[redacted]

Participants. 120 older individuals using the aforementioned applications at the Brookline Senior Living communities, the largest owner and operator of senior living communities across the United States (1000+ communities, 100,000+ residents) where the average age of residents are 85 years old. With respect to study interest across each community, we have reached out to the resident directors at each non-demented community to gauge interest in this program: 84% of the resident directors believed at least some of their constituents would be interested in participating, with 73% of these respondents estimating between 1-10 individuals per site. Given that this is a feasibility study assessing: i) working with this seldomly studied population, ii) the implementation of mobile technology in a senior living community, and iii) the utility of a cognitive assessment that prescribes a personalized intervention regimen, an initial foray into this population with such an approach is well positioned for this particular R21 mechanism.

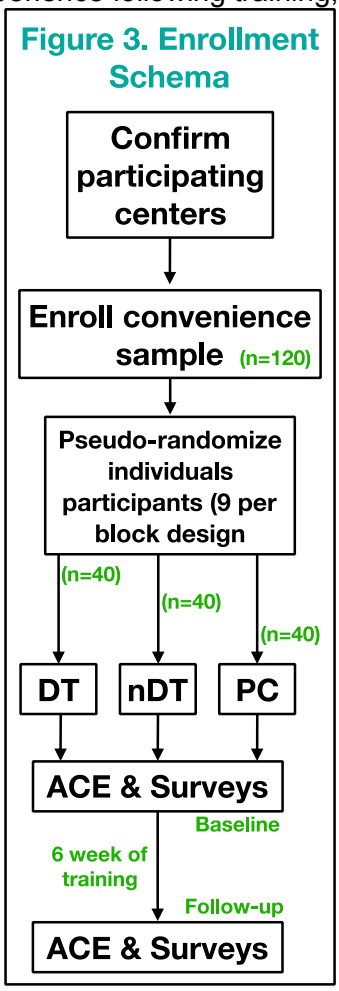
Markers of success. The primary aim of this pilot study is to gather information about the feasibility of utilizing this type of assessment/intervention combination in a senior living community to set up a future R01 application. To that end, our markers to assess feasibility will include: 1) how participating individuals and resident directors accept participating in this project, as assessed through exit surveys with each group, 2) how many eligible participants enrolled/participated/dropped out of this study, 3) what was the quality of the collected data (was there excessive missing/unusable data?), and 4) limited-efficacy testing to examine the expected degree of responsiveness to the two versions of the intervention.

Sample size. A power analysis to determine the needed sample size for this study resulted in us having to recruit a minimum of N=120 (40 in each condition) to achieve a balanced factorial design, which should be quite attainable given the interest indicated by the resident directors. Assuming 25% attrition, our recruitment plan will yield 90 participants, which will allow us to assess changes in performance as a function of training. Given the number of primary comparisons (3 scores of cognitive control at 2 time points (Pre- and Post-training)), there would be 95% power to reveal a group X session interaction on any given outcome, even with only 90 total participants split across the 3 groups. This corresponds to a medium effect size of .53, which is reasonable for a feasibility study of this size given the study-associated logistics. Pre- and post-training outcome data will be modeled using mixed within- and between-subjects GLMs and multivariate regressions[109]. Significant interactions will be interrogated with appropriate follow-up tests between each group, including the direct assessment of effect size comparisons calculated using Satterthwaite's approximation[110].

[redacted]

The goal of this R21 is to test the feasibility of deploying a targeted digital health remediation program for older adults in senior living communities based upon an initial characterization of these abilities. Below we discuss the logistics towards realizing this goal.

Mixed Model Approach. Here we propose to use a sequential exploratory mixed method design[115-119] for this pilot study. Specifically, a quantitative design will be used to: (1) collect descriptive information regarding older adults' perceptions of each app to enhance the UX experience for this particular population to explore the feasibility of self-administration for cognitive assessment and remediation, and (2) make pre-, post-, within- and across-group comparisons of cognitive functioning based on neurocognitive test performance and self-rated assessments. The qualitative approach will begin with local semi-structured interviews regarding the use of each app, first in a group of 10 one-on-one sessions with seniors led by our UX testing consultant (see **Letter of Support**), followed by subsequent interrogation by senior-centric UX group testing group (Longevity Explorers™, see **Letter of Support**) whose members are seniors trained in UX design refinement. Using data gathered from these experiences, we will augment the UX design of each app for subsequent dissemination to the Brookdale Senior Centers for use. Brookdale participants will be asked questions about their experience following training, with feasibility of program participation assessed quantitatively by measuring the number and percentage of sessions completed per participant. Questions at this time point (previously used by Hill and colleagues[90]) will include "Do you feel your everyday thinking abilities have changed from doing the computer exercises and, if so, how? 2. What did you like about doing the computer exercises? 3. What did you dislike about doing the computer exercises? 4. Now that the study is over, would you keep doing the computer exercises?" Responses during said interviews will be transcribed, with frequency tallies of response consistencies per question across participants being tabulated. We will perform thematic analyses for the identification of important patterns/themes[90], creating a coding framework that maximizes coherence amongst categories emerging from the qualitative data[120-122].



Protocol. Following the initial local UX testing, a convenience sample of 120 older adults will be recruited from throughout the Brookdale Senior Centers throughout the United States (see **Figure 3;** see **Recruitment and Retention Plan** for additional participant enrollment details). These individuals will be asked to complete the battery of tasks on the ACE platform (~45min) to characterize cognitive control abilities before and after the assigned intervention. Following their initial assessment, each participant will be randomly assigned (using a pseudo-randomized blocked design using blocks of 9 to ensure equivalent representation across groups) to a one of three intervention types: directed training (DT) on the ACCT platform, non-directed training (nDT) on the ACCT platform, or an expectancy-matched placebo control platform (PC). We will ask each resident director and their residents to refrain from discussing their assigned intervention with other communities to preserve blinding across sites. The total training experience will encompass 6 weeks of training (3 days/week), with each training session lasting 36 minutes (not including self-paced breaks). Each participant in the DT and nDT groups will engage in 12 3-minute blocks of submodules in each training session on the ACCT platform. However, those in the nDT group will play each of the three submodules 4 times equally, while participants in in the DT group will play 12 blocks proportionally weighted towards the cognitive control domain(s) that are most deficient at baseline as determined by their baseline ACE performance, and thus most likely to benefit from directed training. For example, if (following the ACE assessment) a given individual shows deficiencies on their attention and working memory scores but normal performance in their goal-management abilities, they will be prescribed 5 training runs of the attention & working memory modules and only 2 of the goal management module. Customization of each DT participant regime will be accomplished via a web portal at UCSF that transmits personalized training parameters directly to the individual's ACCT application. Each training program contains self-guided instructional videos and practice modules for each treatment, consisting of 6 weeks of training (3 days per week). Training sessions are linked, such that the next session begins at the level attained at the end of the previous session. Participants are provided two types of feedback: 1) real-time feedback – indicating whether the participant successfully detected or classified the target and 2) punctuated feedback – participants advance through a series of "levels" that are reported at the beginning and end of each run. We will provide weekly feedback about intervention use and performance improvement (in addition to daily in-app feedback), in support of it utility found in a recent survey[123]: 79% of health app users indicated that periodic feedback about their app usage encouraged them to continue.

Expectancy-Matched Placebo Control. The placebo control group (PC) will engage in a battery of three apps delivered in the same prescribed manner as the other two groups, which we hypothesize as based on our experience will have minimal positive impact on the cognitive abilities we are assessing: i) an app with 100 different logic games of varying difficulty and length, ii) a language-learning app with 10 language options, and iii) an app that offers a guided Tai Chi program. The total training experience here will also be for 6 weeks (3 days/week), with each training session lasting ~30 minutes where participants will be asked to use each of the submodules for 10 minutes (not including self-paced breaks). We have already determined that this approach generates matched expectancy of benefits compared to our training groups by questioning 100 naïve individuals to predict their expected improvement on each cognitive domain after training on these apps (see [124] for details of expectancy testing). This revealed that placebo training generates equivalent expectations of improvement across each outcome measure as the DT group, thus serving as an effective placebo condition. Furthermore, initial pilot work examining transfer effects following training on this battery has shown no evidence of improved cognitive control with respect to attention or working memory abilities, supporting its utility as a placebo control.

Assessments. All OAs will complete assessments at two periods: baseline and immediately following the intervention. In addition to measuring transfer to benefits to cognitive control (using ACE), we will also assess transfer of gains to functionally-relevant outcome measures, notably the Everyday Cognition Scale (ECog) to assess their ability to perform everyday tasks that demand memory, language, visuospatial abilities, planning, organization, and divided attention[125,126]. The ECog scale has been used in other cognitive interventions trials and proven to be sensitive enough to detect improvements in healthy OAs and differentiate OAs from mild MCI[127,128]. This survey will be sent directly to participants via an automated email campaign from Qualtrics™, with help from local resident mentors to complete these surveys on the same devices. Other surveys sent through this mechanism will include: i) a customized survey assessing participant expectancy across groups to further explore possible uncontrolled placebo effects (see for a description of this approach), ii) distractibility (via the Cognitive Failures Questionnaire)[129], and general health and well-being (SF-36)[130].

Infrastructure Support. Brookdale has already established an elegant infrastructure for sending, tracking, and gathering information as needed across all of their communities. Brookdale has 100,000+ residents in 47 states, divided into 5 geographic divisions, with several communications channels that provide resources on a monthly basis for Resident Programs associates. Each geographic division is led by a Directors of Resident Programs Engagement who supports the Resident Programs Associates in approximately 200+ communities. Each division is divided into approximately 50 areas, with each area supported by a Resident Programs “mentor”, and this team of 50+ mentors directly interacts with 15-20 communities. Resident directors have agreed to assist community residents in downloading and providing in-person help for this study, with Dr. Anguera running a distributed webinar for all resident directors to teach them about these tools prior to study launch. Telephone and email support by the study team will be provided throughout the training period, in addition to active onsite support via resident directors. Each app will be configured to wirelessly transmit data automatically to our secure HIPPA-compliant server at UCSF when each training session is completed, with a custom web-portal facilitating data tracking in real-time to monitor participant adherence and data quality.

Markers of success. The primary aim of this pilot study is to gather information about the feasibility of utilizing this type of assessment/intervention combination in a senior living community to set up a future R01 application. To that end, our markers to assess feasibility will include: 1) how participating individuals and resident directors accept participating in this project, as assessed through exit surveys with each group, 2) how many eligible participants enrolled/participated/dropped out of this study, 3) what was the quality of the collected data (was there excessive missing/unusable data?), and 4) limited-efficacy testing to examine the expected degree of responsiveness to the two versions of the intervention.