A Physical Activity Program to Disrupt Sedentary Time in Older Latinos (PAIS)

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LIST OF ABBREVIATIONS

COI	Conflict of Interest
DHHS	Department of Health and Human Services
DMC	Data Monitoring Committee
DSMB	Data and Safety Monitoring Board
DSMP	Data and Safety Monitoring Plan
FERPA	Family Educational Rights and Privacy Act
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
IBC	Institutional Biosafety Committee
ICD	Informed Consent Document
ICH	International Conference of Harmonization
IDE	Investigational Device Exemption
IDS	Investigational Drug Service
IND	Investigational New Drug
IRB	Institutional Review Board
LAR	Legally Authorized Representative
OHRP	Office of Human Research Protections
OPRS	Office for the Protection of Research Subjects
PHI	Protected Health Information
PI	Principal Investigator
PPRA	Protection of Pupil Rights Amendment
QA/QI	Quality Assurance/Quality Improvement
SAE	Serious Adverse Event
SOP	Standard Operating Procedure

1.0 Project Summary/Abstract

This study has been revised to allow for maximal social distancing in order to expedite the study time line, minimize risk of COVID19 exposure, and ensure participant safety.

The Latino population over age 65 will reach 18% of the total U.S. population by 2050. Currently, over 12% of older adult Latinos have been diagnosed with Alzheimer's disease and related dementias (ADRD). Even more striking, the number of Latinos with ADRD is expected to increase 9-fold over the next 3 decades, representing an epidemic increase of ADRD.[2] The high incidence of ADRD in conjunction with physical function limitations place older Latinos at a high risk for loss of independence and significant caregiver burden. Sedentary time (defined as sitting) has been shown to be associated with reduced cognitive function in healthy older Latinos. Studies are clearly needed to investigate the benefits on cognition and brain connectivity of breaking up and replacing sedentary time with physical activity (PA) in older Latinos. However, in order to develop and deliver a successful intervention we need to understand how to best conduct a lifestyle intervention in the Latino community. Our current understanding is rooted in a Eurocentric view that assumes that interventions that work in one community will work the same way in a different community. This assumption is likely incorrect and represents a significant gap in our ability to develop a successful intervention at the multiple l levels that are required across the socio-ecological model (SEM) to be successful. We propose to investigate the interactive effects of behavior determination to increase PA levels in older Latinos. This study will examine factors that facilitate initiation of and adherence to behavioral change at the individual level using the social cognitive theory, and ecological momentary assessment in an inner-city Chicago Latino Senior community. Our objectives are: 1) to discern the individual characteristics and the social networks within the community that influence behavior change to increase PA levels in the Latino community. 2) To assess the feasibility and acceptability of our PA measures. 3) To test the feasibility and initial impact of an intervention program designed to replace sedentary time with PA that has been designed specifically for older Latinos and delivered at home, to improve cognitive function and brain connectivity. We will achieve these objectives by using phone interviews, ecological momentary assessment, and an ecological momentary intervention within an inner city Chicago Latino senior community. Findings will directly facilitate the development and progression of culturally appropriate intervention(s) that will lead to rapidly translatable programs for older adults at risk for cognitive and physical decline. **This proposal is very relevant to ADRD and aging research** and addresses several areas of focus. 1). Physical Activity promotion, creation, modification and pilot testing of a principle-based intervention to reduce sedentary behavior and increase physical activity. 2). Pilot testing an intervention to enhance mobility in older adults to improve cognitive and physical functioning to prevent or forestall loss of independence. 3). We are harnessing technology to *promote and sustain* a behavioral intervention to achieve healthy aging in older adults.

2.0 Background/Scientific Rationale

The Latino population over age 65 will comprise 18% of the total U.S. population by 2050. Currently, over 12% of older adult Latinos have been diagnosed with Alzheimer's disease and related dementias (ADRD). Even more striking, the number of Latinos with ADRD is expected to increase 9-fold over the next 3 decades, representing an epidemic rate of increase. The high incidence of ADRD in conjunction with physical function limitations place older Latinos at a high risk for loss of independence and significant caregiver burden. Sedentary time (defined as sitting) is a known risk factor for reduced cognitive function in healthy older Latinos. Studies are clearly needed to investigate the benefits on cognition and brain connectivity of breaking up and replacing sedentary time with physical activity (PA) in this population. However, in order to develop and deliver a successful intervention we need to understand how to best conduct a lifestyle intervention in the Latino community. We propose to investigate the interactive effects of behavior determination to increase PA levels in this population. This study will examine factors that facilitate initiation of and adherence to behavioral change at the individual level using social cognitive theory, and ecological momentary assessment in an inner-city Chicago Latino Senior community.

3.0 Objectives/Aims

Successful lifestyle interventions must act on multiple levels across the SEM in order to in order to increase daily physical activity. The SEM underscores the importance of understanding how the individual and the individual's interpersonal community affect behavior change. Our long-term goal is to develop an intervention that is specifically tailored to older Latinos to *prevent or forestall cognitive and physical function decline*. Specifically, we propose to investigate the interactive effects of behavior determination to increase physical activity (PA) levels in older Latinos. Our objectives are

1) to discern the individual characteristics and the social network within the community that influence behavior change to increase PA levels in an inner city Chicago Latino community.

2) To assess the feasibility and acceptability of our PA measures.

3) To test the feasibility of an intervention designed to replace sedentary time with PA that has been designed specifically for older Latinos and delivered in their homes to improve cognitive function.

- **Aim 1 (stage 1A):** Conduct individual phone interviews to determine the individual characteristics and the social networks that influence behavior change to reduce and replace sedentary time with PA within an older adult Chicago Latino community. The focus groups will be 50% male and 50% female to enable comparisons of possible gender-differences.
- **Aim 2 (stage 1A):** Assess the feasibility and acceptability of our PA measures and ecological momentary assessment (EMA) in this community.

- **Aim 3 (stage 1B):** Determine the feasibility and acceptability of an ecological momentary intervention (EMI) program designed to reduce and replace sedentary time with PA in older Latinos, delivered in the home-setting over 6 weeks, compared to participants randomized to receive physical activity guidelines in Spanish.
- **Exploratory aims (stage 1B):** To explore the feasibility and preliminary effect of the EMI intervention on cognitive function in older Latinos, compared to participants randomized to guidelines.

Study Duration: This is a feasibility pilot randomized, controlled trial of a 6-week intervention. Outcome measures will be obtained at baseline and at 6-weeks. Behavior choices and preference data will be continuously captured during the intervention.

4.0 Eligibility

We will randomize 80 older Latinos from a Chicago Latino community center to either the EMI intervention (n=40) or to physical activity guidelines (n=40.

Dr. Ulf Bronas or study designee will assess and determine the subject eligibility. An eligibility checklist will be completed prior to any study participant randomization. Eligibility criteria will be continuously monitored by the PI/RA and document via an eligibility checklist at the baseline and follow-up.

4.1 Inclusion Criteria

- Men and women >55-89 years of age, no history of major head trauma, ownership of a working smartphone, and ability to use video calls.

4.2 Exclusion Criteria

- No ability to use video technology
- Wheelchair dependent
- Diagnosed dementia,
- Participating in a supervised exercise program with intent to increase fitness levels 3 days/week,
- Contraindications to PA per ACSM
  - Requires assistive ambulation;
  - Unstable angina,
  - Claudication
  - severe arthritis,
  - extreme dyspnea on exertion,
  - Class III-IV heart failure;
  - Current uncontrolled sustained arrhythmias,
  - severe/symptomatic aortic or mitral stenosis,
  - hypertrophic obstructive cardiomyopathy,
  - severe pulmonary hypertension,
  - active myocarditis/pericarditis,
  - thrombophlebitis,
  - recent systemic/pulmonary embolus (within 3 months);
  - Revascularization procedures within the previous 6 months;

- Pregnancy

4.3 Excluded or Vulnerable Populations

Vulnerable populations are not included in this study.
The following populations are excluded from this study: 1. Pregnant women: Pregnant women are excluded to limit any potential influence on measures.
Non-English speaking population: Non-English speaking population other than Spanish will be excluded from the study.
Spanish speaking population will be included once IRB approval has been obtained for the Spanish translated versions of the consent, phone app, and study documents.

5.0 Subject Enrollment

Participants are community dwelling adults without dementia. We have established strong relationship with this organization and key stakeholders. Participants will be recruited through a flyer with information about the study posted on organization's website and by word of mouth. We have developed a media recruitment script that will be used as the script for a video presentation that will be posted on a website, TV add, Facebook, and read as a radio add. We will send a notice via the CCTS research match and the TNN Match service using the form titled "research match".

- Participants that contact the study team will be sent the consent form and given as much time as they feel necessary to decide if they would like to participate. Participants will be encouraged to ask any questions at any time throughout the course of the study. Research personnel will be available to answer these questions. Subjects will be informed that participating in this research is voluntary. Subjects will be informed that they may withdraw from the research at any time without penalty. Patient providers are not part of the study team.

6.0 Study Design and Procedures

This research will be performed via telephone/video conference to maximize social distancing and participant safety. The intervention will be performed by the participants at home.

This is a pilot randomized, controlled trial of a 6-week intervention for feasibility. Outcome measures will be obtained at baseline and at 6-weeks. Behavior choices and preference data will be continuously captured during the intervention. We will randomize 80 older Latinos from the Chicago Latino community to either an ecological momentary intervention using fitbits (n=40) or to physical activity guidelines (n=40).

Study interaction 1-baseline test (Approximately 2 hours). Participants will be screened for inclusion/exclusion criteria. If criteria for inclusion in the study are met participants will undergo informed consent process. Following informed e-consent conducted via zoom video/telephone participants will asked about their demographics (demographic

form), and contact information (Face sheet), and then they will be asked about their medical history. Following the medical history we will fill out the Charlson co-morbidity questionnaire, and conduct the following cognitive function measures as approved by the NIH for use via video call: a. Picture vocabulary test, b. Picture sequence test, c. List sorting test, d. Oral reading recognition test, e. Auditory verbal learning test, and the Trail Making test A and B. Following the cognitive function testing, we will conduct a phone/video interview. The interview will be recorded, analyzed and used to develop the intervention.

Following the interview we will conclude the phone call and send the participants an activity monitor to be worn on the waist for 8 days to measure sedentary time: The participants will mail the monitor back to us after 8 days. Once we have received the physical activity monitor we will randomize the participant to intervention or control.

Optional in-person visit (approximately 1 hour) If the participant is willing and able to undergo an MRI scan. No contrast will be used.

- **The MRI Visit will take place about one-week after the initial phone call. Participants will come to the Magnetic Resonance Imaging Center, 3T research center 2242 W. Harrison St. Chicago IL 60612and return the actigraph to us. We will ask participants to do the following:**
- **Have an MRI to take pictures of the brain at a scanning facility. Scanning will last approximately 1 hour during.**
- **Before entering the MRI room, participants will be asked to remove from all metal objects, including jewelry, watches, hair holders, or eyeglasses; and asked to empty pockets of all materials, including keys, wallets, and magnetic cards such as ATM and credit cards. In addition, if the clothing has more than a minimal amount of metal content, they may be asked to change into a hospital gown or other suitable garment. Finally, they may be asked to remove any eye shadow you may be wearing, because eye shadow sometimes contains metallic substances.**
- **Because the MRI machine makes loud noises while it scans, a researcher or technician will provide participants with earplugs to reduce the noise level.**
- **All of the procedures described above will be performed by qualified, licensed personnel and arranged at the participant's convenience. We will inform participants of any abnormalities found in the tests; however, the information obtained from the MRI and cognitive testing is experimental in nature and does not allow for clinical interpretation. We will, however, contact participants if the MRI or cognitive test results warrant a formal clinical follow-up and discuss this with their medical provider (e.g., General**

Practitioner). Ultimately, however, it is up to the participant to follow-up with a doctor for a clinical evaluation

Following the MRI, we will assess cognitive and basic motor function using the NIH toolbox the NIH Toolbox measures for Cognitive function will completed using the standard NIH Ipad (see administration manual):

- **C.2.2 NIH Toolbox Flanker Inhibitory Control and Attention Test page 67**
- **C.2.4 NIH Toolbox Dimensional Change Card Sort Test (DCCS) page 98**
- **C.2.5 NIH Toolbox Pattern Comparison Processing Speed Test page 124**
- **C.2.7 NIH Toolbox Oral Reading Recognition Test page 151**
- **C.2.8 Oral Symbol Digit Test page 154**

Following the NIH Toolbox measures for Cognitive function, the NIH toolbox motor measures will completed using the standard NIH Ipad (see administration manual):

- **Pegboard dexterity test (172)**
- **Balance measures with the addition of iPod app for assessment of sway (179).**
- **Two-minute walk (198)**
- **Grip strength (using handheld dynamometer, 176)**
- **4 meter walk (195)**

Study interaction 2 (Approximately 1 hour): Participants will be notified via telephone which group that were randomized to.

Participants randomized to the intervention group will be sent a fitbit that has been set up to deliver the intervention as described below. We will schedule a telephone call or zoom video call (whichever the participant prefers) to set up the HIPPA compliant EMA system and to provide education about the fitbit and the intervention to disrupt sedentary time.

Intervention (home-setting): We will deliver content in real-time, and in the real-world environment using a wearable sensor, an activity tracker and the Illumivu mEMA smart phone app, which will enable real-time delivery of behavior options and real-time feedback on the effectiveness of behavior choices. Although the intervention will be guided by the interview findings, in general, participants will wear a Fitbit that has been programmed to deliver a notification (a buzz) when activity has ceased for more than 10 minutes. They will receive suggestions on their smartphone app on how to replace sitting time with PA such as standing up 5 times or taking 20 steps, or even performing a short (20 seconds) preferred dance routine. We will capture Fitbit data in a real-time platform (ICardia). Participants will receive reminders from their smartphones to enter

real-time feedback on activity options selected and how successful they were in adopting the option. These data will allow us to track underlying preferences for behaviors and tailor the program accordingly. Participants will receive a message immediately with positive choices for behavioral action. Resulting actions and delivery of the intervention will be automatically captured and downloaded in real time. We will teach them how to use these devices once they are assigned to the intervention group. The sensor and activity tracker will record their everyday physical activity level. When participant stays sedentary too long during a day, the smartphone app will send a real-time reminder with some physical activity options for participant to choose designed based on their preferences and focus group discussions (e.g., standing up 5 times, taking 20 steps, or performing a short dance routine). Resulting actions and delivery of the intervention will be automatically captured and downloaded into the devices in real time.

Participants randomized to the control group will be sent general guidelines for disruption of sedentary time.

Study interaction 3-Follow-up (Approximately 1 hour): At the completion of the 6-week intervention period all participants will be sent an activity monitor to be worn on the waist for 8 days to measure sedentary time: The participants will mail the monitor back to us after 8 days. Once we have received the physical activity monitor we will schedule a phone interview with the participants to understand where they had difficulty and what did or did not work for them. We will then repeat the cognitive function tests and the optional MRI scan.

7.0 Expected Risks/Benefits

Risk associated with the medical history assessment

Discomfort could be felt by participants when answering questions about their medical history.

Risk associated with the cognitive function questionnaires.

There is a slight risk that participants will feel uncomfortable with filling out the questionnaires. Participants could find answering the questions boring and/or tiring. We will monitor the progress and allow participants to take breaks as needed. If they become upset or uncomfortable, they may skip a given question.

Optional MRI scans:

The MRI scans are performed with a powerful magnet without using x-ray radiation or radioactive material. The magnetism of the machine attracts certain metals, which could put a participant at risk. Therefore, people with pacemakers, infusion pumps, metal

prostheses, metallic-backed transdermal patches or metallic shrapnel will be excluded from the study. A checklist will be completed that addresses issues of MRI safety. Some people may feel somewhat closed-in (claustrophobic) during the MRI procedure. The MRI scans can get quite noisy and this may cause some discomfort. We will provide padding, a blanket as well as ear plugs to ensure comfort. Participants will stay in contact with study staff during the entire MRI procedure and can request to stop at any time

Risk associated with the intervention.
There are no known risks associated with activities to break up sedentary time as they are considered usual activities of daily living.

8.0 Data Collection and Management Procedures

- We will use EMI designed to deliver content in real-time, and in the real-world environment. EMI, using a wearable sensor, an activity tracker and the Illumivu mEMA smart phone app, will enable real-time delivery of behavior options and real-time feedback on the effectiveness of behavior choices. This methodology will enable us to create a culturally appropriate intervention that is based on preferences of individuals within their community networks. Although the intervention will be guided by the focus group findings, in general, we expect that participants will wear a Fitbit that has been programmed to deliver a notification (a buzz) when activity has ceased for more than 10 minutes. They will receive a notification on their smartphone app with a suggestion on how to replace sitting time with PA such as standing up 5 times or taking 20 steps, or even performing a short preferred dance routine. We will capture Fitbit data in a real-time platform (ICardia). Participants will receive reminders from their smartphones to enter real-time feedback on the PA options selected and how successful they were in adopting the option. These data will allow us to track underlying preferences for behaviors and tailor the program accordingly. Participants will receive a message immediately with positive choices for behavioral action. Resulting actions and delivery of the intervention will be automatically captured and downloaded in real time.

- **Outcomes: Sedentary time** will be measured using the Actigraph, a validated tool for measuring sedentary time in older adults following standard procedures over 7 days at baseline and at follow up. Sedentary behavior will be defined as: 1) waking activity with an energy expenditure ≤ 1.5 metabolic equivalents occurring in a sitting or reclining posture; 2) vector magnitude counts are <70 counts/15-s and vertical axis counts are <10 counts/15-s. Sedentary interruption will be defined as counts >100/minute. Non-wear time will be considered to be 60 minutes of zero-activity counts. Any counts over 15,000 will be considered erroneous. A valid day will consist of 10 waking hours. At least 5 complete days of data must be available to be included in the analysis.

- **Cognitive and Physical Function Measures** will be assessed using the NIH Toolbox measures.

- **Image acquisition** will be performed on GE 3T MRI research dedicated scanner (MR 750) pre- and post-intervention. After a brief scout image for localization, we will acquire whole brain images using diffusion tensor imaging (DTI); and high-resolution 3D T1-weighted imaging. We will determine and quantify white matter integrity (DTI-FA/MD); and hippocampal volume (T1). These are indices of alterations of brain inter-connections, structure, and function, which are associated with cognitive functioning (details, table 2).

Table 2. Imaging Parameters

Technique	Purpose	Parameters (TE=echo time; TR=repetition time; BW=bandwidth; FOV=field of view; TI=inversion time)
DTI	White matter integrity (FA/MD) quantification	single-shot EPI & parallel imaging using the same 32-channel phased-array head coil; TE/TR~70/5525ms, b-values 0,1000s/mm^2, 33 directions, FOV=20cm^2, matrix 160x160, NEX 2, parallel imaging acceleration factor 2; 6 B0 images, Slice thickness 3 mm
T1/BRAVO	Hippocampal Volume Quantification	Coronal; TI=4.5, Flip=13º, 1.5mm slice thickness, no gap, BW=±25kHz, FOV=22cm^2
T2-FLAIR	White matter hyperintensity quantification	Coronal; TE/TR=104.5/9500ms, TI=2.5sec, FOV 22cm^2
ASL	Cerebrovascular perfusion Cerebral blood flow	axial; Spiral-FSE acquisition; post-label delay time = 1.8 sec, TE/TR=minimum, flip angle=90°, slice thickness = 3-5 mm, matrix size = 128x128, FOV 22cm^2
Resting-state fMRI	Resting state networks	Subjects will be instructed to keep their eyes open, focus on a fixation point, and “not think of anything in particular”. Resting-state data will be acquired: total scan time = 8 minutes.

- **Image Analyses** DTI: FSL with TBSS, we will quantify FA and MD from whole brain and tract specific white matter. T1/FSPGR: Using FreeSurfer, we will extract hippocampal volumes (right and left) as well as sub-fields of the hippocampas adjusted for intracranial volume.T2-FLAIR: Using standard software, we will quantify white matter hyperintensity volumes across the entire brain white matter. We will use a seed-based approach to measure resting state networks of interest. *Functional connectivity networks:* Functional brain networks will be generated using the resting-state fMRI toolbox, CONN (*http://www.nitrc.org/projects/conn*; (Whitfield-Gabrieli and Nieto-Castanon, 2012)). In brief, raw EPI images are realigned, co-registered, normalized, and smoothed before analysis. Any confound effects from motion artifact, white matter, and CSF are regressed out of the signal. Using the same label maps as the structural brain networks, functional brain networks will derived using pairwise BOLD signal correlations.

- **Feasibility and acceptability:** We will conduct formative assessments at the completion of the intervention at week 6. We will derive the number of times the phone app was accessed and the number and types of behavior choices that were made. We will review these data with participants in order to understand where they had difficulty and what did or did not work for them.

9.0 Data Analysis

- We will conduct a thematic analysis to explore themes from individual phone interviews. Feasibility and acceptability will be assessed using descriptive and non-parametric statistics. Exploratory analyses will be conducted to assess for trends and effect sizes. Dr. Alana Steffen of the College of Nursing statistician will conduct all analyses. The apriori stated analysis is listed below.
  This is a pilot study for feasibility**.** For these pilot data we will emphasize descriptive statistics such as means, standard deviations, effect sizes, medians, interquartile ranges, frequencies, and percentages to demonstrate the feasibility of recruitment, adherence, and retention, treatment effects over time, and proof of concept. Our statistical approach for a full trial of these hypotheses will be Generalized Linear Mixed Models (GLMM) with an identity link function for a continuous outcome or a logit link function for a binary outcome. Conceptually, GLMM is a more advanced version of repeated measures ANOVA that can account for potential correlation among multiple measurements over time while having flexibility in fitting outcomes with different distributions (such as normal, binomial or Poisson, etc.). One advantage of this approach over repeated measures ANOVA is that there is no assumption that participants are measured at every, or even the same, time points. Therefore, these models are very flexible at handling missing data. Participants who have a missing observation are not excluded, thus, this produces the intention to treat (ITT) full information maximum likelihood (FIML) model. Conducting these models on pilot data help with sample size calculations for a future R01 submission.
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10.0 Quality Control and Quality Assurance

Data will be continuously evaluated for protocol adherence during weekly meetings with the PIs and the study staff. Dr. Bronas will evaluate all data for quality during weekly study meetings. Biweekly visits will be conducted by the PI to ensure that data collection is carried out according to the protocol.

11.0 Data and Safety Monitoring

Serious adverse events will be monitored and tracked at each follow-up period. Patients will be queried at the phone call and at 6 weeks if they have had any visits to the emergency department or hospitalizations (see attached checklist). We will also ask if they have had any symptoms of cardiac-related problems such as chest, arm or jaw pain while exercising or not exercising. Data will be recorded on an excel spreadsheet and reviewed by the PI at weekly study meetings. Any unanticipated adverse events or problems will be reported to the IRB within 7 days on notification. The PI will monitor safety data. Subjects are free to withdraw from the study at any time. If a subject withdraws from the study we will ask the subject (only once) if they are willing to come

back for the follow-up tests. If the subject does not want to complete the study, no further contact attempts will be conducted and the subject will be discontinued from the study (this will be reported at the annual continuing review).

Adverse Event and Serious Adverse Event Collection and Reporting
Adverse events will be tracked on an ongoing basis for the full sample using an adapted version of the NIA Adverse Event Form (*https://www.nia.nih.gov/research/dgcg/clinical-research-study-investigators-toolbox/adverse-events*) and serious adverse events will be tracked using the NIH Serious Adverse Event Form (*https://www.nia.nih.gov/research/dgcg/clinical-research-study-investigators-toolbox/adverse-events*). Adverse events will be reviewed during semi-annual meetings of the Data Safety Monitoring Committee (see 3.0 below for details). The PI will be informed of serious adverse events as soon as they occur and will notify the Safety Officer (Chair of the Committee) within 24 hours of notification. In addition, adverse events and serious adverse events will be reported to the UIC IRB and NIA consistent with their established protocols and will use the NIA AE/SAE Flow Process to guide this process and timeline (*https://www.nia.nih.gov/research/dgcg/clinical-research-study-investigators-toolbox/adverse-events*).
AEs will be defined as any health-related event that occurs within the intervention or assessment measure sessions. Expected AEs may include strained or sore muscles and fatigue. AE severity will be classified as:

- Mild - if the symptoms are tolerated and do not interfere with the participant's daily life.
- Moderate – if the symptoms cause some concern or some disruption to the participant's daily life, but can be alleviated through rest or relatively simple non-medical intervention.
- Severe – if the symptoms cause a major disruption in their daily life and require medical intervention or drug therapy.

All AEs will be documented using the Adverse Event Form by the PI. The PI will assess the relatedness of the AE to the study intervention and the expectedness of the AE. The PI will follow the Adverse Event flow chart to determine routing and reporting of the AE. All AEs will be reported to the DSMC and IRB in accordance with reporting guidelines. SAEs are not expected to occur within this intervention. However, potential SAEs could be a serious injury related to the intervention, a cardiac event resulting from physical activity, and death. All SAEs will be documented in the Serious Adverse Event form and reported to the NIA program officer and Safety Officer within 48 hours. All participant deaths will be reported to the NIA program officer and Safety Officer within 24 hours. All SAEs will be reported to the DSMC and IRB in accordance with reporting guidelines.

In addition to holding semi-annual DSMC meetings, all AE and SAE data will be reported quarterly by the pilot PI to the NIA project officer and Safety Officer.

1.3 Protection Against Study Risks.
Informed Consent Process. Potential participants will be provided with a copy of the consent form approved by the UIC IRB to follow during the verbal description and also to read on their own. A member of the research team will fully describe the study to the

potential participant(s) verbally, covering all of the content in the consent form, including potential risks and benefits. Potential participants will be given time to read the consent form and invited to ask any questions they may have about the study. Questions will be answered and any identified misunderstandings about the study will be clarified. Individuals interested in participating at this point will be asked to sign the e-consent and will be provided with one copy for their use. The standard consent form template used by the UIC IRB includes all of the basic sections identified in the NIA Informed Consent Checklist (*https://www.nia.nih.gov/research/dgcg/clinical-research-study-investigators-toolbox/informed-consent*).

Protections Against Study Risk. We believe that the potential risks to participants in this study are minimal and are risks that anyone disrupting sedentary time is likely to experience. There may be a small risk of muscle soreness associated with increased physical activity. Participants will be encouraged to (a) consult their health care provider before initiating any new physical activity; and (b) perform physical activities at a pace that is comfortable for them and in a way that is consistent with any recommendations from their medical provider.
Special care will be taken to ensure confidentiality of all data as described above. All project staff will be required to be current in training in Human Research Subjects protection sponsored by the University of Illinois at Chicago. The staff will also receive additional training on confidentiality by the principal investigator.

We do not anticipate any serious adverse events or distress as a result of participating in the proposed research. Any concerns will be immediately reported the principal investigator.

Interim Analysis will not be performed. The pilot intervention will last 6 weeks. The assessments will occur on two occasions (i.e., baseline; immediately post-intervention), so there will not be an opportunity to do an interim analysis during this short term pilot study.

Data and Safety monitoring.

The pilot Principal Investigator (PI) will be responsible for ensuring participants' safety on a daily basis. The pilot will be monitored by a local Data Safety Monitoring Committee and Safety Officer that will not require approval by the NIA. The Safety Officer in conjunction with a Data Safety Monitoring Roybal Center Committee will act in an advisory capacity to the NIA Director to monitor participant safety, evaluate the progress of the study, to review procedures for monitoring the confidentiality of the data, the quality of data collection matter, management, and analyses.

Frequency of Data and Safety Monitoring/ Safety Officer (SO) Reports.
The pilot PI will meet semi-annually with the DSM Committee, either in-person or by teleconference call, to review study progress, data quality, and participants' safety. Written summary reports will be submitted twice a year and will include a detailed analysis of study progress, data and safety issues. Margaret (Peg) Baumann, MD will

serve as chair of the committee, and as SO for any adverse event reports. Other members will include Susan Hughes, PhD (Roybal PI, SPH); Karen Peters, PhD (SPH); and Eileen Collins, PhD (Nursing).
The PI will be informed of serious adverse events as soon as they occur and will notify the SO within 48 hours. In addition, serious adverse events will be reported to the UIC IRB and NIA consistent with their established protocols.
In addition to semi-annual DSMC meetings, all AEs and SAEs will be reported quarterly to the Safety Officer and NIA project officer.

Data Analysis and Coordination
Since this is a single site pilot with a small sample (n=80) with a brief intervention and follow-up period (6 weeks), the pilot PI will coordinate data analysis and will not be blinded to the outcome data or data identifying the pilot participants.

Content of Data and Safety Monitoring Report/ SO Reports.

The content of the SO report will include study status/quality, participant descriptive information, adverse events, and dropout rates/reasons.

DSM Committee/ SO Membership and Affiliation.
The following individuals have accepted positions as part of the DSM Committee. Given the safe guards in place and the relatively low-risk to subjects within this pilot, we are using a local DSM Committee and not requesting review and approval by the NIA.

Susan Hughes, PhD
Professor, School of Public Health and Director, Center for Research on Health and Aging, University of Illinois at Chicago
Dr. Hughes is the Roybal Center PI and will be a DSMC member.

Karen Peters, PhD
Clinical Assistant Professor, School of Public Health, University of Illinois at Chicago
Dr. Peters has a broad background in community-based participatory research and evaluation, with specific training and research experience in community-engaged or -partnered research in both urban and rural areas. She is experienced in the design and conduct of evaluation studies, including data collection, synthesis, production and dissemination of evaluation results to community members that are tailored to their specific needs and interests.

Eileen Collins, PhD
Associate Dean for Research, Office of Research Facilitation and Professor, College of Nursing, University of Illinois at Chicago
Her research focuses on improving physical function and quality of life through cardiovascular and pulmonary rehabilitation interventions. She has been continually

funded for over 20 years by organizations such as NIH, VA and various foundations. Dr. Collins has published over 80 papers in peer-reviewed publications.

Margaret (Peg) Baumann, MD
Geriatric Medicine Physician, Jesse Brown Veterans Administration Medical Center
Dr. Baumann has accepted the position as the local Safety Officer and will work with the study PI and the DSM Committee to review pilot study data and safety monitoring.

Conflict of Interest for SO.

The SO will adhere to the Conflict of Interest Policy and procedures of the University of Illinois.

Protection of Confidentiality.

Data will be presented to the SO and the DSM Committee in a blinded manner during meetings and in written reports. The content of the SO reports and discussions will be treated as confidential. Participant identities will not be known to the SO.

SO Responsibilities.

The responsibilities of the local DSM Committee and the SO include:

- Review the research protocol, informed consent documents and plans for data safety and monitoring;
- Recommend subject recruitment be initiated after receipt of a satisfactory protocol;
- Evaluate the progress of the trial, including periodic assessments of data quality and timeliness, recruitment, accrual and retention, participant risk versus benefit, performance of the trial sites, and other factors that can affect study outcome;
- Consider factors external to the study when relevant information becomes available, such as scientific or therapeutic developments that may have an impact on the safety of the participants or the ethics of the trial;
- Review study performance, make recommendations and assist in the resolution of problems reported by the Principal Investigator;
- Protect the safety of the study participants;
- Report to NIA on the safety and progress of the trial;
- Make recommendations to the NIA and the Principal Investigator concerning continuation, termination or other modifications of the trial based on the observed beneficial or adverse effects of the treatment under study;
- Ensure the confidentiality of the study data and the results of monitoring; and,
- Assist the NIA by commenting on any problems with study conduct, enrollment, sample size, and/or data collection.
-

12.0 Statistical Considerations

We will conduct a thematic analysis to explore themes from interviews and focus groups. Feasibility and acceptability will be assessed using descriptive and non-parametric statistics. Exploratory analyses will be conducted to assess for trends and effect sizes. Dr. Alana Steffen of the College of Nursing statistician will conduct all analyses. The apriori stated analysis is listed below.

This is a pilot study for feasibility. For these pilot data we will emphasize descriptive statistics such as means, standard deviations, effect sizes, medians, interquartile ranges, frequencies, and percentages to demonstrate the feasibility of recruitment, adherence, and retention, treatment effects over time, and proof of concept. Our statistical approach for a full trial of these hypotheses will be Generalized Linear Mixed Models (GLMM) with an identity link function for a continuous outcome or a logit link function for a binary outcome. Conceptually, GLMM is a more advanced version of repeated measures ANOVA that can account for potential correlation among multiple measurements over time while having flexibility in fitting outcomes with different distributions (such as normal, binomial or Poisson, etc.). One advantage of this approach over repeated measures ANOVA is that there is no assumption that participants are measured at every, or even the same, time points. Therefore, these models are very flexible at handling missing data. Participants who have a missing observation are not excluded, thus, this produces the intention to treat (ITT) full information maximum likelihood (FIML) model. Conducting these models on pilot data help with sample size calculations for a future R01 submission.

13.0 Regulatory Requirements

13.1 Informed Consent

Participants are community dwelling adults without dementia, but with concern or that have family members with dementia. We have established strong relationship with key stakeholders. Participants will be recruited through a flyer with information about the study posted on organization's website and by word of mouth. We have developed a media recruitment script that will be used as the script for a video presentation that will be posted on a website, TV add, Facebook, and read as a radio add. We will send a notice via the CCTS research match and the TNN Match service using the form titled "research match".

- Participants that contact the study team will be sent the consent form and given as much time as they feel necessary to decide if they would like to participate. Each interested subject will be mailed a copy of the consent form 1 week prior to scheduling the initial consent phone visit. This will be done to allow potential subjects sufficient time to consider participation. Participants will be encouraged to ask any questions at any time throughout the course of the study. Research personnel will be available to answer these questions. Subjects will be informed that participating in this research is voluntary. Subjects will be informed that they may withdraw from the research at any

time without penalty. Patient providers are not part of the study team. Informed consent will be obtained using procedures and documents understandable to the subject. Individuals who are unable to give informed consent will be excluded from participation in this research. All study personnel will have received the required UIC CITI and HIPAA training prior to initiation of the study. The PI (Ulf Bronas), and the study manager will obtain consent. Informed consent documents will be kept in a locked file cabinet in a locked office separate from other study documents. Only the PI (Ulf Bronas) will have access to these files.

- During the e-consent process, the study will be thoroughly explained and all questions will be answered. Comprehension of all study procedures will be ascertained by non-leading open-ended questions. If participants express an understanding of the study and study procedures and would like to participate in the study, informed e-consent will be obtained. Participants will be able to continue to refer the information or contact the investigator if they have questions.

13.2 Subject Confidentiality

- Precautions to protect subject privacy will be taken throughout the course of the study. All telephone conversations with potential subjects will be conducted in a private setting. No face to face conversations will take place. Strict procedures will be put in place to minimize the risk of breach of confidentiality. All subjects will be assigned a study code. The master list of the subject's name and the linked code will be kept by the study manager in a locked file cabinet in a locked office. All information provided by subjects will kept strictly confidential and will not be reported on an individual basis. None of the information provided by subjects will become part of the medical record. Hard copy data will be stored in a locked office, and electronic data will be stored on a password-protected computer. Hard copy and electronic data will be coded, with the master list kept separately in a secure file in the principal investigator's office. Subjects who refuse to agree to the HIPAA authorization and consent form will not be able to participate in this study. Study data will be coded in numerical order (e.g. PAIS001, PAIS002 etc.). The link to the code will be maintained by the project manager and will be kept in a locked file cabinet in a locked office separate from study data. An electronic copy of the masterfile will be kept in a folder, separate from the data and study forms, on a UIC secured drive. The project manager and PIs will have access to the code. The link to identifiers will be destroyed after 6 years. The study statistician will have access to the de-identified database for analysis purposes.
- Internet-based application/package –Specify: iCardia: Remote collection of Fitbit data and delivery of text-messages will be done via iCardia, a secure, password-protected, internet-based application that has been developed at UIC and is currently hosted in a HIPAA-compliant server at the ACCC Secure Research Environment. Text-messages will be programmed in the iCardia system by the RAs and the PI, based on each person's responses to the interview at baseline and will be sent to study participants based on their preferences captured at baseline. Participants will be able to change their preferred days/hours by responding to the text-messages sent. Participants who no longer wish to receive reminders or text-messages may reply with "STOP." iCardia automatically will stop sending messages if this is received; thus, messages will be immediately discontinued without requiring contact with research

team. iCardia is password protected and will only be accessed by the PI and key research personnel at UIC through an encrypted, Secure Sockets Layer/VPN connection. iCardia will be used in this study for two purposes: (1) to send motivational text-messages about breaking up sedentary time to study participants in the intervention group; and (2) to remotely collect Fitbit data pertaining to participants' physical activity (steps, minutes of activity, intensity of activity, sedentary minutes, etc.). Storing and exportation of Fitbit data from iCardia is done using Subject ID codes only. Text-messages send from iCardia will not contain patient health information or any other sensitive data.

- Ilumivu EMA app for recording of behavior options: All data collected from the mobile app are encrypted before being pushed to the cloud-based storage database. No data are ever stored on the server's file server but always in the database. Access to the database is gated so entry is only permitted to users entering through the approved route (i.e. you can't hack your way into the database by guessing at the URL). Ilumivu's main servers are located in the USA. Data are made accessible to the researchers only by directly accessing the secure site with their verified login credentials and downloading the dataset as a CSV file. Datasets will never be transmitted by email. The mEMA platform does not require any Personally Identifying Information (PII) from participants. The mEMA platform automatically generates a unique identifying code that you give to the user to enter into their mobile app. They key linking this code to any PII is stored outside the mEMA system by the investigators. All the PII data is encrypted and stored in a database separate from the data entered into assessments by your respondent. When the research team downloads the aggregated dataset it will contain no PII. When respondents are completing assessments via the mobile apps then they will never be able to access the web-platform. Designated portions of an ilumivu-based site may only be accessed after supplying a verified user ID and password. Data can be stored either in an encrypted manner or in clear-text. All data are encrypted in transmission
- PI will share data through sharing requests and also work with the Program Officer to identify relevant NIH-recommended data repositories for the pilot data. PI will make the data available for sharing by the time of the online publication of the pilot's main findings. All data will be properly de-identified before sharing.

13.3 Unanticipated Problems

- All study-related, serious, unanticipated adverse events will be reported to the IRB within 48 hours of discovery. Other unanticipated events will be reported to the IRB at the time of continuing review. We will comply with university policies and procedures regarding any unforeseen identifiable data loss.

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Appendices

Eligibility Checklist

Demographic

Face sheet

Charlson Comorbidities

Medical history questionnaire

Telephone script

Interview guide

Participant satisfaction survey