Gamification to Improve Physical Activity in Older Adults: the STEP 4Life Trial

Study Protocol

June 3, 2021

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1. Abstract

Increased physical activity by walking further or more vigorously may prevent or delay the development of Alzheimer's Disease and Related Dementias (ADRD) but reaching higher levels of activity and maintaining it as a long-term habit is difficult to do. This project will use concepts from behavioral science to create a game older adults can play in order to increase their levels of activity while having fun doing it. The game is played with a support partner who is a spouse, family member, or close friend who provides feedback and encouragement to help the game-player reach activity goals and maintain them as habits over time. Participants in the game will use their own smartphone and a wristwatch that tracks activity (such as a FitBit, provided by this study) to set goals, get feedback, and play the game for 12 weeks. Participants will be asked to continue wearing the wristwatch for another 6 weeks to track activity after the game is over. To determine the effectiveness of this game, we will randomly assign 50 people to the game and 50 people to only get the wristwatch but no game component. All participants in this study will be recruited from an online registry of adults age 55-75 who have not been diagnosed with Alzheimer's (GeneMatch) which offers genetic testing on risk for ADRD to all participants. We

will recruit participants to our study who have elevated genetic risk as well as those without specific genetic risks to see if either group responds differently to the game.

2. Overall objectives

The primary objective is to assess the effectiveness of a social incentive-based gamification intervention to increase physical activity over 12 weeks with follow up of 6 weeks after the intervention concludes. We will explore whether participants who know they are higher risk (carriers of the APOE4 gene) are more responsive to the intervention than those who know they are at average risk (non-carriers of APOE4). We will also explore the feasibility of collecting measures of cognition and function remotely using standardized instruments by telephone or video calls.

3. Aims

3.1 Primary outcome: change in mean daily step count from the baseline period to the end of the 12-week intervention period.

3.2 Secondary outcome: mean daily step count during the 6-week follow up period after the end of the intervention.

3.3 Exploratory outcomes: functional measures will include the Timed Up and Go and 30-second Chair Stand Test.[45,46] Cognitive measures will include Verbal Naming, Category Fluency, Trail Making, Number Span, and Blind MOCA.[47]

4. Background

Systematic reviews have demonstrated that higher levels of physical activity are associated with lower risk of developing ADRD even with modest increases in low-intensity exercises.[1-3] Physical Activity Guidelines from the U.S. Department of Health and Human Services also recommend ≥150 minutes/week of moderate intensity physical activity (e.g., brisk walking) for older adults to reduce risks of functional and cognitive decline (including ADRD specifically).[4,5] Physical activity is also recommended by the NIA for people with ADRD and taking daily walks with a support partner is specifically encouraged.[6] Some studies have suggested higher intensity exercise or multi-component interventions may have the greatest impact but the sustainability and scalability of these approaches are major limitations.

Interventions leveraging behavioral economics (BE) to increase physical activity have demonstrated sustainability over prolonged periods after the end of the intervention;[7] however, these approaches have not been applied to populations at risk for ADRD specifically. There are several key components of these interventions which warrant testing in this population. First, gamification leverages BE concepts to motivate behavior change. Gamification is the use of game-design elements such as points and levels in non-game contexts.[9,10] Gamification is an

appealing approach to increase engagement in healthy behaviors because it makes the "hard stuff" fun by turning obligations into goals and challenges.[10] Second, mobile technologies which increasingly used by older adults[11] can be used to accurately,[12] and unobtrusively help set and maintain specific daily and weekly activity goals. Third, social incentives can be used to enhance these effects and reinforce habit formation to prevent regression. Social incentives are powerful influences that motivate individuals to change their behaviors based on social ties or connections.[14-17] For example, an individual's mobility is higher when a family member or friend has increased mobility.[17] On closer inspection, such interactions contain many powerful levers to change human behavior including peer support, accountability, and collaboration. Since social networks are ubiquitous, approaches that harness social incentives could be scaled more broadly at lower cost than interventions relying on health care professionals to motivate and monitor physical activity in older adults at risk for ADRD. Our group has successfully used gamification, mobile technologies, and social incentives to increase activity in several non-ADRD populations.

One challenge to studying behavioral interventions to improve physical activity in the ADRD population has been enrollment with most studies to date enrolling from clinics which limits sampling; prior studies have also used variable definitions of "elevated risk" for dementia. In this study, we identify and recruit participants utilizing a novel, national cohort of individuals with quantifiable risk using genetic testing from the GeneMatch study.[18,19]

5. Study design

5.1 Design

We will conduct a 2-arm, randomized, controlled trial over 12 weeks with 6 weeks of follow-up (18 weeks total) that compares a control group that uses a wearable device to track physical activity to an intervention group that uses the same wearable devices and receives a supportive social incentive-based gamification intervention to adhere to a step goal program. In phase 1 (2 weeks), participant step counts will be monitored and baseline step count will be estimated. In phase 2 (12 weeks), participants will be randomly assigned to the control or intervention group and will set step count goals. In phase 3 (6 weeks), interventions will cease and participant step counts will be monitored. Participants will be considered enrolled in the trial if they complete the run-in period and then are randomized.

5.2 Study duration

The study will begin in Summer 2021. The primary intervention period is 12 weeks. Participants will be enrolled for approximately 20 weeks (2 week run-in, 12 week intervention, 6 week follow up). We expect the entire study to take approximately one year to conduct and analyze outcomes.

5.3 Target population

Adults age 55-75, own a smartphone, enrolled in GeneMatch, know their genetic testing results (APOE4), and able to provide informed consent

5.4 Accrual

We will aim to enroll and randomize 100 participants. We estimate a standard deviation of 2500 steps and a sample of 100 participants allocated in a 1:1 distribution (50 in each arm), will ensure at least 80% power to detect a 1000 step difference. This calculation assumes a 10% dropout rate and a conservative Bonferroni adjustment of the type I error rate with a 2-sided alpha of 0.017.

5.5 Key inclusion criteria

Participants must be age 55-75, own a smartphone, be enrolled in GeneMatch, know their genetic testing results (APOE4), and able to provide informed consent

5.6 Key exclusion criteria

1) Inability to provide informed consent; 2) does not have daily access to a smartphone compatible with the wearable device and not willing to use a device that we can provide them; 3) already enrolled in another physical activity study; 4) unable to ambulate independently; 5) any other medical conditions that would prohibit participation in physical activity program;

6. Subject recruitment

6.1 General

Participants will be recruited from the Alzheimer Prevention Initiative's (API) GeneMatch registry, which is managed by the Banner Alzheimer's Institute. GeneMatch maintains a registry of older adults who live in the United States and do not have a diagnosis of cognitive impairment. GeneMatch will identify potential participants based on age (55-75). GeneMatch will invite these individuals through an email invitation and a study description on their GeneMatch dashboard. Potential participants will have the option to accept or decline the study invitation. If participants accept, they acknowledge that their information will be shared with the study team and that a member of the study team will contact them. Those who decline the invitation will not be contacted again, and none of their information will be shared with the study team. Study coordinators will contact potential participants who accept the invitation via phone/email to further assess interest and answer questions related to the study.

6.2 Populations vulnerable to undue influence or coercion

Not applicable

7. Subject compensation

Participants will receive $100 on a pre-paid debit card (Clincard) upon completion of the study.

8. Study procedures

8.1 Consent

Upon recruitment, potentially interested participants will be directed to the Way to Health internet research portal. Upon reaching the portal, eligibility will be determined based on their responses to screening questions.

The Way to Health portal will take eligible potential participants through an automated online informed consent session. The consent session will be divided into sections and potential participants will have to click a button to advance through each section. This is to help ensure that participants read the consent form thoroughly by breaking down the form into more manageable blocks of text. Successive screens will explain the voluntary nature of the study, the risks and benefits of participation, alternatives to participation, and that participants can cease to participate in the study at any time.

On the final consent screen, potential participants who click a clearly delineated button stating that they agree to participate in the study will be considered to have consented to enroll.

Following consent and the run-in period, the participant will be randomized to intervention or control arm by the web application. The participant will see a description of the details specific to that arm. Participants will be provided with details regarding how to contact the research team via email or phone at any time if they wish to withdraw from the study subsequently or have any questions or concerns about participation. Such contact information will remain present via the subjects Way to Health individual study website dashboard throughout the study. Participants will also be able to access a PDF of the consent form through the study Way to Health site.

Waiver or Alteration of Informed Consent*
Are you requesting a waiver of, or alteration to, the informed consent process? Please choose one of the following and provide justification where appropriate:

No Waiver Requested
Waiver or alteration of required elements of consent
Waiver of written documentation of informed consent: the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality.
X Waiver of written documentation of informed consent: the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context

Written Statement of Research*
Will subjects be provided a written statement of the research?

X Yes
No

8.2 Procedures

Enrollment. Potential participants will complete a screening questionnaire through the Way to Health portal. If the participant successfully passes the screening questions, they can be consented to the study. After screening and consent, participants will complete a survey through the way to health platform to provide demographic information (Age, gender, race, ethnicity, income, education, self-report comorbidities/health conditions) as well as a shipping address for the Fitbit to be sent to. Participants will then receive a Fitbit activity tracker and instructions for setting up the tracker and the Fitbit app on their smartphone. After participants have successfully set up their activity tracker and app, and have linked their Fitbit account to the Way to Health website, they will begin the study run-in period.

Run-In Period. Eligible participants will be mailed a wearable activity tracker that captures data on daily steps counts and asked to use the device for two weeks to get accustomed to it. During this period, we will use a protocol from prior work to estimate a baseline step count using the second week of data. The first week of data will be ignored to diminish the tendency for use of devices in week 1 of receiving a new device to be significantly higher than what might be observed at steady state. To prevent risk of mismeasurement, we will ignore any daily values less than 1000 steps because evidence indicates these values are unlikely to represent capture of actual activity. Once baseline is established, participants will be contacted to conduct goal selection with a step goal of increase of 33%, 40%, 50% or choose a custom goal as long as it is at least 1500 steps greater than baseline. In prior work, we find that on average participants chose ambitious goals and more than half selected a 50% step increase.

Participants with an average of 7500 or greater steps per day during days 8 - 14 of run-in will be ineligible and will not be randomized into the study.

Randomization. After establishing baseline, participants will be randomly assigned to control or interventions using a 1:1 allocation and stratifying on baseline step count (< 4000, 4000-7000 steps, >7000 steps) using an electronic number generator through the WTH platform. All participants will be asked to use the wearable device during the day and at night to measure activity. Each participant will select whether he or she would like to primarily receive study communications by text message, e-mail, or automated interactive voice response phone call.

Cognition and Function Measures. Within 2 weeks of randomization (study weeks 2-4) and within 2 weeks after completing the intervention period (study weeks 15-16), participants will complete online survey-based assessments and virtual (video call) assessments of function (Timed Up and Go and 30-second Chair Stand) and cognition (Verbal Naming; Category Fluency; Trail Making; Number Span; Blind MOCA). The online surveys will be completed through the Way to Health online platform. Research staff will contact participants to schedule and conduct video calls to complete the tests of function and cognition.

Intervention Period.

Control: Participants in the control arm will receive a study device (e.g. FitBit) but no other interventions during the intervention or follow-up periods.

Intervention: Intervention participants will enter a game designed with behavioral economics (BE) concepts to address predictable barriers to behavior change during the 12-week intervention period. The components of the gamification intervention are described below:

Pre-commitment: Each participant signs a contract agreeing to try their best to achieve their daily step goal. Pre-commitment helps to motivate behavior change by increasing perceived accountability.[18,19] *Points*: Each week, participants are endowed 70 points (10/day) prospectively rather than awarded after goal achievement to leverage the BE concept loss aversion that individuals are more motivated by immediate losses than gains.[20-22] Each day that the goal is not met, they are informed that they lost 10 points. Points are replenished at the start of the week to leverage the BE concept of the "fresh start effect" that individuals are more motivated for aspirational behavior around temporal landmarks such as the start of the week.[50] *Levels*: At the end of the week, if the participant has 40 points or more, he or she will advance one level. The levels include: blue (lowest), bronze, silver, gold, platinum (highest). If they have < 40 points, they drop down one level. This creates a sense of achievable goals (goal gradients)[23] and anticipated regret.[24-27] Each participant begins in the middle (silver), so higher levels seem within reach and they will feel a sense of loss from dropping down a level. *Support partner*: Each participant will select a spouse, family member, or friend that they see often to serve as a sponsor and receive a weekly email participant's progress including points, game level, and average step count. This supportive sponsor will help to enhance social incentives to motivate the individual towards his or her goal.[13]

Follow-Up Period. At the end of the 12 week Intervention Period participants will enter a 6 week Follow-Up Period during which interventions will cease but passive data collection of step counts will continue.

Exit Survey. Participants will complete an end-of-study questionnaire on their experience with the wearable device and intervention design. Participants will be asked to describe elements that helped them to achieve their physical activity goals (and elements that did not help) and suggestions on how to improve the design of the interventions.

Upon completion of the study, participants will receive payment of $100 on a pre-paid debit card (Clincard).

8.3 Instruments

Step Count: Daily step count data will be uploaded daily from participants' activity trackers.

Screening Survey: A screening survey will be administered through the study website prior to enrollment to assess eligibility for the study. The survey will query age, use of smart phone, current activity level, participation in other research, ability to safely increase physical activity, availability of study partner, and knowledge of APOE genotype.

Baseline/demographics: After consent and confirmation of eligibility, participants will complete a survey through the way to health platform to provide demographic information (Age, gender, race, ethnicity, income, education, self-report comorbidities/health conditions) as well as a shipping address for the Fitbit to be sent to.

Cognition and Function: During the first two weeks of the intervention period and the first two weeks of the follow up period, participants will complete virtual (video call) assessments of function (Timed Up and Go and 30-second Chair Stand) and cognition (Verbal Naming; Category Fluency; Trail Making; Number Span; Blind MOCA). Research staff will contact participants to schedule and conduct video calls to complete the tests of function and cognition.

Exit survey: Participants will complete an end-of-study questionnaire on their experience with the wearable device and intervention design. Participants will be asked to describe elements that helped them to achieve their physical activity goals (and elements that did not help) and suggestions on how to improve the design of the interventions.

9. Analysis plan

Similar to our prior work,[22,44,54] the primary analysis will fit mixed effect regression models to evaluate changes in physical activity (steps per day and minutes of MVPA) adjusting for each participant's baseline measure, time using calendar month fixed effects, participant random effects, and accounting for repeated measures. Secondary analyses will fit a fully adjusted model including other variables of interest such as participant demographic characteristics and comorbidities. We will also conduct a-priori exploratory subgroup analyses for participants with elevated risk (APOE4 carriers) and higher levels of social support on 1o and 2o outcomes. For these outcomes, we estimate a standard deviation of 2500 steps and a sample of 100 participants allocated in a 1:1 distribution (50 in each arm), will ensure at least 80% power to detect a 1000 step difference. This calculation assumes a 10% dropout rate and a conservative Bonferroni adjustment of the type I error rate with a 2-sided alpha of 0.017.

In exploratory analyses, we will compare results from virtual functional and cognitive tests at the beginning of the study (after randomization) with results during the follow up period (after intervention ends). We do not anticipate major changes in these measures and are not powered to detect minor changes – these are feasibility measures to demonstrate we can conduct virtual performance tests at multiple intervals only.

We will also conduct exploratory subgroup analyses of factors that may influence our primary outcome (change in mean steps/day) such as participant-reported social support and neighborhood walkability as determined by address/zipcode. These are factors that have been associated with steps in our prior work but this pilot will not adequately powered to detect statistical significance (we will explore for trends only).

10. Investigators

Ryan Greysen, MD, MHS, MA is the Principal Investigator (PI). He is the Director of Penn Center for Evidence-based Practice; his research focuses on outcomes of hospitalization for older, vulnerable adults during transitions of care and mobile technologies to engage this population.

Jason Karlawish, MD is Co-Director of the Penn Memory Center and Director of the Penn Program on Precision Medicine for the Brain (P3MB). His research focuses on quality of life and ethical issues of disclosure of gene and biomarkers of Alzheimer's disease risk in older adults.

11. Human research protection

11.1 Data confidentiality

Paper-based records will be kept in a secure location and only be accessible to personnel involved in the study. Computer-based files will only be made available to personnel involved in the study through the use of access privileges and passwords. Wherever feasible, identifiers will be removed from study-related information. Precautions are in place to ensure the data are secure by using passwords and encryption, because the research involves web-based surveys.

11.2. Data Management

The Way to Health web platform will serve as the core mechanism for recruiting and enrolling subjects, transmitting general and intervention-specific messages, collecting activity tracker and online survey data, and providing regular feedback to subjects on their progress in the study.

The Penn Medicine Academic Computing Services (PMACS) will be the hub for the hardware and database infrastructure that will support the project and is where the Way to Health web portal is based. The PMACS is a joint effort of the University of Pennsylvania's Abramson Cancer Center, the Cardiovascular Institute, the Department of Pathology, and the Leonard Davis Institute. The PMACS provides a secure computing environment for a large volume of highly sensitive data, including clinical, genetic, socioeconomic, and financial information. Among the IT projects currently managed by PMACS are: (1) the capture and organization of complex, longitudinal clinical data via web and clinical applications portals from cancer patients enrolled in clinical trials; (2) the integration of genetic array databases and clinical data obtained from patients with cardiovascular disease; (3) computational biology and cytometry database management and analyses; (4) economic and health policy research using Medicare claims from over 40 million Medicare beneficiaries. PMACS requires all users of data or applications on PMACS servers to complete a PMACS-hosted cybersecurity awareness course annually, which stresses federal data security policies under data use agreements with the university. The curriculum includes Health Insurance Portability and Accountability Act (HIPAA) training and covers secure data transfer, passwords, computer security habits and knowledge of what constitutes misuse or inappropriate use of the server. We will implement multiple, redundant protective measures to guarantee the privacy and security of the participant data. All

investigators and research staff with direct access to the identifiable data will be required to undergo annual responsible conduct of research, cybersecurity, and HIPAA certification in accordance with University of Pennsylvania regulations.

Data will be entered into the database through several different mechanisms. Participants will enter their own personal information and respond to surveys through a PHP-based web interface. Activity tracker data will be transmitted from the activity tracker company to the study server through a secure connection. Researchers will have a separate interface that will allow them to manually enter data if needed. For example, to enter data from virtual cognitive and functional tests, researchers will login to Way to Health and complete evaluation forms based on attachments for Timed Up and Go (TUG), 30-second Chair Stand Test (30s CST), Verbal Naming, Category Fluency, Trail Making, Number Span, and Blind MOCA.

Wherever possible, data will be de-identified for analysis. Personal information and research data will be stored in separate SQL tables and will be linked by a computer-generated ID number.

It is unlikely that anyone will need to make corrections to the data, as most of the information is submitted by participants. Furthermore, the web platform will be set up with pre-specified ranges of eligible values for each question to minimize data entry errors. Specifically designated administrators will have the ability to make corrections, however each modification will be logged along with justification for the change. The original data will be preserved in a separate non-modifiable database.

11.3 Subject confidentiality

Research material will be obtained from participant surveys, assessments and from the wearable devices. All participants will provide informed consent for access to these materials. The data to be collected include demographic data (e.g., age, sex, self-identified race), outcome data, and daily activity data collected by the wearable device. Research material that is obtained will be used for research purposes only. The same procedure used for the analysis of automated data sources to ensure protection of patient information will be used for the survey data, in that identifiers will be used only for linkage purposes or to contact participants. The study identification number will be used on all data collection instruments. All study staff will be reminded to appreciate the confidential nature of the data collected and contained in these databases.

Data will be stored, managed, and analyzed on a secure, encrypted server behind the University of Pennsylvania Health System (UPHS) firewall. All study personnel that will use this data are listed on the IRB application and have completed training in HIPAA standards and the CITI human subjects research. Data access will be password protected. Whenever possible, data will be de-identified for analysis.

11.4 Subject privacy

Potential participants will have the option to accept or decline the study invitation. If participants accept, they acknowledge that their information will be shared with the study team and that a member of the study team will contact them. Those who decline the invitation will not be contacted again, and none of their information will be shared with the study team. Enrollment will include a description of the voluntary nature of participation, the study procedures, risks and potential benefits in detail. Potential participants will have the opportunity to ask questions and review the consent form information with family prior to making a decision to participate. Participants will be told that they do not have to answer any questions if they do not wish and can drop out of the study at any time. They will be told that they may or may not benefit directly from the study and that all information will be kept strictly confidential, except as required by law. All efforts will be made by study staff to ensure subject privacy.

11.5 Data disclosure

The following entities, besides the members of the research team, may receive data for this research study: -Fitbit, the company that designs and manufactures the wearable devices used in the study to track participant physical activity. RedCap, a secure web application where participants' informed consent forms will be stored. -Twilio, Inc., the company which processes some study-related messages. Twilio will store patients' phone numbers on their secure computers. -Qualtrics, Inc., the company which processes most study-related surveys. Qualtrics will house de-identified answers to these surveys on their secure servers. -The Office of Human Research Protections at the University of Pennsylvania -Federal and state agencies (for example, the Department of Health and Human Services, the National Institutes of Health, and/or the Office for Human Research Protections), or other domestic or foreign government bodies if required by law and/or necessary for oversight purposes.

11.6 Data safety and monitoring

At the time of enrollment, all patients will be given anticipatory guidance on when to seek medical attention (e.g. when to call their doctor should they feel dizzy, short of breath, chest pain, lightheaded, unstable, or otherwise unwell while ambulating). In addition, participants will be asked to report to the study team any episodes of these symptoms that occur during ambulation to research staff. Participants will also be reminded that they can always contact the study team by phone or email at any time (contact information will be given at the beginning of the study and will also be posted on the Way to Health platform, which can be accessed at any time by the participant). If any concerns of a participant event are identified, the study coordinator will reach out to the participant and complete the event reporting form. This form will be reviewed with the study PI to determine if any action is needed and if the participant can continue safely in the study. Any identified adverse events will be reported to the Institutional Review Board.

A Safety Officer will also be appointed to review IRB protocol and will review adverse events when enrollment is halfway complete. All adverse events that are serious or unexpected (i.e., have not been previously reported for the study's intervention) including death or hospitalization of a participant, will be reported to the IRB, Safety Officer, and NIA Program Officer within 24 hours of the PI's knowledge of the SAE.

Dr. Greysen as the study principal investigator will be responsible for monitoring participant safety, data quality/confidentiality, and evaluating the progress of the study on a daily basis in conjunction with study staff. An NIA-approved SO will have the role/responsibility of reviewing the entire IRB-approved study protocol regarding subject safety and analysis, the informed consent document regarding applicability and readability, and participant recruitment and retention milestones. At the time of interim analysis (50% enrollment), the study team will prepare a safety report to be reviewed by the SO.

11.7 Risk/benefit

11.7.1 Potential study risks

There are minimal risks to participants in this study. The potential risks to study participants include: breach of confidentiality and privacy as information about each participant including their physical activity and health will be recorded; the possibility that answering certain questions may make the participant feel slightly uncomfortable; excessive physical activity could lead to muscle soreness or injury; some skin irritation or rash from wearing the Fitbit watch, although this occurs rarely; increased in physical activity (walking) may increase the risk of falling, although this is also very rare.

We will minimize this risk of confidentiality breach by linking individual identifying information with participant ID numbers only in one single secure file that will only be accessed by the study team in the case of an adverse medical event, participant dropout, or if otherwise deemed necessary by the Principal Investigator. All other identifying information will be discarded after initial contact with the Study Coordinator. All other members of the research team will be able to view only participant ID numbers.

11.7.2 Potential study benefits

Through participation in this study, each participant will have the potential to increase their physical activity, which could improve their health and reduce their risk for cognitive and functional decline. If this approach is effective, it could have tremendous benefits for society if adopted on a wide scale to help individuals increase physical activity. It is expected that other people will gain knowledge from this study and that participation could help understand how to

effectively motivate people to become more physically active. Participants may also receive no benefit from their participation in the study.

11.7.3 Risk/benefit assessment

Anticipated risks of this study should be minimal and the risk/benefit ratio is very favorable. To minimize the chance for serious and unexpected adverse events, study participants will be screened through exclusion criteria. Participants will be told that increased physical activity may improve their health and reduce their risk of cognitive and functional decline.

11.7.4 Alternatives to participation

Participants do not have to be enrolled in the study in order to participate in activities to promote physical activity.

11.8 Resources necessary for human research protection

In addition to efforts of the study investigators (PI Greysen and Co-I Karlawish), this study will be supported by research staff including a Clinical Research Coordinator (50% total effort) and analyst (25% effort). The CRC has participated in previous research trials using FitBit devices and remote monitoring of physical activity by Way to Health. The CRC has also participated in preparation of this study protocol and the PI will oversee execution of this protocol through weekly check-ins and ad hoc meetings as needed. The CRC has office space dedicated in the Division of General Internal Medicine (Blockley Hall) which is adjacent to the PI's office. The office includes a Penn-issued computer with network access. Since this study will be conducted completely virtually, there are no specific facilities other than office space and computing that are needed to conduct this study.

BIBLIOGRAPHY AND REFERENCES CITED

1. Beckett MW, Ardern CI, Rotondi MA. A meta-analysis of prospective studies on the role of physical activity and the prevention of Alzheimer's disease in older adults. *BMC Geriatr.* 2015;15:9.
2. Erickson KI, Hillman C, Stillman CM, et al. Physical Activity, Cognition, and Brain Outcomes: A Review of the 2018 Physical Activity Guidelines. *Med Sci Sports Exerc.* 2019;51(6):1242-1251.
3. Northey JM, Cherbuin N, Pumpa KL, Smee DJ, Rattray B. Exercise interventions for cognitive function in adults older than 50: a systematic review with meta-analysis. *Br J Sports Med.* 2018;52(3):154-160.
4. Ogawa EF, You T, Leveille SG. Potential Benefits of Exergaming for Cognition and Dual-Task Function in Older Adults: A Systematic Review. *J Aging Phys Act.* 2016;24(2):332-336.
5. Saez de Asteasu ML, Martinez-Velilla N, Zambom-Ferraresi F, Casas-Herrero A, Izquierdo M. Role of physical exercise on cognitive function in healthy older adults: A systematic review of randomized clinical trials. *Ageing Res Rev.* 2017;37:117-134.
6. Sofi F, Valecchi D, Bacci D, et al. Physical activity and risk of cognitive decline: a meta-analysis of prospective studies. *J Intern Med.* 2011;269(1):107-117.

7. Centers for Disease Control and Prevention. Facts about physical activity. www.cdc.gov/physicalactivity/data/facts.html, 2017.
8. Andersen LB, Mota J, Di Pietro L. Update on the global pandemic of physical inactivity. *Lancet.* 2016;388(10051):1255-1256.
9. Mohan D, Schell J, Angus DC. Not Thinking Clearly? Play a Game, Seriously! *JAMA.* 2016;316(18):1867-1868.
10. Brown M, O'Neill N, van Woerden H, Eslambolchilar P, Jones M, John A. Gamification and Adherence to Web-Based Mental Health Interventions: A Systematic Review. *JMIR Ment Health.* 2016;3(3):e39.
11. Cugelman B. Gamification: what it is and why it matters to digital health behavior change developers. *JMIR Serious Games.* 2013;1(1):e3.
12. Miller AS, Cafazzo JA, Seto E. A game plan: Gamification design principles in mHealth applications for chronic disease management. *Health Informatics J.* 2016;22(2):184-193.
13. Asch DA, Rosin R. Engineering Social Incentives for Health. *N Engl J Med.* 2016;375(26):2511-2513.
14. Patel MS, Asch DA, Volpp KG. Wearable devices as facilitators, not drivers, of health behavior change. *JAMA.* 2015;313(5):459-460.
15. Patel MS, Benjamin EJ, Volpp KG, et al. Effect of a Social Incentive-based Gamification Intervention Using Wearable Devices and Smartphones on Physical Activity: The BE FIT Randomized Clinical Trial. *Circulation.* 2017;135(25):AP131.
16. Patel MS, Benjamin EJ, Volpp KG, et al. Effect of a Game-Based Intervention Designed to Enhance Social Incentives to Increase Physical Activity Among Families: The BE FIT Randomized Clinical Trial. *JAMA Intern Med.* 2017;177(11):1586-1593.
17. Patel MS, Small DS, Harrison JD, et al. Effectiveness of Behaviorally Designed Gamification Interventions With Social Incentives for Increasing Physical Activity Among Overweight and Obese Adults Across the United States: The STEP UP Randomized Clinical Trial. *JAMA Intern Med.* 2019:1-9.
18. Ariely D, Wertenbroch K. Procrastination, deadlines, and performance: self-control by precommitment. *Psychol Sci.* 2002;13(3):219-224.
19. Rogers T, Milkman KL, Volpp KG. Commitment devices: using initiatives to change behavior. *JAMA.* 2014;311(20):2065-2066.
20. Kahneman D, Tversky A. Prospect Theory: An Analysis of Decision under Risk. *Econometrica.* 1979;47(2):263.
21. Tversky A, Kahneman D. Advances in Prospect-Theory - Cumulative Representation of Uncertainty. *Journal of Risk and Uncertainty.* 1992;5(4):297-323.
22. Patel MS, Asch DA, Rosin R, et al. Framing Financial Incentives to Increase Physical Activity Among Overweight and Obese Adults: A Randomized, Controlled Trial. *Ann Intern Med.* 2016;164(6):385-394.
23. Emanuel EJ, Ubel PA, Kessler JB, et al. Using Behavioral Economics to Design Physician Incentives That Deliver High-Value Care. *Ann Intern Med.* 2016;164(2):114-119.
24. Chapman GB, Coups EJ. Emotions and preventive health behavior: worry, regret, and influenza vaccination. *Health Psychol.* 2006;25(1):82-90.
25. Connolly T, Butler D. Regret in economic and psychological theories of choice. *Journal of Behavioral Decision Making.* 2006;19(2):139-154.
26. Krahmer D, Stone R. Anticipated regret as an explanation of uncertainty aversion. *Economic Theory.* 2013;52(2):709-728.
27. Zeelenberg M, Pieters R. Consequences of regret aversion in real life: The case of the Dutch postcode lottery. *Organizational Behavior and Human Decision Processes.* 2004;93(2):155-168.

28. Harkins KA, Kullgren JT, Bellamy SL, Karlawish J, Glanz K. A Trial of Financial and Social Incentives to Increase Older Adults' Walking. *Am J Prev Med.* 2017.
29. Kullgren JT, Harkins KA, Bellamy SL, et al. A mixed-methods randomized controlled trial of financial incentives and peer networks to promote walking among older adults. *Health Educ Behav.* 2014;41(1 Suppl):43S-50S.
30. Greysen SR, Changolkar S, Small DS, et al. Effect of Behaviorally-Designed Gamification with a Social Support Partner to Increase Mobility after Hospital Discharge: a randomized clinical trial. *JAMA Network Open.* 2021;To be published March 24, 2021.
31. Langbaum JB, Karlawish J, Roberts JS, et al. GeneMatch: A novel recruitment registry using at-home APOE genotyping to enhance referrals to Alzheimer's prevention studies. *Alzheimers Dement.* 2019;15(4):515-524.
32. Centers for Disease Control and Prevention Physical Activity Guidelines. https://health.gov/paguidelines/. Accessed March 3, 2021.
33. U.S. Department of Health and Human Services: Physical Activity Guidelines for Americans. https://health.gov/sites/default/files/2019-09/Physical_Activity_Guidelines_2nd_edition.pdf. Accessed February 25, 2021.
34. National Institute on Aging. Staying Physically Active with Alzheimer's. 2017; https://www.nia.nih.gov/health/staying-physically-active-alzheimers.
35. Patel MS, Chang S, Volpp KG. Improving Health Care by Gamifying It. *Harvard Business Review.* 2019.
36. Kawachi I. It's All in the Game-The Uses of Gamification to Motivate Behavior Change. *JAMA Intern Med.* 2017;177(11):1593-1594.
37. The US digital consumer report. 2014; http://www.nielsen.com/us/en/insights/reports/2014/the-us-digital-consumer-report.html. Accessed March 3, 2021.
38. Case MA, Burwick HA, Volpp KG, Patel MS. Accuracy of smartphone applications and wearable devices for tracking physical activity data. *JAMA.* 2015;313(6):625-626.
39. Christakis NA, Fowler JH. The collective dynamics of smoking in a large social network. *N Engl J Med.* 2008;358(21):2249-2258.
40. Christakis NA, Fowler JH. The spread of obesity in a large social network over 32 years. *N Engl J Med.* 2007;357(4):370-379.
41. Jackson SE, Steptoe A, Wardle J. The influence of partner's behavior on health behavior change: the English Longitudinal Study of Ageing. *JAMA Intern Med.* 2015;175(3):385-392.
42. Bardach SH, Langbaum JB, Kebodeaux CS, Jicha GA. Real-world Site Experiences With GeneMatch: The Role of a Recruitment-related Registry in the Context of Local Site Effort to Support Alzheimer Disease Prevention Research. *Alzheimer Dis Assoc Disord.* 2020.
43. Asch DA, Volpp KG. On the Way to Health. *LDI Issue Brief.* 2012;17(9):1-4.
44. Patel MS, Volpp KG, Rosin R, et al. A Randomized Trial of Social Comparison Feedback and Financial Incentives to Increase Physical Activity. *Am J Health Promot.* 2016;30(6):416-424.
45. Centers for Disease Control and Prevention. Timed Up and Go Test. https://www.cdc.gov/steadi/pdf/TUG_test-print.pdf. Accessed March 3, 2021.
46. Centers for Disease Control and Prevention. 30-Second Chair Stand Test. https://www.cdc.gov/steadi/pdf/STEADI-Assessment-30Sec-508.pdf. Accessed March 3, 2021.
47. National Alzheimer's Coordinating Center (NIA ADRC Program). Uniform Data Set - Neuropsychological Battery (C2T). . 2020:https://naccdata.org/data-collection/forms-documentation/uds-3.
48. Bassett DR, Jr., Wyatt HR, Thompson H, Peters JC, Hill JO. Pedometer-measured physical activity and health behaviors in U.S. adults. *Med Sci Sports Exerc.* 2010;42(10):1819-1825.

49. Kang M, Hart PD, Kim Y. Establishing a threshold for the number of missing days using 7 d pedometer data. *Physiol Meas.* 2012;33(11):1877-1885.
50. Dai H, Milkman KL, Riis J. The Fresh Start Effect: Temporal Landmarks Motivate Aspirational Behavior. *Management Science.* 2014;60(10):2563-2582.
51. Marshall SJ, Levy SS, Tudor-Locke CE, et al. Translating physical activity recommendations into a pedometer-based step goal: 3000 steps in 30 minutes. *Am J Prev Med.* 2009;36(5):410-415.
52. Tudor-Locke C, Sisson SB, Collova T, Lee SM, Swan PD. Pedometer-determined step count guidelines for classifying walking intensity in a young ostensibly healthy population. *Can J Appl Physiol.* 2005;30(6):666-676.
53. Piercy KL, Troiano RP, Ballard RM, et al. The Physical Activity Guidelines for Americans. *JAMA.* 2018;320(19):2020-2028.
54. Patel MS, Asch DA, Rosin R, et al. Individual Versus Team-Based Financial Incentives to Increase Physical Activity: A Randomized, Controlled Trial. *J Gen Intern Med.* 2016;31(7):746-754.