. A systems approach to healthcare: agent-based modeling, community mental health, and population well-being. Artif Intell Med 2015 Feb;63(2):61-71. [doi: 10.1016/j.artmed.2014.08.006] [Medline: 25801593]
9. Bilge U, Saka O. Agent based simulations in healthcare. Stud Health Technol Inform 2006;124:699-704. [Medline: 17108597]
10. Friesen MR, McLeod RD. A survey of agent-based modeling of hospital environments. IEEE Access 2014 [FREE Full text] [doi: 10.1109/ACCESS.2014.2313957]
11. Thompson D, Cullen KW, Redondo MJ, Anderson B. Use of relational agents to improve family communication in type 1 diabetes: methods. JMIR Res Protoc 2016;5(3):e151 [FREE Full text] [doi: 10.2196/resprot.5817] [Medline: 27468762]
12. Neighbour R, Oppenheimer L, Mukhi SN, Friesen MR, McLeod RD. Agent based modeling of “crowdinforming” as a means of load balancing at emergency departments. Online J Public Health Inform 2010;2(3) [FREE Full text] [doi: 10.5210/ojphi.v2i3.3225] [Medline: 23569589]
13. Laskowski M, Demianyk BC, Witt J, Mukhi SN, Friesen MR, McLeod RD. Agent-based modeling of the spread of influenza-like illness in an emergency department: a simulation study. IEEE Trans Inf Technol Biomed 2011 Nov;15(6):877-889. [doi: 10.1109/TITB.2011.2163414] [Medline: 21813364]
14. Li Z, Hayse J, Hlohowskyj I, Smith K, Smith R. Agent-based model for simulation of West Nile virus transmission. 2005 Jun Presented at: Agent Conference on Social Dynamics; June 2005; Chicago p. 459-472 URL: http://mysite.science.uottawa.ca/rsmith43/AgentbasedmodelWNV.pdf
15. Bouden M, Moulin B, Gosselin P. The geosimulation of West Nile virus propagation: a multi-agent and climate sensitive tool for risk management in public health. Int J Health Geogr 2008;7:35 [FREE Full text] [doi: 10.1186/1476-072X-7-35] [Medline: 18606008]
16. Reeves W. Particle systems---a technique for modeling a class of fuzzy objects. ACM SIGGRAPH Comput Graph 1983 Jul 01;17(3):359-375 [FREE Full text] [doi: 10.1145/964967.801167]
17. Dahal K, Chow T. A GIS toolset for automated partitioning of urban lands. Environ Model Softw 2014 May;55:222-234 [FREE Full text] [doi: 10.1016/j.envsoft.2014.01.024]
18. Fecht D, Beale L, Briggs D. A GIS-based urban simulation model for environmental health analysis. Environ Model Softw 2014 Aug;58:1-11 [FREE Full text] [doi: 10.1016/j.envsoft.2014.03.013]
19. Formetta G, Antonello A, Franceschi S, David O, Rigon R. Hydrological modelling with components: A GIS-based open-source framework. Environ Model Softw 2014 May;55:190-200 [FREE Full text] [doi: 10.1016/j.envsoft.2014.01.019]
20. Laranjo L, Rodrigues D, Pereira AM, Ribeiro RT, Boavida JM. Use of electronic health records and geographic information systems in public health surveillance of type 2 diabetes: a feasibility study. JMIR Public Health Surveill 2016;2(1):e12 [FREE Full text] [doi: 10.2196/publichealth.4319] [Medline: 27227147]
21. Frew PM, Archibald M, Schamel J, Saint-Victor D, Fox E, Smith-Bankhead N, et al. An integrated service delivery model to identify persons living with HIV and to provide linkage to HIV treatment and care in prioritized neighborhoods: a geotargeted, program outcome study. JMIR Public Health Surveill 2015;1(2):e16 [FREE Full text] [doi: 10.2196/publichealth.4675] [Medline: 27227134]
22. Epstein J. Generative Social Science: Studies in Agent-Based Computational Modeling. Princeton: Princeton University Press; 2012.
23. Axelrod R, Tesfatsion L. Appendix A: a guide for newcomers to agent-based modeling in the social sciences. In: Handbook of Computational Economics. Amsterdam: North-Holland; 2006:1647-1659.
24. Helbing D, editor. Agent-based simulations and experiments to study emergent social behavior. In: Social Self-Organization. Berlin, Heidelberg: Springer; 2012.

25. Bonabeau E. Agent-based modeling: methods and techniques for simulating human systems. Proc Natl Acad Sci U S A 2002 May 14;99 Suppl 3:7280-7287 [FREE Full text] [doi: 10.1073/pnas.082080899] [Medline: 12011407]
26. Filatova T, Verburg P, Parker D, Stannard C. Spatial agent-based models for socio-ecological systems: Challenges and prospects. Environ Model Softw 2013 Jul;45:1-7 [FREE Full text] [doi: 10.1016/j.envsoft.2013.03.017]
27. Bankes SC. Agent-based modeling: a revolution? Proc Natl Acad Sci U S A 2002 May 14;99 Suppl 3:7199-7200 [FREE Full text] [doi: 10.1073/pnas.072081299] [Medline: 11997445]
28. Hahn H. The Conundrum of Verification and Validation of Social Science-based Models. Procedia Comput Sci 2013;16:878-887 [FREE Full text] [doi: 10.1016/j.procs.2013.01.092]
29. Macal C. Everything you need to know about agent-based modelling and simulation. J Simulation 2016 May 10;10(2):144-156 [FREE Full text] [doi: 10.1057/jos.2016.7]
30. Régnière J, St-Amant R, Béchard A. Natural Resources Canada. Quebec; 2014. BioSIM 10 – User's manual URL: https://cfs.nrcan.gc.ca/publications?id=34818 [accessed 2017-06-30] [WebCite Cache ID 6rcAiaPUK]
31. Government of Manitoba. 2017. Land Use/Land Cover, Manitoba Land Initiative URL: http://mli2.gov.mb.ca/landuse/index.html [accessed 2015-09-29] [WebCite Cache ID 6lCu8bYBT]
32. Sauer J, Hines J, Fallon K, Pardieck D, Ziolkowski J, Link WA. The North American Breeding Bird Survey, Results and Analysis 1966 - 2013 Version 01.30.2015. Laurel, MD: USGS Patuxent Wildlife Research Center; 2015. URL: http://www.mbr-pwrc.usgs.gov/bbs/ [accessed 2015-04-24] [WebCite Cache ID 6lCuLOI3C]
33. Bird Studies Canada. 2015. Manitoba Breeding Bird Atlas (2010-2014): raw breeding evidence URL: [WebCite Cache ID 6rcBSvVVN]
34. Rich T, Beardmore C, Berlanga H, Blancher P, Bradstreet M, Butcher G. Partners in Flight North American Landbird Conservation Plan. Ithaca, NY: Cornell Lab Ornithol; 2013. PIF population estimates database URL: http://rmbo.org/pifpopestimates/ [accessed 2016-10-12] [WebCite Cache ID 6lCujjYkq]
35. Bird Studies Canada on behalf of the North American Bird Conservation Initiative. 2014. NABCI bird conservation regions URL: http://www.birdscanada.org/research/gislab/index.jsp?targetpg=bcr [accessed 2016-10-12] [WebCite Cache ID 6lCutWRT8]
36. Carey B, Christianson W, Courcelles A, Cuthbert C, de March L, Smet KD. Finding Birds In Southern Manitoba. Manitoba: Manitoba Naturalists Society; 2006.
37. Boreal Avian Model Project. 2010. BAM effective detection radius URL: http://www.borealbirds.ca/index.php/bam_edr [accessed 2016-05-17] [WebCite Cache ID 6lCvGYU0G]
38. Manitoba Breeding Bird Atlas. Winnipeg: Manitoba Breeding Bird Atlas; 2010. Guide For Point Counters URL: http://www.birdatlas.mb.ca/download/Point_Counting_Guide_April_22.pdf [accessed 2016-10-12] [WebCite Cache ID 6lCvQMj23]
39. The Birds of North America Online. Ithaca, NY: Cornell Laboratory of Ornithology; 2015. URL: https://birdsna.org/Species-Account/bna/home [accessed 2017-07-11] [WebCite Cache ID 6rriBUDDp]
40. Neighbour R, Mukhi SN, Friesen MR, McLeod RD, Crowley M. Vehicular Traffic Modeling Governed by Cellular Phone Trajectories. : IEEE; 2012 Presented at: IEEE Vehicular Technology Conference (VTC Fall); 3-6 Sept. 2012; Quebec City, QC p. 1-5 URL: http://ieeexplore.ieee.org/document/6398876/ [doi: 10.1109/VTCFall.2012.6398876]
41. Borkowski M, McLeod RD. Epidemic Modeling with Discrete Space Scheduled Walkers. : IEEE; 2008 Presented at: IEEE 19th International Conference on Systems Engineering. ICSENG '08; 2008; Las Vegas, NV URL: http://ieeexplore.ieee.org/document/4616694/ [doi: 10.1109/ICSEng.2008.28]
42. Murray-Rust D, Robinson D, Guillem E, Karali E, Rounsevell M. An open framework for agent based modelling of agricultural land use change. Environ Model Softw 2014 Nov;61:19-38 [FREE Full text] [doi: 10.1016/j.envsoft.2014.06.027]
43. Downes C, Collins B. The Canadian Breeding Bird Survey, 1966-94. In: Canadian Wildlife Service Progress Note No. 210. Ottawa, ON: Environment Canada; 1996.
44. Kirk DA, Diamond AW, Smith AR, Holland GE, Chytyk P. Population Changes in Boreal Forest Birds in Saskatchewan and Manitoba. Wilson Bull 1997;109(1):1-27 [FREE Full text]
45. Majumder MS, Santillana M, Mekaru SR, McGinnis DP, Khan K, Brownstein JS. Utilizing nontraditional data sources for rear real-time estimation of transmission dynamics during the 2015-2016 Colombian Zika virus disease outbreak. JMIR Public Health Surveill 2016;2(1):e30 [FREE Full text] [doi: 10.2196/publichealth.5814] [Medline: 27251981]
46. Ewing DA, Cobbold CA, Purse BV, Nunn MA, White SM. Modelling the effect of temperature on the seasonal population dynamics of temperate mosquitoes. J Theor Biol 2016 Jul 7;400:65-79 [FREE Full text] [doi: 10.1016/j.jtbi.2016.04.008] [Medline: 27084359]
47. Marini G, Poletti P, Giacobini M, Pugliese A, Merler S, Rosà R. The role of climatic and density dependent factors in shaping mosquito population dynamics: the case of Culex pipiens in northwestern Italy. PLoS One 2016;11(4):e0154018 [FREE Full text] [doi: 10.1371/journal.pone.0154018] [Medline: 27105065]

Abbreviations

ABM: Agent-Based Model

BAM: Boreal Avian Modelling
BCR: Bird Conservation Region
DBF: DataBase File
DE: differential equation
EDR: Effective Detection Radius
FID: Feature ID
GIS: Geographic Information System
ID: identification
MS: Microsoft
MBBA: Manitoba Breeding Bird Atlas
PIF: Partners In Flight
SQL: Structured Query Language
USGS: United States Geological Survey
UTM: Universal Transverse Mercator
Vmp: minimum power speed
Vmr: maximum range speed
WNV: West Nile Virus

Edited by P Sullivan; submitted 16.06.16; peer-reviewed by G Marini, JT Amenyo; comments to author 04.10.16; revised version received 12.10.16; accepted 05.06.17; published 17.07.17.

Please cite as:
Nasrinpour HR, Reimer AA, Friesen MR, McLeod RD
Data Preparation for West Nile Virus Agent-Based Modelling: Protocol for Processing Bird Population Estimates and Incorporating ArcMap in AnyLogic
JMIR Res Protoc 2017;6(7):e138
URL: http://www.researchprotocols.org/2017/7/e138/
doi:10.2196/resprot.6213
PMID:28716770

Protocol

Cross-Sectional Study of Chronic Obstructive Pulmonary Disease Prevalence Among Smokers, Ex-Smokers, and Never-Smokers in Almaty, Kazakhstan: Study Protocol

Almaz Sharman[1], MD, PhD; Baurzhan Zhussupov[1], MSc Epi; Dana Sharman[1], MPH, MD; Assel Stambekova[1], MD; Sattar Yeraliyev[1], MD

Kazakhstan Academy ∘ f Preventive Medicine, Almaty, Kazakhstan

Corresponding Author:
Baurzhan Zhussupov, MSc Epi
Kazakhstan Academy ∘ f Preventive Medicine
66 Klochkov St.
Almaty,
Kazakhstan
Phone: 7 727 317 88 55
Email: baurzhan.zhussupov@gmail.com

Abstract

Background: Chronic obstructive pulmonary disease (COPD) is significantly underdiagnosed in Kazakhstan, and there is no previously conducted study on COPD prevalence in the country.

Objective: The purpose of this study is to assess the prevalence of COPD among individuals aged 40 to 59 years based on results of spirometry before and after bronchodilator, presence of structural changes in the lungs (emphysema, inflammatory changes, and thickening of the walls of the large and small airways) detected by computer tomography, and the symptoms of COPD. The study has 3 study groups: smokers of conventional cigarettes, those who had quit smoking 1 to 5 years ago, and those who haven't smoked cigarettes.

Methods: This is an observational study with a cross-sectional design among individuals aged 40 to 59 years in Almaty, Kazakhstan. The sample of 900 individuals of both sexes contains 500 smokers, 200 ex-smokers, and 200 never-smokers. Study measures include spirometry, chest computed tomography, electrocardiography, physical exams, laboratory testing of serum, anthropometry, and 6-minute walk test. Data are collected by computer-assisted personal interviewing with tablets. The questionnaire was designed to explore possible COPD risk factors including history of smoking, current smoking, level of smoking exposure (in pack-years), passive smoking, occupational and environmental hazards, and covariates: age, gender, ethnicity, education, occupation, and self-reported morbidity. COPD Assessment Test (CAT) is used to collect information about COPD symptoms.

Results: We have completed the participant recruitment and study procedures. Currently, we are working on data processing and data analysis. The authors anticipate the preliminary results should be available by September 2017. Study results will be published in peer-reviewed scientific journals.

Conclusions: This is the first study in Kazakhstan that assesses prevalence of COPD and its comorbidities in the adult population aged 40 to 59 years. The results of the study will be useful for improving COPD preventive measures, better COPD screening, identification, and registration. Findings of the study will also contribute to global knowledge on the epidemiology of COPD.

Trial Registration: ClinicalTrials.gov NCT02926534; https://clinicaltrials.gov/ct2/show/NCT02926534 (Archived by WebCite at http://www.webcitation.org/6rjwGsPOZ)

(JMIR Res Protoc 2017;6(7):e143) doi:10.2196/resprot.7422

KEYWORDS

COPD; Kazakhstan; cross-sectional; study protocol; tobacco smoking, risk factors

Introduction

Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of death worldwide [1]. The number of affected individuals and deaths from COPD are expected to increase as the population ages [2]. In Russia, the largest neighboring country of Kazakhstan, the prevalence of symptomatic COPD in the adult population was estimated to be 15.3% [3]. An estimated 1.4 million individuals in Kazakhstan may be affected by COPD. This estimate is based on studies that have been conducted in other countries in the World Health Organization European Region [4] but not in Kazakhstan, because a study on the prevalence of COPD has not been conducted in the country yet. COPD is significantly underdiagnosed in Kazakhstan. In 2013, the rate of reported COPD cases was 315.9 per 100,000 or around 53,000 registered cases of COPD [5]. A better understanding of the epidemiology and social and other determinants of the disease is needed in order to recognize the true magnitude of the problem and develop effective treatments and prevention strategies.

Various criteria for COPD have been used in population-based studies. The most common criterion is airflow obstruction detected by spirometry testing, defined as a postbronchodilator ratio of forced expiratory volume in 1 second (FEV_1) to forced vital capacity (FVC) less than 0.7 or 70% [6]. This criterion is simple to implement and widely used in epidemiological surveys. However, COPD prevalence based on this could be slightly biased—overestimated in old subjects and underestimated in younger ones [7]. For this reason, the fifth percentile of the FEV_1/FVC ratio or the lower limit of normal distribution of the FEV_1/FVC ratio defined for specific age-gender group is also recommended for use in epidemiological studies [8].

Respiratory symptoms [9] and physical examination [10] were frequently used to evaluate COPD prevalence. However, collecting such data is more important for establishing the clinical diagnosis of COPD [6]. The specific symptoms of COPD include progressive dyspnea, cough, and sputum production [6]. The COPD Assessment Test (CAT) was specially designed to measure how COPD symptoms lead to health status impairment. The test is derived from 8 items, and the score varies from 0 to 40. The cut-off point for the CAT is 10, after which regular treatment for symptoms is recommended [6]. Although a physical examination is rarely used in COPD diagnosis, particularly in detecting mild to moderate COPD, thoracic examination of patients with severe disease can usually reveal the following signs: hyperinflation, wheezing, diffusely decreased breath sounds, hyperresonance on percussion, and prolonged expiration [11].

Chest computed tomography (CT) scan is recommended for subjects with airflow limitation and signs and symptoms suggestive of COPD for making an accurate diagnosis of COPD to exclude other conditions [12]. CT scan also helps to separate COPD patients into 2 main phenotypes, emphysema and small airway disease [13]. CT images can be visually assessed by qualified observers to describe patterns of altered lung structure or quantified for assessment of the extent of emphysema, gas trapping, and airway abnormality [14]. Some studies suggested that severity of emphysema detected by CT scan is associated with greater lung function decline even if airway obstruction is not currently presented [15,16]. As a result, CT-detected emphysema may predict future development of airflow obstruction [16,17].

Tobacco smoking, occupational and environmental exposures including workplace dusts and chemicals, and smoke from home cooking and heating fuels are the main risk factors for COPD [8]. In addition, advanced age, chronic respiratory infections such as tuberculosis, low socioeconomic status, and being underweight may influence COPD development [18,19]. Genetic predisposition also plays an important role in COPD development. Originally described more than 50 years ago, α_1-antitrypsin deficiency may cause COPD and accounts for 1% to 2% of all COPD cases. There are other genome variants currently being investigated as candidates for COPD genes, but only the Z variant of α_1-antitrypsin is accepted as a COPD gene at the present time [20].

Comorbidities are frequently found in persons with COPD. Some of them have risk factors, which are the same as for COPD, particularly tobacco smoking and aging. Moreover, systemic inflammation and chronic hypoxia present in COPD patients may cause other health-related conditions. Common comorbidities include heart disease, lung cancer, osteoporosis, metabolic syndrome and diabetes, anemia, anxiety, cognitive decline, and sleep disorders [21,22]. Specific comorbidities increase mortality and poor outcome in COPD, so management of main comorbidities has been included to COPD guidelines [6].

The aim of the study is to assess the prevalence of COPD among smokers, ex-smokers, and never-smokers aged 40 to 59 years based on pulmonary function assessment (spirometry), structural changes (emphysema and large and small airway inflammation with thickening) identified by high-resolution CT, COPD symptoms, and exercise limitations. In addition, the study objectives include comparing the prevalence of health conditions considered as COPD comorbidities (heart disease, hypertension, metabolic syndrome, diabetes mellitus) in 3 study groups and their interaction with COPD.

Methods

Study Design

This is an observational study with a cross-sectional design to assess the prevalence of COPD in Almaty, Kazakhstan, among individuals aged 40 to 59 years based on results of spirometry, the presence of structural changes in the lungs, and symptoms of COPD.

The study population is 3 groups of male and female residents of Almaty, the largest city in Kazakhstan, with a population of 1.7 million people, 9% of whom are aged 40 to 59 years. Members of the first group include current smokers with more than a 10 pack-year history of smoking (smokers). The second group comprises individuals who quit smoking from 1 to 5 years ago and have more than a 10 pack-year history of smoking (ex-smokers). The third group comprises persons who have

never smoked regularly (ie, smoked less than 100 cigarettes in their lifetime) (never-smokers).

We recruited individuals who are 40 years of age or older because most people are at least 40 years old when the symptoms of COPD first appear [23]. The same age limit is selected for many COPD prevalence studies [24-26]. The upper age was set at 59 years to avoid survival bias [27] possibly leading to underestimating the effects of risk factors on COPD. We have taken into account that the life expectancy at birth among males was only 66 years in Kazakhstan in 2015 [28].

Inclusion and Exclusion Criteria

Male and female participants aged 40 to 59 years who have a 10 pack-year and more of smoking history (for smokers and ex-smokers) or fewer than 100 cigarettes in their lifetime (for never-smokers) and are able to provide informed consent can be included in this study.

Exclusion criteria:

- Pregnancy
- Fever (37°C or higher) at the time of the visit or during the 2 weeks preceding the visit
- Legally incapable
- Chronic infectious and noninfectious lung disease except asthma (eg, pulmonary fibrosis, bronchiectasis, cystic fibrosis, tuberculosis)
- Resection of at least one lobe (or performing procedures to reduce lung volume)
- Any cancer; receiving a course of radiation or chemotherapy at the time of the visit
- Suspected lung cancer (presence of significant lung neoplasm)
- Presence of metal in the chest
- Ophthalmic surgery within the last 12 months prior to the visit
- Myocardial infarction or other form of acute or chronic coronary insufficiency or cardiac arrhythmia diagnosed at least 6 months prior to the visit
- Myocardial infarction or other form of acute or chronic coronary insufficiency or cardiac arrhythmia for which an individual regularly receives medication
- Severely elevated blood pressure (equal to or greater than a systolic 180 or diastolic of 100)
- History of cerebrovascular accident
- Thoracic or abdominal surgery within the last 6 months
- Contraindications to use salbutamol or its analogs
- CT scan or other research using ionizing radiation within the last 6 months

Sampling

According to the Burden of Obstructive Lung Disease (BOLD) protocol, a minimal sample size of 600 is recommended to achieve an acceptable level of precision for estimating COPD prevalence [29]. Our goal is for a sample size of 900 including 500 smokers, 200 ex-smokers, and 200 never-smokers. We have used the National Health and Nutrition Examination Surveys data to assume COPD prevalence in these 3 groups [30]. The sample size of 500 allows for achieving the precision of 3.5% with the expected prevalence of obstructive impairment of 20%. The sample size of 200 and the expected prevalence of pulmonary obstruction of 10% and 2% among ex-smokers and never-smokers, respectively, provides sample estimates with 4.2% and 1.9% precision, respectively [31].

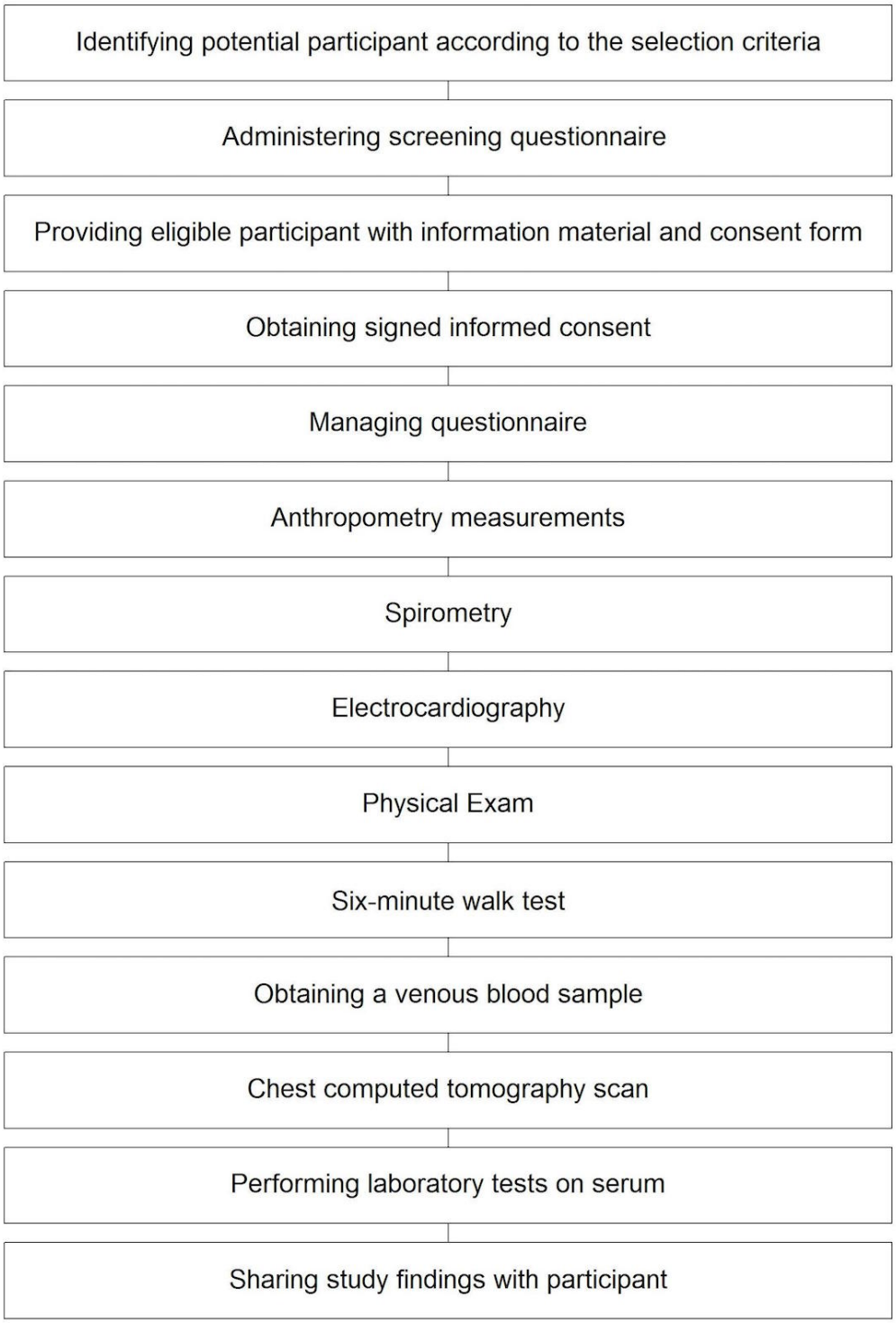
The 3 study groups are planned to have the same gender and age distribution by implementing age-gender quota to eliminate age and gender potential confounding effect to the associations between smoking status and outcomes.

It was shown that the sample characteristics depend on recruitment method used [32]. To recruit study participants, active and passive approaches are used. Participants are recruited by using personal networks of investigators and persons who are already participating in the study (snowball), placing an advertisement of the study in social media (Facebook) targeting those individuals who are potentially eligible to participate (live in Almaty, specific age group), and meeting with the owners and managerial staff of several large companies located in Almaty to explain the benefits of participation in the study. Employees of these companies who are potentially eligible to participate in the study are contacted by phone calls.

Study Procedures

The study flow is shown in Figure 1. Participants are expected to attend 2 to 3 visits for the study, for a total of about 3 hours. Completing study procedures for each participant, including sharing the study results with the participant, is expected to take up to 2 weeks.

Figure 1. Patient recruitment, enrollment, and data collection and sharing.



Spirometry

Spirometry is performed by trained investigators, with 3 technically satisfactory maneuvers performed by each study participant. The largest value of FEV_1 and the respective value FVC are selected to calculate ratio of FEV_1 to FVC. The CardioTouch 3000-S (BiTech Medical Corp), a 12-lead resting electrocardiogram (ECG) machine with a spirometer with a measuring accuracy that complies with American Thoracic Society requirements [33], is used to perform lung function

tests. Calibration of the spirometer was performed every day before using it. A 3-L syringe was pumped through to check that accuracy did not exceed a tolerance of 3% [33].

Computed Tomography

Study subjects undergo 64-channel CT scans of the chest (Philips Brilliance CT 64). Subjects with restrictive (FEV_1/FVC from 70% to 80%) and obstructive (FEV_1/FVC less than 70%) lung diseases or signs and symptoms of COPD found during the physical examination and survey undergo inspiratory-expiratory CT scans obtained at the following settings: detector collimation 0.6-0.75 mm, 0.625-0.9 mm reconstructed slice thickness, 0.45-0.625 mm slice interval, 120 kV, 200 (inspiratory) and 50 (expiratory) mAs. Other subjects have only inspiratory CT scans: 0.8 mm reconstructed slice thickness, 0.4 mm slice interval, smooth reconstruction algorithm iDose 7, matrix size 512×512, range = –500 to 1500, 120 kV, 40 mAs [34].

CT scans are evaluated by 3 independent qualified observers to produce semiquantified measures that characterize the extent of emphysema, severity of bronchial dilatation, traction bronchiectasis, bronchial wall thickening, and small airway disease. We use the Bhala scoring system [35] modified by Tulek at al [36]. The kappa test will be used to evaluate interrater reliability of visual CT scan analysis. The median score by 3 observers will be recorded for each participant.

Electrocardiography

A standard 12-lead ECG is performed with the CardioTouch 3000-S for each study subject by employing strictly standardized procedures. Research staff members were trained to properly place electrodes. At least 4 cardiac cycles are taken from each of 12 leads. The machine runs at 50 mm/sec. The following ECG parameters are evaluated by a trained clinical researcher: waves and complexes, presence and description of ECG abnormalities including pathologic q-waves, ST elevation, ST depression, T-wave inversion, hypertrophy, QRS axis deviation, block, and arrhythmia. ECGs were visually inspected for technical errors and were interpreted by a qualified cardiologist. The prevalence of specific ECG abnormalities as well as grouped abnormalities will be reported for each study group. Associations between COPD and ECG abnormalities, crude and adjusted by sex, age, and smoking status, will be measured and presented.

Physical Exam

Clinical investigators were trained to conduct the pulmonary (percussion and inspection) exam and technique for listening to second heart sounds. Two Stanford Medicine 25 modules were used as study materials in hands-on sessions [37,38]. The prevalence of individual pathological findings will be presented for each study group. Associations between pathological findings from 2 exams and COPD will be evaluated.

Anthropometry

Anthropometry measures include height, weight, waist circumference, heart rate, blood pressure, and pulse oximetry.

Six-Minute Walk Test

All study subjects will take a 6-minute walk test to evaluate functional exercise capacity. Investigators assess whether contraindication exists or not. Absolute contraindications are unstable angina and myocardial infarction during the previous month. Relative contraindications are blood pressure more than 180/100 mm Hg and a resting heart rate of more than 120 beats per minute [39]. Subjects with any of the contraindications are referred to the clinical coordinator for a decision about the conduct of the test. Posttest dyspnea is measured using the Borg scale [40].

Laboratory Data

Serum from each participant is tested for blood cholesterol level, high-density lipoprotein (HDL), low-density lipoprotein (LDL)), triglycerides, C-reactive protein, fibrinogen, glucose, hepatitis B and C IgM and IgG antigens and antibodies, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) liver enzymes, and α_1-antitrypsin.

Questionnaire

The questionnaire was designed to collect data on possible COPD risk factors including history of smoking; current smoking; level of smoking exposure (in pack-year); passive smoking; and occupational and environmental hazards including dusts, chemicals, and indoor fuel pollution. The questionnaire contains the following covariates: age, gender, ethnicity, education, occupation, and self-reported morbidity. CAT is used to collect Information about COPD symptoms. The test was designed and validated for use in routine clinical practice to evaluate the health status of patients with COPD [41]. Computer-assisted personal interviewing (CAPI) with tablets has been implemented to collect, store, and transmit data related to a personal survey interview.

The questionnaire was piloted by interviewing 7 testers—3 smokers, 2 ex-smokers, and 2 never-smokers. After completing pilot interviews, the testers were asked to answer specific questions and then provide comments and suggestions on the whole questionnaire. The questions that were not clear enough were identified and have been improved.

Statistical Analysis

Data from all CAPI devices will be exported to one database, and R version 3.3.1 (The R Foundation) will be used for data analysis. Descriptive analyses will be performed using mean, median, interquartile interval, and standard deviation for quantitative variables and frequency tables for categorical variables. Depending on the nature of outcome and exposure variables, type of data distribution, and the sample size, bivariate comparisons will be made by the following tests: chi-square test, Fisher's exact test, analysis of variance, *t* test, and the Mann-Whitney test.

A multivariable analysis (generalized linear models) will be conducted to control for confounding. Presence of effect modification/interaction terms will be explored. An alpha <.05 will be considered significant. To construct the optimal model, backward elimination will be used. The full models will contain all independent effects and some important interactions.

Mediators (variables that lie on the causal pathway between exposure and outcome) will not be included in the model. To avoid multicollinearity, we will examine the tolerance for each independent variable. If the tolerance value is less than 0.1, we will omit a variable from the analysis. The optimal model will be defined based on the Akaike Information Criterion. Model diagnostic plots will be generated to test model assumptions (eg, normality of deviance residuals).

Ethics Approval

The National Central Ethics Committee under the Ministry of Health and Social Development in the Republic of Kazakhstan approved this study on August 19, 2016. The study has been registered at ClinicalTrials.gov [NCT02926534].

Results

We have completed the participant recruitment and study procedures. Currently, we are working on data processing and data analysis. The authors anticipate the preliminary results should be available by September 2017. Study results will be published in peer-reviewed scientific journals.

Discussion

To the best of our knowledge, this is the first study in Kazakhstan that assesses COPD prevalence in the general population aged 40 to 59 years, specifically smokers, ex-smokers, and never-smokers. The study also aims to investigate COPD comorbidities and their interaction with COPD. Improving COPD preventive measures, COPD screening, identification, and registration requires obtaining this epidemiological information. Study strengths include its relatively large sample size and collection of comprehensive medical, behavioral, and other health-related data from each study participant.

However, there remain some limitations. First, the study is observational. Thus, the possibility of unidentified or unmeasured confounders exists. We are going to conduct the sensitivity analysis to assess a covariate that could eliminate the effect of smoking on COPD. Second, the study is cross-sectional, and the time when COPD occurred cannot be identified. The values of potential confounders measured in the study could differ from ones when symptoms of COPD first appeared and could be diagnosed. As a result, causal inferences cannot be made. Third, the study includes many components to be measured, which makes it impossible to employ probability sampling to select participants. The main risk of nonprobability sampling is that the distribution of important covariates in the sample will differ significantly from their distribution in the study population. We employ quota sampling to set quotas for gender and age, 2 important covariates for COPD, to balance them in the sample. In addition, we measure all known important covariates or confounders to make the desired adjustments in our data analysis. Fourth, the study is conducted in one city, Almaty, which reduces the generalizability of the study results to the country population. Finally, we expect some measurement bias that arises from errors in the data collection. For example, participants could avoid socially undesirable answers. To reduce the latter bias, all data collection procedures were tested and the research staff members were trained.

Acknowledgments

This study is supported with resources and the use of facilities at Kazakhstan Academy ◦ f Preventive Medicine, the HealthCity Clinic, and Synergy Group Kazakhstan. The project is partially funded by a grant from Philip Morris International (IIS.PMI.2016.001). This funder had no role in collection, analysis, or interpretation of data or in writing the manuscript.

Authors' Contributions

The study was designed by AS, DS, and BZ. AS and BZ drafted the manuscript. All authors critically revised the manuscript. All authors read and approved the final manuscript.

Conflicts of Interest

None declared.

References

1. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012 Dec 15;380(9859):2095-2128. [doi: 10.1016/S0140-6736(12)61728-0] [Medline: 23245604]
2. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study. Lancet 1997 May 24;349(9064):1498-1504. [doi: 10.1016/S0140-6736(96)07492-2] [Medline: 9167458]
3. Chuchalin AG, Khaltaev N, Antonov NS, Galkin DV, Manakov LG, Antonini P, et al. Chronic respiratory diseases and risk factors in 12 regions of the Russian Federation. Int J Chron Obstruct Pulmon Dis 2014;9:963-974 [FREE Full text] [doi: 10.2147/COPD.S67283] [Medline: 25246783]
4. Adeloye D, Chua S, Lee C, Basquill C, Papana A, Theodoratou E, et al. Global and regional estimates of COPD prevalence: systematic review and meta-analysis. J Glob Health 2015 Dec;5(2):020415 [FREE Full text] [doi: 10.7189/jogh.05-020415] [Medline: 26755942]

5. National Center for the Problems of Forming the Healthy Lifestyle: press release. URL: http://www.hls.kz/rus/press-releases_1_61 [accessed 2017-07-06] [WebCite Cache ID 6qQFCdjB]
6. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of COPD. URL: http://goldcopd.org/global-strategy-diagnosis-management-prevention-copd-2016/ [accessed 2017-01-25] [WebCite Cache ID 6nmH3nBW5]
7. Swanney MP, Ruppel G, Enright PL, Pedersen OF, Crapo RO, Miller MR, et al. Using the lower limit of normal for the FEV1/FVC ratio reduces the misclassification of airway obstruction. Thorax 2008 Dec;63(12):1046-1051. [doi: 10.1136/thx.2008.098483] [Medline: 18786983]
8. Bakke PS, Rönmark E, Eagan T, Pistelli F, Annesi-Maesano I, Maly M, et al. Recommendations for epidemiological studies on COPD. Eur Respir J 2011 Dec;38(6):1261-1277 [FREE Full text] [doi: 10.1183/09031936.00193809] [Medline: 22130763]
9. Lundbäck B, Stjernberg N, Nyström L, Forsberg B, Lindström M, Lundbäck K, et al. Epidemiology of respiratory symptoms, lung function and important determinants. Report from the Obstructive Lung Disease in Northern Sweden Project. Tuber Lung Dis 1994 Apr;75(2):116-126. [doi: 10.1016/0962-8479(94)90040-X] [Medline: 8032044]
10. Bakke P, Eide GE, Hanoa R, Gulsvik A. Occupational dust or gas exposure and prevalences of respiratory symptoms and asthma in a general population. Eur Respir J 1991 Mar;4(3):273-278. [Medline: 1864342]
11. Koff RS. Fundamentals of lung auscultation. N Engl J Med 2014 May 22;370(21):2053. [doi: 10.1056/NEJMc1403766#SA3] [Medline: 24849098]
12. Make BJ, Martinez FJ. Assessment of patients with chronic obstructive pulmonary disease. Proc Am Thorac Soc 2008 Dec 15;5(9):884-890 [FREE Full text] [doi: 10.1513/pats.200808-093QC] [Medline: 19056711]
13. Pistolesi M, Camiciottoli G, Paoletti M, Marmai C, Lavorini F, Meoni E, et al. Identification of a predominant COPD phenotype in clinical practice. Respir Med 2008 Mar;102(3):367-376 [FREE Full text] [doi: 10.1016/j.rmed.2007.10.019] [Medline: 18248806]
14. Lynch DA, Austin JHM, Hogg JC, Grenier PA, Kauczor H, Bankier AA, et al. CT-definable subtypes of chronic obstructive pulmonary disease: a statement of the Fleischner Society. Radiology 2015 Oct;277(1):192-205 [FREE Full text] [doi: 10.1148/radiol.2015141579] [Medline: 25961632]
15. Mohamed HFAA, Zanen P, Gietema H, Kruitwagen CLJJ, Isgum I, Mol C, et al. CT-quantified emphysema in male heavy smokers: association with lung function decline. Thorax 2011 Sep;66(9):782-787. [doi: 10.1136/thx.2010.145995] [Medline: 21474499]
16. Koo H, Jin KN, Kim DK, Chung HS, Lee C. Association of incidental emphysema with annual lung function decline and future development of airflow limitation. Int J Chron Obstruct Pulmon Dis 2016;11:161-166 [FREE Full text] [doi: 10.2147/COPD.S96809] [Medline: 26893550]
17. Sin DD, Leipsic J, Man SFP. CT in COPD: just a pretty picture or really worth a thousand words (or dollars)? Thorax 2011 Sep;66(9):741-742. [doi: 10.1136/thx.2011.161430] [Medline: 21572118]
18. Rosenberg SR, Kalhan R, Mannino DM. Epidemiology of chronic obstructive pulmonary disease: prevalence, morbidity, mortality, and risk factors. Semin Respir Crit Care Med 2015 Aug;36(4):457-469. [doi: 10.1055/s-0035-1555607] [Medline: 26238634]
19. Lee SJ, Kim SW, Kong KA, Ryu YJ, Lee JH, Chang JH. Risk factors for chronic obstructive pulmonary disease among never-smokers in Korea. Int J Chron Obstruct Pulmon Dis 2015;10:497-506 [FREE Full text] [doi: 10.2147/COPD.S77662] [Medline: 25784796]
20. Berndt A, Leme AS, Shapiro SD. Emerging genetics of COPD. EMBO Mol Med 2012 Nov;4(11):1144-1155 [FREE Full text] [doi: 10.1002/emmm.201100627] [Medline: 23090857]
21. Cavaillès A, Brinchault-Rabin G, Dixmier A, Goupil F, Gut-Gobert C, Marchand-Adam S, et al. Comorbidities of COPD. Eur Respir Rev 2013 Dec;22(130):454-475 [FREE Full text] [doi: 10.1183/09059180.00008612] [Medline: 24293462]
22. Chatila WM, Thomashow BM, Minai OA, Criner GJ, Make BJ. Comorbidities in chronic obstructive pulmonary disease. Proc Am Thorac Soc 2008 May 01;5(4):549-555 [FREE Full text] [doi: 10.1513/pats.200709-148ET] [Medline: 18453370]
23. Shavelle RM, Paculdo DR, Kush SJ, Mannino DM, Strauss DJ. Life expectancy and years of life lost in chronic obstructive pulmonary disease: findings from the NHANES III Follow-up Study. Int J Chron Obstruct Pulmon Dis 2009;4:137-148 [FREE Full text] [Medline: 19436692]
24. Daldoul H, Denguezli M, Jithoo A, Gnatiuc L, Buist S, Burney P, et al. Prevalence of COPD and tobacco smoking in Tunisia—results from the BOLD study. Int J Environ Res Public Health 2013 Dec 17;10(12):7257-7271 [FREE Full text] [doi: 10.3390/ijerph10127257] [Medline: 24351745]
25. Alhamad EH, Alorainy HS, Lababidi H, Al-Hajjaj MS. The prevalence of chronic obstructive pulmonary disease in Riyadh, Saudi Arabia: a BOLD study. Int J Tuberc Lung Dis 2015 Oct;19(10):1252-1257. [doi: 10.5588/ijtld.14.0939] [Medline: 26459542]
26. Danielsson P, Ólafsdóttir IS, Benediktsdóttir B, Gíslason T, Janson C. The prevalence of chronic obstructive pulmonary disease in Uppsala, Sweden—the Burden of Obstructive Lung Disease (BOLD) study: cross-sectional population-based study. Clin Respir J 2012 Apr;6(2):120-127. [doi: 10.1111/j.1752-699X.2011.00257.x] [Medline: 21651748]
27. Rothman RJ, Greenland S, Lash TL. Modern Epidemiology. Third Edition. Philadelphia: Lippincott-Williams & Wilkins Publishers; 2008.

28. World Health Organization. The WHO country health profile of Kazakhstan. URL: http://www.who.int/countries/kaz/en/ [accessed 2017-05-14] [WebCite Cache ID 6qS2v7MOo]
29. Buist AS, Vollmer WM, Sullivan SD, Weiss KB, Lee TA, Menezes AMB, et al. The Burden of Obstructive Lung Disease Initiative (BOLD): rationale and design. COPD 2005 Jun;2(2):277-283. [Medline: 17136954]
30. Ford ES, Mannino DM, Wheaton AG, Giles WH, Presley-Cantrell L, Croft JB. Trends in the prevalence of obstructive and restrictive lung function among adults in the United States: findings from the National Health and Nutrition Examination surveys from 1988-1994 to 2007-2010. Chest 2013 May;143(5):1395-1406 [FREE Full text] [doi: 10.1378/chest.12-1135] [Medline: 23715520]
31. Lohr SL. Sampling: Design and Analysis. 2nd Edition. Boston: Cengage Learning; 2010.
32. Hoving C, Mudde AN. Effect of recruitment method and setting on the composition of samples consisting of adult smokers. Patient Educ Couns 2007 Jan;65(1):79-86. [doi: 10.1016/j.pec.2006.05.008] [Medline: 16872796]
33. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. Eur Respir J 2005 Aug;26(2):319-338 [FREE Full text] [doi: 10.1183/09031936.05.00034805] [Medline: 16055882]
34. Beigelman-Aubry C. Advanced chest imaging. URL: http://clinical.netforum.healthcare.philips.com/us_en/Explore/Abstracts/CT/Advanced-chest-imaging [accessed 2017-07-06] [WebCite Cache ID 6qSQyIBzY]
35. Bhalla M, Turcios N, Aponte V, Jenkins M, Leitman BS, McCauley DI, et al. Cystic fibrosis: scoring system with thin-section CT. Radiology 1991 Jun;179(3):783-788. [doi: 10.1148/radiology.179.3.2027992] [Medline: 2027992]
36. Tulek B, Kivrak AS, Ozbek S, Kanat F, Suerdem M. Phenotyping of chronic obstructive pulmonary disease using the modified Bhalla scoring system for high-resolution computed tomography. Can Respir J 2013;20(2):91-96 [FREE Full text] [Medline: 23616965]
37. Stanford Medicine 25. Pulmonary exam: percussion and inspection URL: http://stanfordmedicine25.stanford.edu/the25/pulmonary.html [accessed 2017-07-06] [WebCite Cache ID 6nmHVisJP]
38. Stanford Medicine 25. Cardiac second sounds URL: http://stanfordmedicine25.stanford.edu/the25/cardiac.html [accessed 2017-01-25] [WebCite Cache ID 6nmHu2tbb]
39. American Thoracic Society. ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med 2002 Jul 1;166(1):111-117. [doi: 10.1164/ajrccm.166.1.at1102] [Medline: 12091180]
40. Mahler DA, Horowitz MB. Perception of breathlessness during exercise in patients with respiratory disease. Med Sci Sports Exerc 1994 Sep;26(9):1078-1081. [Medline: 7808239]
41. Jones PW, Harding G, Berry P, Wiklund I, Chen W, Kline LN. Development and first validation of the COPD Assessment Test. Eur Respir J 2009 Sep;34(3):648-654 [FREE Full text] [doi: 10.1183/09031936.00102509] [Medline: 19720809]

Abbreviations

BOLD: Burden of Obstructive Lung Disease
CAT: COPD Assessment Test
CAPI: computer-assisted personal interviewing
COPD: chronic obstructive pulmonary disease
CT: computed tomography
ECG: electrocardiogram
FEV1: forced expiratory volume in 1 second
FVC: forced vital capacity

Edited by G Eysenbach; submitted 27.01.17; peer-reviewed by F Pourmalek; comments to author 20.03.17; revised version received 16.05.17; accepted 23.05.17; published 25.07.17.

Please cite as:
Sharman A, Zhussupov B, Sharman D, Stambekova A, Yeraliyev S
Cross-Sectional Study of Chronic Obstructive Pulmonary Disease Prevalence Among Smokers, Ex-Smokers, and Never-Smokers in Almaty, Kazakhstan: Study Protocol
JMIR Res Protoc 2017;6(7):e143
URL: http://www.researchprotocols.org/2017/7/e143/
doi:10.2196/resprot.7422
PMID:28743683

Publisher:
JMIR Publications
130 Queens Quay East.
Toronto, ON, M5A 3Y5
Phone: (+1) 416-583-2040
Email: support@jmir.org