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STUDY TITLE:
A Smartphone Application to Improve Physical Activity in Underactive Older Adults with Mild Cognitive Impairment/Mild Dementia

PI NAME: Stacey Schepens Niemiec, PhD, OTR/L, DipACLM

STUDY PROCEDURES

Background/Rationale

Despite the health benefits of physical activity (physical activity), community-living seniors with dementia have 26% lower physical activity levels than their cognitively healthy peers. Health-related smartphone applications (apps), which are now frequently used to improve health behaviors, provide a promising approach to increase older adults' physical activity; however, not only are few apps scientifically evaluated or tailored for older adults, but no physical activity apps have been adapted for older persons with cognitive impairment despite their need for health-supportive tools.

Objectives/Purpose

This supplemental grant will build on Aim 1 of an R21 parent grant (HS-16-00670)—to assess the usability, feasibility, and acceptability of Moving Up—by adding a focus on older smartphone users with a diagnosis of mild cognitive impairment (MCI)/mild dementia.

Participants (Sample)

Inclusion Criteria

Target Users:

- 65+ years old;
- English speaking;
- resides in local Los Angeles area or the Pacific Time Zone;
- cognitive function in line with a diagnosis ranging from MCI to mild dementia (of any form)—a diagnosis is not required. When applicable, cognitive status will be verified through ADRC participant database, health care provider documentation/verbal confirmation, clinical documentation indicating cognitive/functional assessment scores falling within the MCI/mild dementia range, and/or a MoCA Blind/Telephone administered at screening. See Screening form for details of the decision-making flow for eligibility based on diagnosis and cognitive status.
- reports <150 minutes of moderate to vigorous physical activity per week as per a single-item screener;
- self-reported ability to safely engage in regular walking;
- smartphone owner of a compatible smartphone for ≥1 month;
- willing and available second family member/friend/caregiver who owns a smartphone and can attend training sessions; and
- observed ability to reliably access and operate a smartphone during training.

Exclusion Criteria

Target Users:

- unwillingness to meet at local community venues and/or via online meetings
- unwillingness to comply with study procedures for the length of the study
- inability to participate in English
- residing outside of the local LA area and do not have the capacity to participate remotely or commuting to the USC study site
- recent cognitive status does not fall within an acceptable MCI/mild dementia range as determined through MoCA if diagnosis was unverified by health care provider or by ADRC

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- recent cognitive status is below what is acceptable for MCI/mild dementia as determined through MoCA if diagnosis was verified by health care provider or ADRC
- individual has diminished decisional capacity and does not have an LAR available for surrogate signing.

Recruitment, Screening, & Consent

Recruitment Tools

- Flyers
- Telephone scripts
- Verbal (personal solicitation)
- Websites/social media outlets
- Other
    - ADRC database (health history & cog. scores), provider referrals, Healthy Minds Volunt. List, ResearchMatch.org, Keck Med Clinical Trials Website, Alzheimer's Prevention Registry (including announcements on Facebook pg), CARE Registry, Keck data request

Recruitment Methods

ADRC staff and healthcare providers will be responsible for identification of prospective participants (target users) from their subject/participant database. Their contact information will be sent to the study staff who will call the prospective participant (target user) to discuss the study and screen for eligibility. If prospective participants see a flyer, they may call the study team and provide their own contact information if interested, or submit an inquiry through the study's Keck Recruitment Website (link included in 24.2). Registries for which we are approved will provide contact information of participants through the registry: Healthy Minds Database, Collaborative Approach for Asian Americans & Pacific Islanders Research & Education (CARE) Registry, Alzheimer's Prevention Registry, Keck Data Request.

Screening Procedures

Target app users/study partners: As a part of the recruitment phase, researchers will use the Screening Form (labeled "Screening form Most Smartphone MCI study" uploaded in 21.2) to screen individuals for potential participation in the study. The form is used to gather information on demographics, health, physical activity, and cognition to determine preliminary eligibility. A screening consent is also included at this stage as described below in "Consent Procedures." In addition, the need for a Legally Authorized Representative to be present for the remainder of screening will also be assessed via two questions on this screening tool under the "'Mini' Decisional Capacity" heading: (1) Based on our conversation so far, can you please tell me main purpose of the study?; and (2) Please tell me why you might be interested in participating. Should the individual demonstrate diminished capacity even after re-education or a second discussion on a different day, and they do not have an appointed LAR, screening will be discontinued and the person will be deemed ineligible. The screening form will be reviewed by the project coordinator or PI for final eligibility determination.

The ADRC or health care provider/facility will identify potentially eligible participants and refer them to us. In line with the facility's privacy requirements, we will access enrolled participants' ADRC records and extract specified data using our Data Collection and Extraction form (see Data Collection and Extraction Form). These data will be used to characterize the population (e.g. cognitive status, functional abilities). All data will be entered into REDCap. If the participant is not a registered patient linked to the ADRC where data are available confirming clinical diagnosis of MCI/mild ADRD, and instead is a referral from a provider or self-reports a diagnosis of MCI/mild ADRD, we will seek confirmation from the individual's health care provider. Documentation/confirmation of diagnosis and/or cognitive status from their health care provider will only be gathered if feasible/reasonable to obtain, as this information will only be used to characterize the final sample (e.g., number of participants with a formal, verified diagnosis of MCI/mild dementia). Individuals who self-report thinking or memory problems but have no known diagnosis of MCI/mild ADRD will not be asked for verification of diagnosis. For all prospective participants, we will administer the Montreal Cognitive

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Assessment (MoCA Blind/Telephone version in 20.1) to screen for the level of cognition required to be eligible for the study and to corroborate the self-reported diagnosis (when applicable). The decisional process related to diagnosis (when applicable) and cognitive status can be found in form Screening form Most Smartphone MCI study (see diagram in appendix) attached in section 21.2. If a potential participant screens out because they score too high on the MoCA, they will be informed that they are being excluded from the study because they obtained a score on the MoCA that exceeds the range for mildly impaired cognition; and that while the study team cannot provide a diagnosis, if the individual has concerns about their level of cognition and/or wants to undergo further testing, they should make an appointment with their primary care physician. The individual will be responsible for the costs of any medical care or testing that they pursue. The study team will also make resources available, such as Alzheimer's LA (https://www.alzheimersla.org/) and AARP (AARP.org). For dissemination purposes, we will identify the number of enrolled participants who had a clinical diagnosis as confirmed by the ADRC or health care provider, those who self-reported a clinical diagnosis without ability to produce confirmation from their provider, and those who self-reported thinking or memory problems with no known diagnosis of MCI/mild ADRD.

The study team will conduct a Keck data request through the USC Clinical Data Warehouse to boost recruitment.

The inclusion criteria will be:

- Diagnoses: G31.84 Mild Cognitive Impairment, so stated OR 331.83 Mild Cognitive Impairment, so stated
- Age: >=65 years

The exclusion criteria will be:

- No diagnosis of Mild Cognitive Impairment
- Age: <65 years
- Residence outside of the Pacific Time Zone

The following identifiers will be requested:

- Name
- Date of birth
- Address
- Email
- Phone

Consent Procedures

A screening consent is included in the screening procedures to allow the study team to retain data collected during this process from target study participants. This consent includes a brief description of the study, what will be done with screening data if individuals are eligible/ineligible and if they are eligible that data will be linked to their main study data if they decide to participate. A mini decisional capacity is conducted at this point to determine if the person can continue through the screening process without an LAR present. Re-education or a rescheduled discussion of the study will be offered as needed to improve understanding or the availability of an LAR will be determined to continue with the screening and enrollment process.

Target app users/study partners: Standard informed consenting procedures will be followed. Prior to initiating informed consent procedures with target app users, a thorough decisional capacity assessment of the individual will be completed using the Decisional Capacity Assessment (labeled "Decisional Capacity Assessment 042519" uploaded in 22c.5.2). Target users will be provided a consent form (in electronic and/or hard copy format) that describes enrollment in the study. Before proceeding with study activities, all individuals will be asked about the status of an LAR and that person will be involved in the consenting process based on decisional capacity results. Individuals who have decisional capacity and do not require an LAR to co-sign will sign the consent form independently. They will have the option of participating in the study with or without a study partner. Individuals who have the decisional capacity but also have an LAR who typically co-consents will co-sign the consent forms if desired by the individual. Surrogate consenters/LARs will sign on behalf of individuals who do not have decisional capacity. If a person has diminished decisional capacity and has no LAR

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appointed, or does not have a study partner available to participate, they will be excluded from the study. Individuals who enroll will also complete a HIPAA Authorization during the consent process. Study partners who will be participating in orientation sessions and interview/assessment sessions will be given an informed consent form.

Methods

App Description

The Moving Up-A app will be provided to target user participants for both the 2-week and 2-month studies. Moving Up-A is a multi-feature PA suite that blends basic activity tracking and evidence-based behavior change techniques in the form of specialty functions. These functions include: (a) implicit and explicit messaging that promotes positive views of aging, (b) sedentary activity monitoring with peer-generated suggestions for minimizing inactivity, and (c) activity coaching. The app connects with the smartphone accelerometers/native activity trackers and other smartphone internal motion sensors to track steps over time. It serves as an interface for participants to review steps taken, stand and move progress, messages and tasks.

The 2-week protocol has a schedule of approximately 36 notifications/messages planned to be sent across the 2-week period through the app directly. The 2-month protocol has as many as 154 notifications/messages planned to be sent across the 8-week period through the app. This may work out to approximately 3 prompts a day. There is some variation in number of messages/notifications/tasks depending on a person's progress toward goals, responses to tasks, or self-selected reminder frequency. A sample of messages sent through the app is attached in 21.2 and labeled, "Sample Messages Sent through Moving Up-A." Tasks sent within this calendar of notifications are very short to complete (~5-10 minutes). Sample tasks include check-marking an activity inventory of what one plans to do in the next week, completing a sentence unscrambling task, and check-marking what barriers they encounter to physical activity. Tasks and surveys participants complete are detailed in "Tasks/Surveys Received in the App" and are attached in 21.2.

The study partners receive a mirrored version of the messaging schedule and will receive approximately the same number of notifications as the target user. Because messages depend somewhat on interactions with the app and responses to tasks, this is why we say "approximately the same number."

Instances of app opening, pages/tabs/messages/notifications viewed, and profile and goal changes are recorded on the backend of the app and stored in the secured USC Deriva server. The auto-tracked data stored in Deriva (serving as our data collection tool) are listed in the "Data Reports of Auto-tracked App Content" uploaded in 21.2.

Activity Monitoring for Outcomes

The ActivPAL activity monitor, used for measurement purposes separate from the in-app activity tracker, is a small device worn on the thigh over a 2-week period for the 2-week study or two 4-day periods for the 2-month study, to provide baseline information on postural changes and estimated energy expenditures, using static and dynamic acceleration. Details of procedures for the 2-week and 2-month studies are described below.

2-week Study Procedures

Following informed consent procedures, participant dyads (target users and their study partners) will complete a background questionnaire (online or hard copy) and download the Moving Up-A app prior to an orientation session to the app. These activities which can be done in advance of orientation help to reduce the participant burden, cognitive load, and time commitment on orientation day. However, questionnaires and app set-up may be completed at the orientation session if in-person participation is the most feasible and appropriate method of participation. The target user background form (labeled "01. Background Questionnaire_04-25-19 (bsl)(0.04)" and uploaded to 21.2) is to be completed by the target user with assistance from the study partner as needed. Information in this form is used to characterize the target user participants. The Study Partner Demographics form (labeled “Study Partner Demographics(0.01)” and uploaded to 21.2) is a questionnaire to be completed by the study partner and gathers

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background information about that individual and their relationship with the participant. This information is used to characterize the study partner participants. Target users and study partners will also complete a questionnaire (online or hard copy) designed to gather profile and goals information in order to pre-fill this information into the app settings prior to orientation (labeled “Profile Set Up Sheet_participant fillable” and uploaded to 21.2). The study team will schedule all upcoming appointments with the target users and study partners. The agreed-upon appointments will be added to a calendar at the end of a Welcome Letter (labeled "Welcome Letter_online" or "Welcome Letter_inperson" and uploaded to 40.1) that is sent to participant dyads.

The orientation session will be held either in-person or online and will be attended by the participant dyads together. Dyads will ideally be in the same physical location for this session, but if the target user’s cognition does not require in-person support from the study partner (e.g., the dyad attends online, but each from their own home), then the dyad will be accommodated as such. At orientation, the Moving Up-A app and in-app pedometer will be loaded onto/connected to participant dyads’ phones to be utilized for 2 weeks. If the participant's phone is incompatible with the in-app pedometer, we will distribute a basic external pedometer (described in 20.1) for them to carry to track activity. The session will last approximately 2.5 hours in total, including breaks, when all activities including paperwork and app download are conducted at the visit. Dyads will be introduced to the Information Collected in App form (labeled “Information Collected in App” and uploaded to 40.1). This form serves as a guide for the researcher to inform participants about the type of data that will be collected in the app throughout the duration of the study, and what happens to the app following study completion. Dyads will be taught how to use the app features and given a user manual. Study partners will be instructed to observe and note the target user’s interactions with the app and use the app themselves if they choose.

Additionally, to conclude the orientation participant dyads will be introduced to the activPAL activity monitor the target user will wear for 2 weeks and complete an activity log, with assistance as required. This will occur in one of two ways: (1) participant dyads will be mailed an activity monitor packet (labeled "04. Activity Monitor Packet_Instructions and Tracking Log_2wk" and uploaded to 21.2), including paper-based instructions for wear/care, a link to video-based instructions (Self-application: https://youtu.be/3Gjrj_hzF4E, Assisted application: https://youtu.be/WjkKel7RUxo, and Re-application: https://youtu.be/Au3xpkCNhzw), tracking log, and a pre-addressed/postage pre-paid envelope; or (2) if activity monitor donning is deemed best accomplished via direct contact, target users will be fitted with the activity monitor in-person and the study partner educated about monitor wear/care and tracking log. Telephone/video-call assistance will be made available to dyads in either case to ensure proper and maintained activity monitor fit over the study duration.

The participants will receive similar tasks and prompts during the study. Users may receive more tailored messages based on various tasks, such as the Occupational Inventory, which asks what they expect to be doing in the next week. Additional prompts will be sent based on participant goals and level of physical activity (e.g., they will receive a prompt to stand if they have not yet met their set standing goal for the day). The app will automatically track and store data on the number of pages a participant views, frequency of app access, number of push notifications opened, number of steps taken per day/week, changes to step goals/profile, and survey responses. Such collected data will be automatically recorded by the app backend and sent to and stored on the USC Deriva server.

During the first week of study participation, target users (with study partners in attendance as available) will be contacted via phone or Zoom tele/video conference 3-4 times to gather initial user impressions, provide tentative support on app features, and troubleshoot as needed (telephone check-in prompt document is labeled "Check-In Phone Call and Technical Support Calls Flow" and uploaded to 19.1). To the extent possible, content of the calls will be tailored to reflect app content that was recently delivered to the users and based on their individual usage behaviors. If applicable to the user feedback provided during these check-in calls, portions of the uMARS and/or the post-study interview may be completed during the calls. A REDCap form will be completed after each call to summarize the

feedback received, and the post-study interview summary form may be partially filled out at this time. If target users and/or study partners report difficulties during their check-in calls, the study team may send short videos to remind them about how to use the app or resolve specific issues. Check-in calls may last from 10–30 minutes depending on user needs and questions. They will be audio/video recorded with the participants' and study partners' permission. If study partners were unable to attend any of the first-week check-in calls with the target user, a separate call will be made to the study partner at the end of this week to ensure their perspective/feedback is collected in at least one call. During the second week of study participation, we expect to make no more than 3 brief check-calls to the target users, occurring as necessary based on the target user's support needs. Reminder text messages (or calls, depending on participant preference) will be sent to user dyads for scheduling purposes in advance of check-in calls or follow-up visits, as well as to provide encouragement to check the app.

Upon completion of the 2-week smartphone app trial period, dyads will attend an approximately 1-hour follow-up session, either in-person or online. Using a semi-structured interview guide (Interview Guide - Participants and partners in 19.1), dyads will be queried about such topics as potential efficacy to impact physical activity and suggestions for enhancement. Dyads will also complete the remainder of the user experience survey (online or hard copy; labeled "uMARS 070919.docx(0.01)" in 21.2) to gather participant feedback on app engagement, functionality, aesthetics, information appraisal, subjective quality, and perceived impact of the app. If some questions from the interview guide or uMARS form were previously completed during check-in calls, these questions will not be asked again at this session. Dyads will also return the activity monitors and accompanying logs either in-person or via mail.

2-month Study Procedures

A new cohort of 15 target users (with their study partners) will partake in the second iterative stage of app development. All methods described above will apply with a few exceptions. First, users will utilize the app for two months (as opposed to two weeks). Second, target users and study partners will keep a bi-weekly diary (handwritten, audio recorded, or typed based on user preference) of their user experiences across the two months (on their own schedule). Third, check-in calls will take place as follows:

- Week 1: three scheduled check ins
- Week 2: two check ins as needed
- Week 3: one check in as needed
- Week 4: one scheduled check in at end of week to discuss thoughts thus far
- Week 5: check ins as needed
- Week 6: check ins as needed
- Week 7: check ins as needed
- Week 8: none

Fourth, externally worn activPAL activity monitors will be utilized twice in 4-day bouts (during the first and last weeks of the trial period). Activity monitors will be either donned in-person or mailed for self-donning at the initial assessment/orientation session and participant dyads instructed to mail back monitors after four full days of wear. Participant dyads will be mailed a new activity monitor for the target user to be worn for the final week of the beta-testing period. This monitor will be returned at follow-up either in-person or via mail.

Statistical Considerations

Sample Size:

As this is a feasibility study, statistically significant results are not a priority; data will only be interpreted for the purposes of feasibility and not efficacy of the intervention. To determine feasibility of the phone-based activity monitors to collect activity-related data, with 15 target users in each phase, we have 80% power to find a statistically significant correlation of 0.65 between activity measured using target users' phones and an activity monitor. We have 80% power to detect an effect size of 0.78 for change in physical activity over the two-month development phase. This large of an effect size is unlikely, but our results will better inform our sample size determination for future studies. For expert

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stakeholders, sample size (n=15) was determined based on available funds for participant stipend and research personnel capacity.

Statistical Considerations & Analysis:

Descriptive statistics will be used to summarize target user and study partner characteristics, user experiences from experience questionnaires, and user interaction with the app. Data captured through audio recordings of interviews will be transcribed verbatim. Diary data will be cleaned and compiled. Using qualitative data analysis software, we will code data based on pre-established and emergent themes, adjusting processes as needed. When relevant, diary data will be compared with findings from interviews.

For the two-month development phase, one study endpoint is the feasibility in change in mean daily physical activity, which will be calculated for each target user over the days for which external activity monitor data are available. Paired sample t-tests or Wilcoxon signed rank tests, as appropriate, will be used to compare pre-post changes in mean daily physical activity. To analyze activity patterns from the smartphone monitors, we will fit mixed effects linear regression models. We will analyze app usage in the two-month development phase using mixed effects zero-inflated negative binomial regression.

The Moving Up-A package will be considered: feasible if we identify a theme of potential for long-term impact based on user responses, a general improvement in patterns of physical activity (e.g., upward trend in step count slope, downward trend in sedentary time slope), and/or usage patterns that indicate high interactivity with the app (e.g., accessing features ≥3x/week); usable if target users and study partners report that the app is easy to use, if they can navigate app features with general ease, and if reported issues are fixable; and acceptable if target users and study partners respond with generally positive comments about the features during interviews and in their user experience diaries.