ONLINE SUPPLEMENT 1

Effects of "Light-Touch" Counseling by Humans vs. Computers to Increase Weekly Walking in Underserved Populations: The COMPASS Randomized Clinical Trial Design and Methods

Abby C. King, PhD, et al. Stanford University School of Medicine

1. Introduction

Physical inactivity is responsible for nearly 10% of major non-communicable diseases (NCDs) worldwide.[1] In the U.S., population-level data suggest that increasing regular moderate physical activity could reduce annual medical costs by as much as $76.6 billion.[2] While national guidelines for physical activity promotion emphasize the importance of appealing and convenient physical activities such as walking,[3] a significant proportion of Americans (33%) remains inactive.[4] This is particularly true for older (45% inactive), low-income (46% inactive), and Latino adults (44% inactive),[4] who have high rates of obesity and other chronic conditions (e.g., Type 2 diabetes)[5] in combination with often reduced access to programs to improve physical and mental health.[6]

Few physical activity programs have taken into account the cultural preferences and needs of Latino Americans—among the fastest growing segments of the U.S. population, including aging adults.[7] The major objective of the COMPASS Trial is to systematically compare culturally adapted and individually tailored physical activity counseling for midlife and older Latino adults delivered through two different communication channels: trained peer advisors (called *promotores de salud)* vs. a virtual advisor (i.e., a computer-based embodied conversational agent named "Carmen"). Peer or lay health advisors, which have been in existence in Latino communities for decades,[8] are typically members of the community in which they work, sharing the community's culture, language, and environment.[9,10-12] However, few such programs have specifically targeted physical activity counseling.[13] Similarly, while evidence suggests that aging adults as well as Latinos and other racial/ethnic minorities are increasingly using computer technology and e-Health platforms,[14] most people targeted by e-Health programs have been well educated, younger (<50 years), and White.[14-17] These circumstances increase concerns that e-Health may intensify the "digital divide" and exacerbate health disparities for under-represented communities.[14,18,19] In particular, restricted computer access and lower computer, health, and language literacy levels are significant barriers for underserved populations.[14] Few websites have been designed for persons with less than a high school education,[14] and few e-Health programs incorporate cultural factors in health communications.[20] For web-based programs that do offer information in Spanish, content quality often has been substandard.[21] This may help to explain why only 42% of Latino adults ages 50 and older use the Internet, compared with 57% of non-Latinos.[19] In response to these often-cited barriers, the state-of-the-science "virtual advisor" computer technology being employed in COMPASS requires minimal computer skills or literacy, and provides personally and culturally tailored physical activity advice and support in multiple languages.[22]

The COMPASS Trial allows for a direct determination of program comparative effectiveness for the Peer vs. Virtual Advisor programs. It also provides the opportunity to explore which Latino adult subgroups may do best with which type of communication channel. Given the dearth of community-based clinical trials in the health promotion area that have specifically targeted low-income aging Latinos, the COMPASS Trial also presents a unique opportunity to evaluate recruitment channels of particular relevance to Latino adults. The study design and procedures, including recruitment, intervention, and assessment procedures, constitute the major focus of this paper.

2. Methods and Procedures

The Stanford University School of Medicine Institutional Review Board approved the study protocol for the COMPASS (Computerized Physical Activity Support for Seniors) Trial. All study materials, including informed consent and recruitment, intervention, and assessment forms, were produced in English and underwent thorough translation into Spanish by certified translators. Participants provided written consent upon reviewing the consent form with a bilingual staff member. The trial was registered at Clinicaltrials.gov (#NCT02111213).

2.1. Study design

The primary aim of this randomized trial is to test whether the Virtual Advisor intervention is as efficacious as the Peer Advisor intervention in promoting significant 12-month increases in weekly minutes of walking—a form of moderate-intensity activity that is readily accessible and appealing to substantial numbers of midlife and older adults across the socioeconomic spectrum.[3,23] The study employs a cluster-randomized design of community centers located in neighborhoods with at least 20% midlife and older Latino residents.[24] In addition to location, other factors that were considered in choosing community centers included interest and willingness of center staff to participate in the study, appropriate space to accommodate computer equipment for the Virtual Advisor or Peer Advisor sessions, and a steady flow of Latino midlife and older adults who utilize the center's regular programs and services. Community centers were matched by geographic location and randomized to either the Peer Advisor or Virtual Advisor intervention arm. The comparative effectiveness of these two interventions constitutes the major objective of the study and is the focus of this paper. In light of the extensive 80-year physical activity and health evidence

base demonstrating the important impacts of regular physical activity on individual and population health, particularly among older, inactive populations like the one being targeted, it was deemed unethical to include a placebo arm.[25,26]

2.2. Study location and participants

The study is located in two San Francisco Bay Area counties—Santa Clara and San Mateo counties. Approximately 26% of the population across these two counties report being of Latino or Hispanic ethnicity [www.census.gov, 2015 American Community Survey]. Latinos in the western U.S. come largely from Mexico and Central America.[24] Of those born outside the US, approximately 50% have lived here for 15 or more years.

The following study eligibility criteria were used to enroll study participants: (a) ages 50 years and older; (b) insufficiently active,[3] i.e., engaged in less than 100 minutes/week of moderate intensity activity over the past month; based on initial study physical activity screening items (see below), followed by a final baseline physical activity determination using the full CHAMPS questionnaire; [27] (c) able to safely engage in moderate forms of physical activities such as walking based on the Physical Activity Readiness Questionnaire;[27] (d) living within close proximity (i.e., within 5 miles) to one of the study-designated community centers to allow regular (e.g., weekly) attendance to the community center-based intervention sessions; (e) able to read and understand English or Spanish sufficiently to provide informed consent and participate in all study procedures; and f) planning to live in the area for the next twelve months. The study screen, typically by phone, to determine physical activity status included the following questions: 1) In the last three months have you regularly participated (at least two times per week) in any physical activity that has increased your breathing, such as aerobics, brisk walking, dancing, swimming, or playing sports. If the participants answered "yes", they were asked to describe how many days per week they regularly exercised and how many minutes per day. These numbers were multiplied to calculate the total number of minutes per week. If the total number was 100 min or more, the individual was deemed ineligible. If the total number of minutes per week was reported as < 100, then individuals were asked to report, in a typical or normal week over the past four weeks, the total number of minutes per week they engaged in dance, walking or hiking uphill, walking fast or briskly for exercise, and water exercises other than swimming. In- dividuals were deemed eligible if participation in the above exercises totaled < 100 min per week. A final determination of study eligibility based on physical activity status occurred at baseline using the full CHAMPS questionnaire.

2.3. Study participant recruitment and screening methods

To enhance external validity, three complementary recruitment methods were employed: geographically defined targeted mass mailings, cultural media-based promotion, and community outreach.[28-30] For the geographically defined targeted mass mailings, mailing addresses of residents in geographically defined Census block groups near the community centers were accessed via a private mail service company and selected based on age and Latino ethnicity. Introductory bilingual letters describing the study and business reply cards were sent to households, along with a toll-free number to call to obtain further study information and undergo initial screening for study eligibility. Those individuals judged to be initially eligible based on the telephone screen were invited to attend a group study orientation session at their designated community center, during which time the study objectives and procedures were explained in further detail, all questions were answered, and interested individuals were scheduled for an individual baseline assessment visit also held at the community center. Those individuals found to be eligible and willing to enroll in the study were scheduled for an initial individual intervention session at the community center.

To broaden the types of individuals enrolled in the trial, the targeted mass mailings were augmented with bilingual media-based promotion and community outreach.[28-30] The media promotional methods included study announcements placed in local Latino newspapers. As part of community outreach activities, study information was placed at participating community centers and was made available at local stakeholder events attended by bilingual study staff, such as health and resource fairs, back to school nights, Parent Teacher Association (PTA) meetings, local school council events, and parent group meetings, as well as neighborhood libraries, churches, local health clinics serving Latino adults, and local grocery stores.[31] Study participants and others who expressed interest in the study also were encouraged to refer others or share study information.

2.4. Study participant retention methods

To promote high levels of participant retention across the 12-month intervention and assessment period, group-based study orientation sessions were employed following the telephone screening process and prior to baseline assessment to ensure that all individuals considering study participation were fully informed about the study objectives, what would be expected of them throughout the study, and what they in turn could expect from the study

staff. The interactive group session included the weighing of the pros and cons of participating in the study, along with related motivational interviewing techniques and behavioral strategies, such as structuring of realistic expectations related to study outcomes. This type of pre-enrollment educational session has been associated with high levels of study retention in health behavior change trials across periods lasting up to 18 months.[32]

Modest remuneration for participation in each of the three study assessment points consisted of a $10/assessment gift card, used as a small "thank-you" for assessment completion. Use of small remunerations for completion of the scientific assessments only (and not intervention participation) are typically included in behavioral intervention studies to help defray any costs or inconvenience accompanying completion of the scientific assessments. The modest size of this remuneration is commensurate with standard ethical practice in helping to ensure that prospective participants do not sign up for a study simply because of a large remuneration. There is no evidence that we are aware of indicating that small remuneration for scientific assessment completion impacts participation levels in the types of behavioral interventions being tested. In fact, recent evidence reviews of studies that have formally tested the effects of providing monetary incentives or rewards specifically for physical activity behavior change in diverse populations report that unless such incentives are tied directly to achieving a specific physical activity goal, they have not been found to provide additional benefit beyond that provided by a behavioral intervention alone.[26,33]

2.5. Peer Advisor recruitment and screening methods

Recruitment of Peer Advisors was accomplished using a variety of strategies. Study interventionists worked with the community center staff to identify activities within the community center through which Peer Advisors might be recruited. In addition, study staff requested referrals of people who attended the community centers regularly and who center staff identified as potentially viable candidates for the Peer Advisor role. In addition to collaborating with the community centers directly, Peer Advisor recruitment was also conducted through collaborating with different agencies external to the community centers. These agencies included local social and civic service agencies along with educational institutions such as schools and libraries. In addition, some recruitment efforts occurred through partnering with local fitness centers and targeting their physically active population as potential study peer advisors.

Peer Advisor eligibility criteria consisted of the following: (a) ages 30 years and older; (b) physically active on a regular basis (i.e., engaged in approximately 150 minutes/week or more of moderate intensity physical activity over the past 12 months); (c) free of any medical problems that might make it difficult to participate in regular physical activity or serve as a Peer Advisor in the study (e.g., any unstable chronic conditions); (d) willing to participate in the peer advisor 12-hour training program and volunteer an average of 2-3 hours per week to advise their participants on physical activity; (e) willing to participate in monthly Peer Advisor supervision meetings; (f) able to read and understand English or Spanish sufficiently to provide informed consent and participate in all study procedures; and (g) planning to live in the area for the next 12 months. Peer Advisor selection and training consisted of screening interested individuals by phone to determine initial eligibility. Eligible individuals then attended an orientation session during which time the study objectives and procedures were explained in further detail, all questions were answered, and interested individuals provided informed consent related to study confidentiality protocols and information sharing. Individuals then completed a 12-hour Peer Advisor training program based on the successful peer advisor physical activity training programs conducted previously by the Stanford team.[34-36]

2.6. Peer Advisor oversight and quality assurance methods

Ongoing Peer Advisor oversight and quality assurance have been accomplished through monthly Peer Advisor supervision meetings, periodic review of Peer Advisor logs and notes completed after each Peer Advisor-participant advising session, and random check-ins by study staff with study participants. Each monthly study staff-led, group-based Peer Advisor supervision meeting lasts approximately 120 minutes and focuses on the following activities: (a) sharing among Peer Advisors of their experiences and challenges with their participants, along with receipt of problem-solving advice and ideas from study staff and other Peer Advisors; (b) ongoing physical activity-relevant information and updates; and (c) provision of relevant resources such as tip pages and newsletters that Peer Advisors can use in their meetings with their participants.

2.7. Peer Advisor retention methods

In addition to the monthly supervision meetings, other Peer Advisor retention methods include annual informational and motivational workshops provided by Stanford investigators and staff, modest monetary remuneration for the general time commitment accompanying Peer Advisor activities as well as to help defray any travel costs to the centers (i.e., a $10 local store gift card received upon completion of each participant introductory

intervention session; a monthly store gift card commensurate with the number of participant advising sessions completed that month, equaling $5.00 per advising session), intermittent receipt of low-cost project incentives (e.g., project apparel, project mugs and tote bags), and a certificate of completion honoring each Peer Advisor's contributions to the project at the end of his or her study advising period.

2.8. Development and delivery of study interventions

The two physical activity interventions are based on the theoretically derived cognitive-behavioral advice and support strategies used in the evidence-based Active Choices physical activity counseling program and similar behaviorally based interventions in the field.[37-40] The primary behavioral theory utilized in the program is Social Cognitive Theory[41] combined with the contextual framework of the Transtheoretical Model.[42] Social Cognitive Theory (SCT) recognizes the dynamic interplay of cognitive, behavioral, and social factors in influencing behavior change.[41] Among the variables derived from SCT are self-efficacy, the use of self-regulatory skills (e.g., self-monitoring, goal-setting), factors related to the physical activity behavior itself (e.g., format, intensity), and social environmental factors (e.g., modeling, social support, feedback from others), as predictors of physical activity participation.[43] Applications of the Transtheoretical Model to the health promotion area include the use of a range of behavioral and cognitive strategies aimed at an individual's motivational readiness to change a particular behavior (e.g., consciousness raising and other cognitive approaches in the preparation and action phases early in the program; reinforcement management and related behavioral approaches in the later phase of the program).[42]

The Virtual Advisor program consists of an embodied conversational agent (ECA)--an interactive, animated computer character that simulates face-to-face counseling and support using simple speech as well as nonverbal behaviors (e.g., facial cues, hand gestures).[44,45] Individuals interact with it through touching one of several simple conversation boxes shown on the screen throughout the interaction, which eliminates the need to utilize a computer mouse, track pad, or keyboard. The conversation boxes are aimed at less than an eighth-grade education level.[44,46]

The ECA communication interface has been shown to be effective in changing behavior in individuals with little to no computer experience and low levels of health literacy.[46] The initial adaptation of the Virtual Advisor program to the Latino population being targeted was accomplished through a smaller intervention study that preceded the current trial[22] that was based on earlier work with embodied conversational agents (i.e., virtual advisors) conducted by Bickmore et al.[45] This work was augmented with information from King et al.'s Active Choices physical activity intervention program.[38] The formative testing and pilot work that was conducted also suggested that "Carmen", the virtual advisor, could be acceptable to other midlife and older ethnic minority groups as well, including Asian, Filipino, and African-American adults. The intervention protocol derived from this prior work was applied, in conjunction with similar intervention work with peer advisors,[47] in establishing a parallel physical activity counseling program delivered in the trained Peer Advisor arm.[47]

Both individually adapted programs are delivered at each participant's designated community center and focus in particular on walking and similar forms of moderate-intensity physical activity. Both interventions begin with an introductory session that covers the following information:[38] (a) review of the participant's physical activity history, long-term goals, and anticipated barriers to and facilitators of regular physical activity; (b) provision of information on the physical activity national guidelines, safety tips, and community center resources; (c) co-creation of a weekly physical activity plan; (d) training in the regular use of a pedometer and a project calendar to log steps and walking minutes; and (e) scheduling of the next intervention appointment.

Following the introductory session, each session follows a standard counseling protocol that is similar across the two interventions and which generally consists of the following elements: greetings and introductory social dialogue, checking for important health changes, review of pedometer-measured steps and minutes walked since the last advising session, acknowledgement of successes, problem-solving around barriers to physical activity, provision of relevant information to continue with physical activity or to overcome barriers, goal-setting for the period between the current and the next advising session, scheduling of the next advising session, and summary and wrap up. The typical advising session for each intervention was developed to average approximately 10-15 minutes, and the general schedule of advising sessions for both arms over the one-year intervention period, based on previous research,[34,38] is as follows: weekly sessions for the first two months; and twice-per-month sessions for the remaining 10 months.

In the *Human Advisor* arm, peer advisors meet with their individual participants in a location within the community center that affords privacy. The *Virtual Advisor,* meanwhile, is housed on a dedicated computer (supplied by the study) located in a private, secure area at each designated community center receiving that

intervention. Participants are trained in a brief introductory session with project staff and are provided with a private log-in to initiate sessions with the advisor. Similar to the Peer Advising arm, participants are taught to use an Omron pedometer (Omron Healthcare, Inc., model HJ-720ITC**,** Lake Forest, Ill, 60045, USA), which provides a valid, reliable daily step count under prescribed and self-paced walking conditions in normal-weight and overweight adults.[48] Participants are instructed to wear the pedometer on a daily basis, and download it on the Virtual Advisor computer via USB port at each session. The Omron can reliably store data for up to 41 days. Participants also complete a brief survey of personalized information at enrollment (e.g., favorite entertainment, names of supportive relatives/friends) that is programmed into the computer to personalize Virtual Advisor dialogue. Participants are encouraged to wear headphones during Virtual Advisor sessions to ensure privacy. As described earlier, Virtual Advisor and Peer Advisor sessions include individualized social interaction, progress review based on downloaded pedometer information, personalized feedback and problem solving, and goal setting based on current progress.[49] Educational information can be received if desired in both arms.

2.9. Intervention fidelity and quality assurance

To maintain intervention fidelity and quality assurance in the Peer Advisor arm, trained staff members conduct regular quality control checks and activities as described above.[34,50] Virtual Advisor quality assurance includes regular monitoring of system performance and backup along with participant log-in activity, and ongoing availability of a study helpline for participants and center staff to call for assistance in correcting any problems. A designated Stanford staff member is in regular contact (twice a month or more frequently as needed) with the Virtual Advisor programming and oversight team at Northeastern University to ensure that any problems that occur can be resolved in a timely manner.

2.10. Assessment: Primary outcome measures

The primary outcome is change in walking activity across the 12-month intervention period. Walking is assessed at three time points (baseline, six months, 12 months) using the four walking items from the validated CHAMPS questionnaire (interview format) for older adults, which is available in English and Spanish.[51-53] The CHAMPS questionnaire assesses usual weekly minutes of walking over the previous 4 weeks.

Such validated self-report instruments represent the most direct and reliable means for assessing walking patterns, given that device-based assessment tools (pedometers, accelerometers) typically capture more general movement levels beyond walking behavior and can be less accurate and sensitive to change in older adults with low levels of physical activity. The CHAMPS walking items have been significantly associated with pedometer steps in previous studies, and were sensitive to change in the earlier conducted Virtual Advisor physical activity intervention study in a similar group of midlife and older Latino adults.[22] The CHAMPS total activity as well as moderate and more vigorous physical activity (MVPA) variables have been consistently associated with objective physical activity measures in prior studies and therefore will be evaluated as secondary measures of physical activity in the COMPASS Trial.[54,55] We will also describe the proportion of each arm meeting the national physical activity recommendations of at least 150 minutes/week of MVPA.[3]

Physical activity measurement using the CHAMPS is accompanied by the validated Actigraph® accelerometer (model wGT3X) at each of the three assessment time points.[56] The accelerometer provides objective information related to overall physical activity amounts and intensity (though not the types of activities engaged in). The accelerometry protocol from a large study of 860 older adults is being applied.[57] The activity monitor is worn on the hip during waking hours for seven consecutive days at each time point, ensuring a sufficient number of days of physical activity data (at least five days is considered as complete data) commensurate with current physical activity studies in older adults.[58] Participants are instructed to wear the accelerometer for at least eight hours per day during their waking hours, commensurate with other studies aimed at expanding data inclusivity.[59,60] Wear-time validity will be determined through applying the wear and non-wear time analysis and classification algorithms reported by Choi et al.,[61] and analysis and interpretation of the accelerometry data will be based on our prior investigations and those of other older adult populations.[62]

2.11. Secondary outcome measures

Secondary outcome variables of particular importance to aging Latino populations include the following: sedentary behavior, measured using a validated one-week recall survey responsive to change in older adults;[63] body mass index (BMI), derived using standard clinical assessment protocols for height and weight;[53] resting blood pressure and heart rate, using standard protocols;[53] and quality of life and well-being, measured with the 10-item

Vitality Plus Scale assessing well-being constructs associated with regular physical activity in aging adults, including sleep quality, energy, mood, and pain.[64]

In addition to the above outcomes, program safety and adverse events are being tracked in both intervention arms using standardized forms and protocols used in prior physical activity intervention trials.[34,39] Also, overall participant acceptability ratings of the novel Virtual Advisor intervention are being assessed at the end of the 12-month intervention period via a 19-item computer program acceptability scale,[65] a 4-item cultural congruity scale,[66] and the Working Alliance Inventory's 12-item bonding subscale.[22,67] Similar program acceptability questionnaires are being collected in the Peer Advisor arm at 12 months.[34]

2.14. Randomization of community centers to study arms

Block randomization by county locale was used to assign ten community centers to the two major study arms. Centers were randomized in pairs (1:1 allocation) by locale to either Virtual or Human advisors based on a computerized randomization sequence (SAS PROC Plan statistical software; Cary, NC) by staff not involved in study assessment or intervention procedures. Allocation concealment was in place for each block of centers during the randomization process to minimize selection bias with respect to subsequent blocks. Assessment staff members are blinded to randomization assignment and masked to prior assessment data for each participant.

2.15. Sample size calculation and data analysis plan

Sample size estimates have been developed to test the study's primary question related to whether the Virtual Advisor intervention is no worse than the intervention delivered by trained human advisors, i.e., a test of non-inferiority.[68] Using a one-tailed 95% confidence interval, the threshold of clinical significance between the two treatments, Δ, has been developed to demonstrate clinical noninferiority of the new intervention (Virtual Advisor) if the confidence interval lay completely above – Δ, while clinical noninferiority of the Peer Advisor intervention will be demonstrated if the confidence interval lay completely below + Δ. The 30 minutes of walking/week noninferiority margin was chosen based on the physical activity evidence base showing that adding as little as an additional 30-minute episode per week can confer meaningful health benefits for aging adults, including lowered risks of premature all-cause mortality,[25,26,69,70] as well as acute improvements in cognitive function[26]—outcomes of great interest among older adults. The noninferiority margin was based on a clinically meaningful difference, in one direction, between arms of 30 minutes walking/week,[25] and a within-arm standard deviation of 90, accounting for clustering within centers.[71]

We calculated that a sample of 113 per arm (226 total) would provide 80% power to demonstrate noninferiority between the two interventions using a simple pre-post analysis. We plan to use a mixed-effects linear regression model. Mixed-effects linear regression effectively addresses both missing data and early dropout in "intention-to-treat" analysis.[72,73,74] Twenty-one additional participants were recruited to protect against loss to follow-up. Similar mixed-effects linear regression techniques will be used to address the secondary outcomes of interest, e.g., intervention impacts on well-being variables across the study period.

Analysis Plan

Descriptive statistics summarize baseline characteristics. Baseline between-arm differences are tested using independent-sample t-tests for continuous variables and Pearson chi-square or exact tests for categorical variables. The primary noninferiority hypothesis is tested using a mixed-effects linear regression model (SAS, 15.1**)**. Change in total 12-month walking minutes/week is the primary outcome, with centered arm assignment as the independent variable, and centered baseline walking value, the interaction between centered arm assignment and centered baseline value, community site, and sex as covariates.[75] To account for the cluster-randomization design, community center is included as a random intercept term.[76] Extreme values of the 12-month outcomes are limited by winsorization to three standard deviations above the mean.[77] To account for missing data, multiple imputations are performed by replacing missing 12-month values with a set of plausible values using the option of imputation by fully conditional specification methods (10 imputations were done). Imputation results are then combined.[78,79] All reported outcomes use intention-to-treat (ITT) methods. Using a 1-sided 95% confidence interval constructed for the between-group difference in the primary outcome, noninferiority is deemed demonstrated if the lower limit of the confidence interval lay to the right of the noninferiority margin of -30.[80] For completeness,[80] both ITT and per-protocol analyses will be reported. Intervention participation variables are compared using t-tests. Within-arm pre-post t-tests on outcomes are undertaken for descriptive purposes.

3. Descriptive Results

3.1. Selection and description of study community centers

Ten community centers located in Santa Clara and San Mateo Counties, California with at least 20% Latino households (range = 21-55% Latino households) living within a one- to five-mile radius from the center were identified and expressed interest in serving as a study intervention site. These sites were block-randomized by locale to either the Human or Virtual Advisor arms. Soon after recruitment (to the Human Advisor arm) and prior to participant enrollment, one center experienced unforeseen changes in its administration that disrupted center operations and precluded center participation in the study. To ensure comparable participant enrollment in each study arm, additional participants were enrolled at the remaining four community centers assigned to that intervention arm.

In each center, there were center staff who were willing to support the research team in reserving meeting space for clinical assessments, recruitment meetings, and, when relevant, Human Advisor meetings. For the sites that received the Virtual Advisor, designated staff members were instructed on how to maintain the computer kiosk (i.e., refilling printer paper, providing minor technical support related to the computer such as making sure that it was switched on and that the touch screen remained clean, and contacting a member of the research team if needed.)

All participating community centers offered, as part of their usual activities, a nutrition program for older adults as well as nonphysical activity-oriented classes and activities, such as bingo, karaoke, and arts and crafts. Additionally, 89% offered weekly physical activity classes and had at least one general computer available for older adults visiting their center.

3.2. Study participants enrolled and recruitment sources

A total of 245 participants are enrolled in the primary trial (Human Advisor arm: n = 122; Virtual Advisor arm: n = 123). The study participants range in age from 50 to 87 years, and 79% are women, with about half of participants reporting being married or living with a partner. The predominance of women is common in such health promotion intervention studies, as is the reluctance of participants, especially from such lower-income communities, to report their household incomes. Forty-four percent of participants have high school or lower levels of education.

The highest recruitment yield (88.7% of enrolled subjects) was obtained from the geographically defined and demographically targeted bilingual mass mailings aimed at the Census blocks surrounding the community centers. The total number of targeted letters mailed describing the study and inviting individuals to contact the study team for more information was 107,930. The total cost of the targeted mailing recruitment strategy equaled approximately $69,900.00.

3.3. Results related to recruitment and enrollment of Peer Advisors

During the recruitment process for Peer Advisors, 230 individuals expressed initial interest, and 119 individuals were found to be eligible based on the study's Peer Advisor eligibility criteria. Of these individuals, 56 completed the Peer Advisor training requirement, and 36 initiated Peer Advisor activities with at least one participant. Over the course of the intervention period, six Peer Advisors had to relinquish their peer advisor activities due to a move out of the area, medical illness, or the initiation of a new job which put constraints on their time. Their study participants were transferred successfully to other Peer Advisors with minimal difficulties.

4. Discussion

The COMPASS Trial is among the first studies to systematically compare the effectiveness of physical activity advice delivered by humans versus automated advisors in aging Latino adults. Insufficiently active Latino adults are at elevated risk for a variety of chronic diseases and conditions, yet have rarely been targeted for tailored physical activity advice and support using communication sources (i.e., trained peer advisors, virtual advisors) that have great potential for population transferability and reach. The use of community centers for intervention delivery provides a readily available intervention access point in many communities across the U.S., and the one-year intervention period will provide insights related to initial physical activity adoption and more sustained behavioral maintenance. The multi-faceted recruitment plan allows for a more diverse and potentially generalizable sample, and the particularly high yield of the targeted mass mailings is notable, given its less frequent use in a number of community-based research studies. At least one study has shown that personalized direct mailings can increase response rates for Latino adults relative to non- targeted approaches. [81] While community-based *promotores de salud* (i.e., lay or peer advisors) are a known and effective mechanism for health promotion in Latino populations, the method has been limited by the ability to scale. If the technology-enabled Virtual Advisor proves comparable and cost-sensitive relative to the Peer Advisor arm, it represents a scalable and replicable solution that could be readily integrated into current community and senior center infrastructures.

While the primary aim of this trial is to compare the 12-month effectiveness of the Virtual Advisor relative to Peer Advisors, a similarly compelling goal is to explore, through the planned moderator analyses, which participant subgroups may do best with which type of intervention. Referred to as "the whiches conundrum",[82-84] ascertaining how best to target different interventions to different subgroups of people represents among the most important challenges currently facing the behavioral health and precision medicine fields.[82] Similarly, the planned mediator analyses will provide initial information on which types of variables may be of particular importance for achieving intervention-related impacts on physical activity levels.

5. Conclusion

If the promising preliminary Virtual Advisor evidence obtained from the original pilot study [22] is confirmed in this comparative effectiveness trial, this intervention will represent a potentially low-cost, readily accessible option that could be broadly disseminated across a range of community settings (e.g., clinics, pharmacies, libraries, residential settings). As such, it has substantial potential to reduce the health disparities gap by influencing a key health behavior in underserved populations.[85]

HUMAN SUBJECTS

Note: All investigators participating in the proposed research have completed the Human Participant Protections Education for Research Teams certification process in compliance with NIH and Stanford University or Northeastern University guidelines.

I. Consent Procedures

Prior to undergoing the initial telephone or face-to-face screening, the screening procedures will be explained and individuals will give verbal consent to answer initial eligibility questions (age, ethnicity, proximity to community center). Those who are initially eligible will then proceed to an information session where the study activities and procedures will be explained in greater detail. If interested in continuing at that point, individuals will read and sign an informed consent form approved by the Human Use Committee at Stanford Medical School. This consent form will describe the study assessment and intervention components of the project, and their rights as research participants. The consent form will inform individuals that all information is strictly confidential and will not be released to anyone without their written consent. They will be reminded that as volunteers they can terminate their participation at any time without negative consequences. They will be provided information to contact the Medical Committee for the Use of Human Subjects in Research at Stanford Medical School.

II. Potential Risks

The potential risks involved in this project include psychological complications resulting from the assessment procedures or medical risks associated with moderate intensity physical activity programs in persons in this older age group.

Psychological risks of the evaluation. There is a remote risk that persons completing questionnaires focusing on behavioral or psychological content may become distressed. There is no evidence that any permanent psychological dysfunction has resulted from such assessments.

Medical risks of physical activity programs. The major risks of physical activity programs by initially inactive persons aged 50 years and over are orthopedic and cardio-respiratory. Orthopedic problems primarily are of the overuse variety and usually can be treated by rest and change in the mode of physical activity. Frequent minor problems can occur, including temporary soreness or irritation of muscles, tendons and joints. The likelihood of orthopedic and cardio-respiratory risks are greatly minimized through the use of a moderate-intensity physical activity program that involves mild to moderate-intensity walking, as proposed in the current study, and a supervised, individualized, progressive approach to physical activity as proposed in the current program.

III. Minimizing Potential Risk

Study assessments will be conducted at the community centers by extensively trained and supervised study staff.

Physical activity programs. To ensure participant safety in this study, we will apply the set of screening and oversight procedures that are recommended in the American College of Sports Medicine's (ACSM) guidelines and that we have used successfully in our research studies over the past 30 years. As recommended in the current ACSM guidelines, to screen potential participants for appropriateness for the physical activity program, we will have each

individual complete the Physical Activity Readiness Questionnaire (PAR-Q), an extensively validated and used screening questionnaire that has been used throughout Canada and the U.S. to screen individuals for community-based physical activity programs. If individuals answer 'yes' to any of the medically related screening items, they will be directed to get physician clearance prior to entry into the study. This protocol has been shown to ensure participant safety without creating unnecessary medical expenses and barriers to participation for persons not deemed at risk for physical activity-related complications---an important issue for the low-income population being targeted. The use of a mild form of physical activity (walking) also diminishes risk. In addition, participants will be regularly monitored for any level of physical discomfort or injury as part of the virtual advisor and lay advisor programs, and all subjects will be evaluated for adverse events as part of the study assessments conducted every 6 months using the standard forms approved for use by the Stanford Institutional Review Board.

The risks of injury resulting from participating in the prescribed physical activity programs will be minimized in several ways:

- Exclusion from the study of any person with overt cardiovascular or orthopedic disease.

- Individualized physical activity program aimed at slow, gradual progression of physical activity amount.

- The use of moderate-intensity physical activity programs, involving walking, for all study participants.

- Ongoing personalized instruction of participants as part of the evidence-based physical activity advisor programs.

- Ongoing attention to and advice related to the experience of physical discomfort during physical activity as part of both evidence-based physical activity advisor programs. (In addition, standard advice from the current U.S. Department of Health and Human Services' national physical activity recommendations concerning physical activity safety is provided as part of the health education attention-control program.)

The content of the moderate-intensity physical activity program that is being targeted is commensurate with the current national guidelines for physical activity promotion in older adults.

Confidentiality of participant data. Confidentiality of participant data will be maintained by handling individual data by ID number, rather than by name; storing all individual data in locked file cabinets and secured, password protected electronic hard drives and data servers; and not disclosing individual data to anyone other than project staff, except as requested by the participant in writing.

Adverse event monitoring and reporting. Adverse events information will be collected at all assessment points and recorded on standard forms that have been used in our other studies. We will collect information on all potential types of adverse events, including musculo-skeletal soreness and injury, as well as major medical events including injuries or conditions that result in health care provider visits, hospitalization, etc. Consistent with NIH and Stanford IRB policy, adverse events will be promptly reported in writing to the NIH and Stanford IRB.

IV. Risks versus Benefits

We believe the risks involved with the proposed physical activity interventions and associated tests are very small. Our own experience in studies involving the assessments proposed and the encouragement of progressive, moderate intensity physical activity in screened participants in this age group has been very positive. We are not aware of a single long-term adverse reaction to such physical activity programs among the over 3,000 study subjects we have monitored over the past 30 years.

We believe that all participants will benefit by learning (from the study questionnaires) about their health status and physical activity levels. Those who successfully improve their physical activity levels will have achieved desired goals. Over the study period, all participants will benefit from receiving health information.

We believe society will benefit from the results of this project in that it will inform further research aimed at developing effective and appropriate physical activity programs for under-served ethnic minorities. It will shed light on how best to deliver physical activity advice to enhance adoption and maintenance of PA among Latinos using state-of-the-art informational technology that could conceivably be utilized in a range of community and home settings, thus substantially broadening the reach of the physical activity counseling program to underserved populations at potentially lower-cost than traditional face-to-face or health care provider-delivered approaches. These are public health issues of immense proportions, particularly with the continued growth of the elderly segment

of the U.S. population and the substantial prevalence of inactivity among that population segment. In summary, we believe the risks can be kept very low whereas the benefits to participants and society are quite substantial.

Data and Safety Monitoring Plan

In addition to ongoing (weekly) project oversight by our senior investigators, the project's Data and Safety Oversight Committee, will meet at regular intervals (e.g., semi-annually or more frequently as indicated) throughout the project period to provide input and feedback related to study recruitment and retention rates, study eligibility determination issues, data completion rates, and adverse events. During the study, participants will regularly monitor any discomfort that they are experiencing from the moderate-intensity physical activity program (consisting of walking) and will report them to their physical activity advisor on a weekly basis. We will use this information to revise the interventions as necessary to ensure that any risks of injury or discomfort are minimized.

References

1. Lee IM, Shiroma EJ, Lobelo F, et al. Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. *Lancet.* 2012;380(9838):219-229.
2. Pratt M, Macera CA, Wang G. Higher direct medical costs associated with physical inactivity. *The Physician and Sportsmedicine.* 2000;28:63-70.
3. Physical Activity Guidelines Advisory Committee. *Report of the Physical Activity Guidelines Advisory Committee, 2008.* Washington, DC: U.S. Department of Health and Human Services;2008.
4. Pleis JR, Ward BW, Lucas JW. *Summary health statistics for U.S. adults: National Health Interview Survey, 2009.* Atlanta, CA: CDC;2010.
5. Livingston G, Minushkin S, Cohn D. *Hispanics and health care in the United States: Access, information and knowledge.* Pew Hispanic Center;2008.
6. Silvia CA. Barriers to physical activity in the Hispanic community. *J Public Health Policy.* 2003;24(1):41-58.
7. Vincent GK, Velkoff AK. *The Next Four Decades, The Older Population in the United States: 2010 to 2050.* Washington, DC: U.S. Census Bureau;2010.
8. World Health Organization. *The Community Health Worker.* Geneva Switzerland: Office of Publications, World Health Organization;1990.
9. Eng E, Parker E, Harlan C. Health advisor interventions strategies: a continuum from natural helping to paraprofessional helping. *Health Educ Behav.* 1997;24(4):510-522.
10. Love MB, Gardner K, Legion V. Community Health Workers: Who they are and what they do. *Health Educ Behav.* 1997;24(4):510-522.
11. Ayala GX, Vaz L, Earp JA, Elder JP, Cherrington A. Outcome effectiveness of the lay health advisor model among Latinos in the United States: an examination by role. *Health Educ Res.* 2010;25(5):815-840.
12. Viswanathan M, Kraschnewski J, Nishikawa B, et al. *Outcomes of community health work interventions. Evidence Report.* Rockville, MD: Agency for Healthcare Research and Quality; June 2009 2009. Technology Assessment No. 181.
13. Vega WA, González HM. Latinos "aging in place": Issues and potential solutions. In: Angel JL, Torres-Gil F, Markides K, eds. *Aging, Health, and Longevity in the Mexican-Origin Population.* New York, NY: Springer; 2012:193-205.
14. Viswanath K, Kreuter MW. Health disparities, communication inequalities, and eHealth. *Am J Prev Med.* 2007;32(5 Suppl):S131-133.
15. Glasgow RE. eHealth evaluation and dissemination research. *Am J Prev Med.* 2007;32(5 Suppl):S119-126.
16. Norman CD, Skinner HA. eHealth Literacy: Essential skills for consumer health in a networked world. *J Med Internet Res.* 2006;8(2):e9.
17. Norman GJ, Zabinski MF, Adams MA, Rosenberg DE, Yaroch AL, Atienza AA. A review of eHealth interventions for physical activity and dietary behavior change. *Am J Prev Med.* 2007;33(4):336-345.
18. Curry SJ. eHealth research and healthcare delivery beyond intervention effectiveness. *Am J Prev Med.* 2007;32(5 Suppl):S127-130.
19. Livingston G. *The Latino digital divide: The native born versus the foreign born.* Washington, DC: Pew Research Center; July 28, 2010 2010.
20. Kreuter MW, McClure SM. The role of culture in health communication. *Annu Rev Public Health.* 2004;25:439-455.

21. Cardelle AJF, Rodriguez EG. The quality of Spanish health information websites: An emerging disparity. *Journal of Prevention & Intervention in the Community.* 2005;29:85-102.
22. King AC, Bickmore TW, Campero MI, Pruitt LA, Yin JL. Employing "virtual advisors" in preventive care for underserved communities: Results from the COMPASS study. *J Health Commun Int Perspect.* 2013;18(12):1449-1464.
23. Murphy MH, Nevill AM, Murtagh EM, Holder RL. The effect of walking on fitness, fatness and resting blood pressure: a meta-analysis of randomised, controlled trials. *Prev Med.* 2007;44(5):377-385.
24. U.S. Census Bureau. U.S. 2010 Census Data. 2011; Census Summary File 1. Available at: http://2010.census.gov/2010census/data/ Accessed December 3, 2011.
25. Physical Activity Guidelines Advisory Committee. *Physical Activity Guidelines Advisory Committee Report, 2008.* Washington, DC: US Department of Health and Human Services;2008.
26. Physical Activity Guidelines Advisory Committee. *2018 Physical Activity Guidelines Advisory Committee Scientific Report.* Washington, DC: U.S. Department of Health and Human Services;2018.
27. Thomas S, Reading J, Shephard RJ. Revision of the Physical Activity Readiness Questionnaire (PAR-Q). *Canadian J Sports Sci.* 1992;17:338-345.
28. King AC, Harris RB, Haskell WL. Effect of recruitment strategy on types of subjects entered into a primary prevention clinical trial. *Annals of Epidemiology.* 1994;4:312-320.
29. Kiernan M, Phillips K, Fair JM, King AC. Using direct mail to recruit Hispanic adults into a dietary intervention: an experimental study. *Ann Behav Med.* 2000;22(1):89-93.
30. Brown SD, Lee K, Schoffman DE, King AC, Crawley LM, Kiernan M. Minority recruitment into clinical trials: Experimental findings and practical implications. *Contemp Clin Trials.* 2012;33(4):620-623.
31. Soto J, Campero MI, Castro CM, King AC. Lessons from recruiting Latino older adults into the LIFE trial. Society of Behavioral Medicine 33rd Annual Meeting and Scientific Sessions: Rapid Communications; April 13, 2012, 2012; New Orleans, LA.
32. Goldberg JH, Kiernan M. Innovative techniques to address retention in a behavioral weight-loss trial. *Health Educ Res.* 2005;20(4):439-447.
33. King AC, Whitt-Glover MC, Marquez DX, et al. Physical Activity Promotion: Highlights from the 2018 Physical Activity Guidelines Advisory Committee Systematic Review. *Med Sci Sports Exerc.* 2019;51(6):1340-1353.
34. Castro CM, Pruitt LA, Buman MP, King AC. Physical activity program delivery by professionals versus volunteers: The TEAM randomized trial. *Health Psychol.* 2011;30(3):285-294.
35. Wilcox S, Dowda M, Griffin SF, et al. Results of the first year of Active for Life: Translation of two evidence-based physical activity programs for older adults into community settings. *Am J Public Health.* 2006;96:1201-1209.
36. Griffin SF, Wilcox S, Ory MG, et al. Results from the Active for Life process evaluation: program delivery fidelity and adaptations. *Health Educ Res.* 2010;25(2):325-342.
37. King AC, Haskell WL, Taylor CB, Kraemer HC, DeBusk RF. Group- vs home-based exercise training in healthy older men and women. A community-based clinical trial. *JAMA.* 1991;266(11):1535-1542.
38. King AC, Friedman RM, Marcus BH, et al. Ongoing physical activity advice by humans versus computers: The Community Health Advice by Telephone (CHAT) Trial. *Health Psychol.* 2007;26:718-727.
39. King AC, Castro CM, Buman MP, Hekler EB, Urizar G, Ahn DG. Behavioral impacts of sequentially versus simultaneously delivered dietary plus physical activity interventions: The CALM Trial. *Ann Behav Med.* 2013;46(2):157-168.
40. Wilcox S, Dowda M, Leviton LC, et al. Active for Life: final results from the translation of two physical activity programs. *Am J Prev Med.* 2008;35(4):340-351.
41. Bandura A. Social cognitive theory: an agentic perspective. *Annual Reviews of Psychology.* 2001;52:1-26.
42. Marshall SJ, Biddle SJH. The transtheoretical model of behavior change: a meta-analysis of applications to physical activity and exercise. *Annals of Behavioral Medicine.* 2001;23:229-246.
43. King AC. Interventions to promote physical activity in older adults. *Journal of Gerontology: Biological Sciences and Medical Sciences.* 2001;56A(Special Issue II):36-46.
44. Bickmore T, Caruso L, Clough-Gorr K, Heeren T. 'It's just like you talk to a friend' - Relational agents for older adults. *Interacting with Computers.* 2005;17:711-735.
45. Bickmore T, Gruber A, Picard R. Establishing the computer-patient working alliance in automated health behavior change interventions. *Patient Educ & Counseling.* 2005;59:21-30.
46. Bickmore T, Pfeifer LM, Byron D, et al. Usability of conversational agents by patients with inadequate health literacy: evidence from two clinical trials. *J Health Commun.* 2010;15 Suppl 2:197-210.

47. Castro CM, Pruitt LA, French SH, Cassayre CL, King AC. Successful peer mentoring for physical activity:12-month results of the TEAM trial. *Annals of Behavioral Medicine.* 2008;35:S081.
48. Holbrook EA, Barreira TV, Kang M. Validity and reliability of Omron pedometers for prescribed and self-paced walking. *Med Sci Sports Exerc.* 2009;41(3):669-673.
49. Umstattd MR, Wilcox S, Saunders R, Watkins K, Dowda M. Self-regulation and physical activity: the relationship in older adults. *Am J Health Behav.* 2008;32(2):115-124.
50. King AC, Sallis JF, Dunn AL, et al. Overview of the Activity Counseling Trial (ACT) intervention for promoting physical activity in primary care settings. *Medicine and Science in Sports and Exercise.* 1998;30:1086-1096.
51. Stewart AL, Mills KM, King AC, Haskell WL, Gillis D, Ritter PL. CHAMPS physical activity questionnaire for older adults: outcomes for interventions. *Med Sci Sports Exerc.* 2001;33(7):1126-1141.
52. Hekler EB, Buman MP, Dunton GF, Atienza AA, King AC. Are daily fluctuations in perceived environment associated with walking after controlling for implementation intentions? *Psychology & Health.* 2012;27(9):1009-1020.
53. Pahor M, Guralnik JM, Ambrosius WT, et al. Effect of structured physical activity on prevention of major mobility disability in older adults: The LIFE Study Randomized Clinical Trial. *JAMA.* 2014;311(23):2387-2396.
54. Harada ND, Chiu V, King AC, Stewart AL. An evaluation of three self-report physical activity instruments for older adults. *Medicine and Science in Sports and Exercise.* 2001;33:962-970.
55. Hekler EB, Buman MP, Haskell WL, et al. Reliability and validity of CHAMPS self-reported sedentary to vigorous intensity physical activity in older adults. *J Phys Act Health.* 2012;9:225-236.
56. Feito Y, Bassett DR, Thompson DL. Evaluation of activity monitors in controlled and free-living environments. *Med Sci Sports Exerc.* 2011;44(4):733-741.
57. King AC, Sallis JF, Frank LD, et al. Aging in neighborhoods differing in walkability and income: Associations with physical activity and obesity in older adults. *Soc Sci Med.* 2011;73:1525-1533.
58. Hart TL, Swartz AM, Cashin SE, Strath SJ. How many days of monitoring predict physical activity and sedentary behaviour in older adults? *Int J Behav Nutr Phys Act.* 2011;8:62-68.
59. Evenson KR, Wen F, Metzger JS, Herring AH. Physical activity and sedentary behavior patterns using accelerometry from a national sample of United States adults. *Int J Behav Nutr Phys Act.* 2015;12:20.
60. Evenson KR, Wen F, Herring AH. Associations of Accelerometry-Assessed and Self-Reported Physical Activity and Sedentary Behavior With All-Cause and Cardiovascular Mortality Among US Adults. *Am J Epidemiol.* 2016;184(9):621-632.
61. Choi L, Liu Z, Matthews CE, Buchowski MS. Validation of accelerometer wear and nonwear time classification algorithm. *Med Sci Sports Exerc.* 2011;43(2):357-364.
62. Rejeski WJ, Marsh AP, Brubaker PH, et al. Analysis and interpretation of accelerometry data in older adults: The LIFE Study. *J Gerontol A Biol Sci Med Sci.* 2016;71(4):521-528.
63. Gardiner PA, Clark BK, Healy GN, Eakin EG, Winkler EAH, Owen N. Measuring older adults' sedentary time: reliability, validity, and responsiveness. *Med Sci Sports Exerc.* 2011;43(11):2127-2133.
64. Myers AM, Malott OW, Gray E, et al. Measuring accumulated health-related benefits of exercise participation for older adults: The Vitality Plus Scale. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences.* 1999;54A:M456-M466.
65. Delcourt MAB, Kinzie MB. Attitudes toward computer technologies (ACT) and self-efficacy for computer technologies (SCT). In. Montreal, Quebec, Canada: McGill University; 1990.
66. Yin L, Bickmore T, Cortes D. The impact of linguistic and cultural congruity on persuasion by conversational agents. Proceedings of the 10th Intelligent Virtual Agents Conference (IVA); 2010; Philadelphia, PA.
67. Horvath A, Greenberg L. Development and validation of the Working Alliance Inventory. *J Counseling Psychol.* 1989;36(2):223-233.
68. Kaul S, Diamond GA. Good enough: A primer on the analysis and interpretation of noninferiority trials. *Ann Intern Med.* 2006;145(1):62-69.
69. Sundquist K, Qvist J, Sundquist J, Johansson SE. Frequent and occasional physical activity in the elderly: a 12-year follow-up study of mortality. *Am J Prev Med.* 2004;27(1):22-27.
70. Kushi LH, Fee RM, Folsom AR, Mink PJ, Anderson KE, Sellers TA. Physical activity and mortality in postmenopausal women. *JAMA.* 1997;277:1287-1292.

71. Albright CL, Pruitt L, Castro C, Gonzalez A, Woo S, King AC. Modifying physical activity in a multiethnic sample of low-income women: one-year results from the IMPACT (Increasing Motivation for Physical ACTivity) project. *Ann Behav Med.* 2005;30(3):191-200.
72. Gibbons RD, Hedeker D, Waternaux C, Kraemer HC, Greenhouse JB. Some conceptual and statistical issues in the analysis of longitudinal psychiatric data. *Archives of General Psychiatry.* 1993;50:739-750.
73. Laird N, Lange N, Stram D. Maximum likelihood computations with repeated measures: application. *J Am Statistical Assoc.* 1987;82:97-105.
74. Kraemer HC, Blasey C. *How many subjects? Statistical power analysis in research, 2nd edition.* Los Angeles: Sage Publications, Inc.; 2016.
75. Finney JW, Mitchell RE, Cronkite RC, Moos RH. Methodological issues in estimating main and interactive effects: examples from coping/social support and stress field. *J Health Soc Behav.* 1984;25:85-98.
76. West BT, Welch KB, Galecki AT. *Linear Mixed Models: A Practical Guide Using Statistical Software.* Boca Raton, FL: CRC Press; 2006.
77. Tan WY, Tabatabai MA. A modified winsorized regression procedure for linear models. *J Statistical Computation and Simulation.* 2007;30(4):299-313.
78. Little RJA, Rubin DB. *Statistical Analysis with Missing Data, Second Edition.* New York: John Wiley & Sons; 2002.
79. SAS Institute Inc. *SAS/STAT User's Guide: Version 15.1.* Cary, NC: SAS Institute, Inc.; 2018.
80. Kaji AH, Lewis RJ. Noninferiority Trials: Is a new treatment almost as effective as another? *JAMA.* 2015;313(23):2371-2372.
81. Preacher K, Hayes A. Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. *Behavior Research Methods.* 2008;40:879-891.
82. King AC. Behavioral medicine in the 21st century: transforming "the Road Less Traveled" into the "American Way of Life". *Ann Behav Med.* 2014;47(1):71-78.
83. King AC, Ahn DF, Atienza AA, Kraemer HC. Exploring refinements in targeted behavioral medicine intervention to advance public health. *Ann Behav Med.* 2008;35(3):251-260.
84. Hekler EB, Buman MP, Otten J, et al. Determining who responds better to a computer- vs. human-delivered physical activity intervention: results from the community health advice by telephone (CHAT) trial. *Int J Behav Nutr Phys Act.* 2013;10:109-118.
85. Munoz RF. Using evidence-based internet interventions to reduce health disparities worldwide. *J Med Internet Res.* 2010;12(5):e60.