STUDY PROTOCOL COVER PAGE

STUDY TITLE:
In-home cycling for individuals with Parkinson disease

NCT IDENTIFICATION NUMBER:
NCT04300023

DATE OF DOCUMENT:
January 24, 2019

Layperson summary

This study is part of a larger multipart study. In the current phase, we will examine the effects of social engagement during in-home exercise on a small sample of individuals with Parkinson Disease (PD). This pilot investigation will directly measure the effect of social support and engagement on exercise outcomes for rural dwelling individuals with PD.

Research Project Protocol

Running Title:
In-home cycling for individuals with Parkinson disease

Full Title:
Examining the reach, effectiveness and maintenance of social engagement on exercise outcomes: in-home cycling for individuals with Parkinson disease

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Protocol Version:
01/24/2019

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Funding Sponsor:
Wisconsin Alumni Research Foundation (WARF) – Fall Competition
Pickett PI

Institute for Clinical and Translational Research - KL2 Award
Pickett PI

Project Summary

The benefits of exercise for individuals with Parkinson disease (PD) have been well documented; however, individuals with PD living in rural and underserved urban settings are largely unable or unwilling to participate in group exercise programs due in large part to their distance from such programs and financial considerations. Additionally, community based programs which provide social support and engagement have been shown to benefit elderly individuals as well as individuals with pathology, but are equally unattainable to this group. Taking the exercise to these individuals via telemedicine or tele-exercise may be an ideal means of delivering this type of intervention.

The long-term goal of this project is to improve outcomes for underserved populations of individuals with Parkinson disease (PD) by providing access to in-home physical activity via a telehealth approach. Approximately one million Americans currently live with a diagnosis of PD and it has been estimated that delaying the progression by 20% would result in a $75,891 savings per individual based on reduced health care costs, income maintenance, increased duration of life and improved quality of life. However, individuals with PD of lower socioeconomic status, people of color and rural dwelling seniors have been critically underserved by clinical and academic programming resulting in poorer health outcomes.

These two studies will examine: 1) the Reach, Effectiveness, Implementation and Maintenance and 2) the optimal delivery method for an in-home exercise intervention program for individuals with PD living in underserved communities. We will deliver a managed and meaningful exercise intervention that not only addresses the benefits of physical activity for individuals with PD, but also offers a social connection to research staff outside of the participant's typical caregiver(s).

Study 1

Examine the reach, effectiveness and maintenance of an in-home, partnered cycling program for underserved individuals with PD.

Study 2

Examine the effects of social engagement during in-home exercise on a small sample of individuals with Parkinson Disease (PD). This pilot investigation will directly measure the effect of social support and engagement for rural dwelling individuals with PD.

Background and Significance

It has been estimated that delaying the progression of PD by 20% would result in a life time savings of $75,891 per individual based on lost income, health care costs, duration of life and quality of life (Johnson, Diener, Kaltenboeck, Birnbaum, & Siderowf, 2013). With approximately one million Americans currently living with a diagnosis of PD (de Lau & Breteler, 2006), the possible savings generated by quality interventions is remarkable. The currently accepted mechanisms for treatment of PD related symptoms include pharmacological, surgical and exercise related interventions; however, a large percentage of individuals have limited access to care (Dorsey & Willis, 2013). In many cases the limitations to receiving proper care are due to limited physical mobility, loss of driving ability, and distance from or access to a suitable healthcare provider (van der Marck et al., 2013). These limitations are particularly devastating for underserved individuals in lower socioeconomic status populations (SES) who may be fully unaware of current options for treatment and without access to programming that meets their needs. For example, individuals with PD in communities of color have far less access to and knowledge of activity-based intervention options.

In addition to postural instability, resting tremor, bradykinesia and rigidity (the four cardinal symptoms of PD), individuals with PD frequently report depression (Zesiewicz, Gold, Chari, & Hauser, 1999), cognitive impairment and dementia (Hely, Reid, Adena, Halliday, & Morris, 2008), and sleep disorders (Kumar, Bhatia, & Behari, 2002), among a host of other signs and symptoms. In the past ten years increasing evidence indicates that exercise, when well coupled with pharmacological approaches, may offer significant improvement in a number of areas affected by PD including: gait-related measures such as walking speed, stride length, balance and mobility (Alberts, Linder, Penko, Lowe, & Phillips, 2011; Earhart & Falvo, 2013; Hackney & Earhart, 2010; Herman, Giladi, & Hausdorff, 2009; Mehrholz et al., 2010), quality of life (Li et al., 2014; Nocera, Amano, Vallabhajosula, & Hass, 2013), depression (Boulgarides, Barakatt, & Coleman-Salgado, 2014; Sharma, Robbins, Wagner, & Colgrove, 2015) and sleep (Frazzitta et al., 2015; Wassom, Lyons, Pahwa, & Liu, 2015), just to name a few. Immediate improvements related to treadmill walking have been reported with only a single session (Frenkel-Toledo et al., 2005). Similarly, an anecdotal report of two days of tandem cycling reported symptom and handwriting improvements in a single individual with PD (Alberts et al., 2011). Numerous long term studies have shown improvements in gait-related measures with some research indicating that the benefits may be sustained for as long as five weeks after training (Herman, Giladi, Gruendlinger, & Hausdorff, 2007). What has not been explored well in the literature is the impact of these interventions on functional measures such as activities of daily living (ADLs). Additionally, while numerous effectiveness studies have been conducted on a myriad of interventions for individuals with PD, very few of these interventions have been progressed through a dissemination and implementation model to make them accessible and impactful to individuals living with PD and their care teams.

Focusing beyond the benefits of general exercise, a growing body of literature in both animal models (Poulton & Muir, 2005; Tillerson, Caudle, Reveron, & Miller, 2003) and humans (Alberts et al., 2011; Ridgel, Vitek, & Alberts, 2009) has demonstrated improvement of PD motor symptoms following “forced exercise” programs. In this context, forced exercise (FE) is defined as exercising at a rate greater than the individual’s preferred voluntary rate. Following eight weeks of either FE or voluntary rate exercise, individuals with PD who exercised in a FE group showed improvement in clinical ratings of their PD symptoms, biomechanical measures of dexterity and aerobic fitness. In contrast, individuals who exercised at their voluntary exertion level showed improvement in aerobic fitness only (Ridgel et al., 2009). An obvious challenge in the implementation of a FE model is how to progressively increase the intensity of the exercise while maintaining adherence**.**

Evidence indicates that group based exercise programs are more beneficial for a number of factors including program adherence and enjoyment (Shanahan et al., 2017; Zhou, Grady, & Chen, 2017). Although difficult to tease apart, the benefit of these social programs is thought to be in the person-to-person interactions that occur around the activity. This introduces a feasibly and scalability limitation to remotely delivered, in-home exercise interventions as it is not feasible to travel to the homes of more than a few individuals each day. One way to address this limitation is through person-to-person internet-based communication programs such as Skype© and FaceTime©. These tools allow the participants to communicate hands free while also allowing the clinician or researcher to visually monitor the participant. Face-to-face interactions with the participants allow for a member of the research team to monitor and provide feedback about exercise intensity. The social aspect of the experience is also enhanced when both parties can see each other. The difficulty in delivery of such an intervention is two-fold. First, how to use an internet-based communication tool with individuals who

may not have access to the necessary high-speed internet options; and second the scalability of one-on-one interactions with each participant. Additionally, it is unknown at this time if the face-to-face interaction is beneficial to the individual with PD.

Also missing from this literature is delivery of activity-focused interventions of any kind to individuals with PD in low SES communities. An unpublished zip code based demographic analysis of the 114 participants in a recently completed NIH R01 funded study on effective exercise approaches for individuals with PD found participants in the study resided in communities with only 31.3% of the households earned less than $25,000 per year and 26.2% of the population earned more than $100,000 per year. These percentages are vastly different that the 39.6% of the MO population that earns less than $25,000 and 13.3% that earns over $100,000. For individuals in lower SES communities, access to exercise programs is lacking.

The two studies described here seek to address the above highlighted problems in intervention implementation for individuals with PD in underserved communities. We will examine the effectiveness, feasibility, and ideal methodological approach for delivery of an in-home exercise program. This intervention will allow the individuals enrolled to participate in regular exercise and a community activity that promotes social support and engagement. Additionally, we will compare a solo versus partnered protocol to examine the possible benefits of partnered, socially supported exercise.

Specific Aims

Study 1

SPECIFIC AIM 1: Examine the reach and maintenance of an in-home cycling program for underserved individuals with PD. Reach will be assessed by examining the demographic characteristics of the individuals enrolled and through the administration of a questionnaire on objective and subjective socioeconomic status to better understand their level of accessibility to services, perceived barriers and economic status. We will also explore the implementation of a health coach to promote effective maintenance of the program after the 6-month intervention. Finally, we will conduct two interviews to better understand strengths and weakness of the program and to better address the needs of the participants in future studies.

Hypothesis 1a: Demographic characteristics including race and socioeconomic status of the enrolled participants will not statistically differ from the characteristics of the state of WI.
Hypothesis 1b: Feedback from participant interviews will inform future delivery of the in-home cycling program.

SPECIFIC AIM 2: Determine the effectiveness of a 6-month in-home, progressive, tele-exercise cycling program and 3-month health coach follow-up for underserved populations of individuals with PD.

Hypothesis 2a: Participants will improve performance of activities of daily living from baseline to posttest. These effects will be maintained at 3-month follow-up.

Hypothesis 2b: Participants will significantly improve measures of gait and balance performance and non-significantly improve fall rate from baseline to posttest. These effects will be maintained at 3-month follow-up in the group piloting implementation of a health coach, but not in solo follow-up group. Falls data will allow for effect size calculations for future applications.

Hypothesis 2c: Activity level as measured by an activity monitor will increase from baseline to posttest. This effect will be maintained at 3-month follow-up in health coach group, but not in the solo group.

Study 2

SPECIFIC AIM 1: Determine whether incorporation of social interaction during physical activity significantly improves task adherence and increases task stamina as compared to solo cycling.

Hypothesis 1a: Those individuals participating in socially engaged cycling will complete a significantly greater number of cycling sessions than individuals in the solo cycling group.

Hypothesis 1b: Individuals in the social cycling group will cycle for longer durations at each session than solo cyclists, despite the long term goal being 30 minutes per session for both groups.

SPECIFIC AIM 2: Determine whether incorporation of social interaction during physical activity significantly improves activities of daily living, fall rate and quantity of movement for individuals with PD. The primary variables for this aim are Performance Assessment of Self-care Skills Assessment scores, gait velocity and step count.

Hypothesis 2a: Socially engaged exercise will result in significantly greater improvement in measures of instrumented activities of daily living (IADL; as measured by the Performance Assessment of Self-care Skills (PASS) assessment) as compared to solo cycling.

Hypothesis 2b: Fall rate will be non-significantly improved with socially engaged cycling but not with solo cycling. Weekly calls will be placed to both groups to record fall rate. Falls data will allow for effect size calculations for future applications.

Hypothesis 2c: Overall activity level, as measured by an activity monitor, will increase with socially engaged cycling but not with solo cycling.

Study Duration: This study will be conducted over the next 4 years including all data analysis, manuscript and grant proposal submissions.

Research Design

This pilot study will utilize two separate experimental designs to address: 1) the Reach, Effectiveness, Implementation and Maintenance and 2) the optimal delivery method for an in-home exercise intervention program for individuals with PD living in underserved communities. Both studies will utilize paired, randomly assigned groups to explore the given questions. Pairs will be based on disease severity (UPDRS III scores) and age.

Study 1: The proposed pilot study will utilize the RE-AIM framework (Reach, Effectiveness, Adoption, Implementation and Maintenance) to focus on the reach and effectiveness of a 6-month triweekly in-home cycling program and then pilot a health coach model to promote maintenance for the subsequent 3-month period. 40 qualified individuals will be paired based on disease severity (score on subsection III of the UPDRS) and age and randomly assigned to either the cycling group or the normal care control group for 6 months. For those in the cycling group, participants will interact via Skype with study team members during all cycling sessions. This intervention will allow the individuals enrolled to participate in regular exercise and a community activity that promotes social support and engagement. The proposed pilot maintenance model for the 3-month period following the intervention will implement a health coach model with scheduled sessions every other week to discuss goals and motivation while decreasing the total contact time with the participant. Individuals in the normal care control group will crossover and complete the cycling intervention following the initial 6 months.

Study 2: 12 people with PD, living in rural settings or with barriers to travel and who have reported that proximity to community-based exercise is a primary barrier to enrollment will be enrolled in the study. Qualified individuals will be paired based on disease severity (score on subsection III of the UPDRS) and age and randomly assigned to either the social cycling group or solo cycling group for 6 months. Both groups will have an exercise bike delivered to their home, custom fit to their needs and installed in a safe location. Sessions will consist of up to 30 minutes of cycling. Those in the social group will cycling while engaged in social interaction with a research staff member, thus providing a social/community aspect that would not otherwise be present. Those in the solo group will have a target duration and intensity but will exercise without a partner.

For both studies

Participants:

Inclusion and exclusion criteria is identical for both studies.

Inclusion criteria for all enrolled participants include:

1) 45 years of age or older
2) diagnosis of idiopathic “definite PD” (Racette, Rundle, Parsian, & Perlmutter, 1999) based upon established criteria (Calne, Snow, & Lee, 1992; Hughes, Daniel, Kilford, & Lees, 1992)
3) vision at or corrected to 20/40 or better
4) ability to independently ambulate for at least 10 minutes continuously
5) no reported vestibular or neurological disease (stroke or muscle disease) beyond their diagnosed PD
6) score of greater than or equal to 78 (no evidence of dementia) on the telephone adaptation of the modified mini-mental state exam (Norton et al, 1999) .
7) English Speaking

Exclusion criteria for all enrolled participants include:

1) contraindication for exercise
2) history of muscular or orthopedic diagnosis

3) inability to participate in the full duration of the study.
4) currently exercising for 20 or more minutes per week.

Participant Identification and Study Recruitment: To recruit prospective participants to this study, we will utilize flyers, email, website and Facebook postings, presentations at support group meetings and special events, as well as word of mouth.

Flyers will only be posted after gaining permission at the site in question. To this end, we will contact other research colleagues at the University of Wisconsin, who are also working with elderly individuals and individuals with Parkinson disease (PD), including the Speech & Language Disorders Clinic of the Communication Sciences & Disorders Department and the UW Hospital Movement Disorders Clinic. Additionally, we will work with surrounding rural community hospitals asking them to post and handout the materials for their patients and patients' caregivers. We will also request permission through the UW Health Sports Medicine Fitness Center (UWHSMFC) in Madison, WI to disseminate the flyer to their Parkinson disease fitness classes, Falls Free Living class and similar programs targeted for elderly individuals and those with PD. We will also approach individuals at locations throughout the state where PD support classes and programing for elders is currently taking place. We will also work with the Wisconsin Chapter of the American Parkinson Disease Association, the Wisconsin Institute for Healthy Aging (WIHA), the Community Academic-Aging Research Network (CAARN), the Collaborative Center for Health Equity, and the Aging and Disability Research Centers (ADRC) of Milwaukee and Southwest WI to post notifications on their website and social networking accounts, as well as make presentations at local chapter support groups, events, and fundraisers. Finally, we will utilize the Sensory Motor Integration Laboratory's website and Facebook account to disseminate electronic information about the study.

Privacy and Confidentiality: One potential risk of participating in this study is that confidential information about the participants may be accidentally disclosed. If a participant's current diagnosis of PD is not known to others, the potential to cause damage to their psychological well-being as well as to their reputation exists.

To decrease this risk, data will be stored in a double secured location. In a locked filing cabinet (paper data) or on a secure network server.

All data collection sessions will occur in the private setting of the Sensory Motor Integration Lab. While multiple participants may be in the lab for data collections simultaneously, the lab is divided into three separate data collection areas which allows each participant to have maximum privacy.

All data will be coded at the time of data collection. All participants will be assigned an identification number prior to data collection and all documents and files will be named using this ID. All data will be stored on computers which will be kept in the SMIL during data collection and transferred to the School of Education's secure server either via an Ethernet connection or through UW Box. All data analysis will be performed on computers in the SMIL or in the faculty office of the PI. A password is necessary for access to the computers and they all are equipped with automatic log off. Data being moved from one location to another will be moved via UW Box or the School of Education's secure network. Access to these computers are limited to SMIL staff, therefore identification of any subjects or data is unlikely. Coded data will be kept indefinitely.

Monitoring Software: Activity tracker and Ride Social accounts will be established with dummy identifiers (SMIL1, SMIL2). The only link that will exist between the individual's identifiers and the accounts will be on the participant code document. Data will be downloaded from the web accounts weekly and logged in the participants data file. The only concern that currently exists is if the individual attempts to reset or create their own account for either tool and discloses their personal information. Individuals will be instructed at the beginning of the study that an account has been made for them and they should not attempt to make a new account.

Video Data: All video data will be stored on the School of Education server in a directory designated to the SMIL lab. Only specified lab personnel have access to the network server directory. The server is maintained by the School of Education and is backed-up nightly. Dartfish video analysis software will be used to obscure facial features of participants.

Contact information: Each participant will have a sealed folder which contains their emergency contact information including instructions for the local 911 operator and contact information for an identified contact person. The sealed folders marked with the participant names will be kept locked in the PI's research office. These folders are to be unsealed only in the case of an emergency. All folders and their contents will be destroyed once the individual completes the three-month follow-up or if they withdraw from the study.

Data Sharing: Dr. Pickett will be responsible for deciding when/to whom to disseminate coded data, and will work with other researchers if necessary to confirm that they have proper IRB approval/etc., as necessary. Required UW-Madison IRB approval would be obtained prior to the release of any data.

Substudies: Two separate studies will occur as part of the larger experiment.
Study 1
Examine the reach, effectiveness and maintenance of an in-home, partnered cycling program for underserved individuals with PD.

Study 2
Examine the effects of social engagement during in-home exercise on a small sample of individuals with Parkinson Disease (PD). This pilot investigation will directly measure the effect of social support and engagement for rural dwelling individuals with PD.

Screening for eligibility
The screening mechanism is the same for both substudies.

Interested individuals will initiate contact with the study team either via the listed phone numbers, emails or by completing the on-line survey requesting more information and granting permission to contact. Interested individuals will be contacted by a member of the research team to describe the study, confirm his/her interest in the study, perform a phone screening, and, if appropriate, schedule evaluation appointments. In the event that the prospective participant cannot be reached or does not return the contact, the research team member will initiate no more than three follow-up attempts. The phone screen assess inclusion and exclusion criteria including the Telephone Adaptation of the Modified Mini-Mental State Exam (Norton et al., 1999).

Enrollment
The enrollment mechanism is the same for both substudies.

Once a person has indicated a desire to participate, we will: 1) work with them to schedule a study visit; 2) enter their name and contact information onto the participant database; and 3) mail a packet of materials. The packet will include an informational cover letter summarizing the program, details on the evaluation appointment (date, time, location, parking instructions, etc.), and instructions for participants to complete the appropriate forms (medical history and current medication list, Patient Questionnaire portion of the UPDRS and the Pittsburgh Sleep Quality Index) and bring the forms to their evaluation appointment. Participants will receive a reminder phone call two days prior to the scheduled study visit. During this call a member of the research team will discuss the informed consent process and any additional questions the person may have about study participation.

Baseline
The baseline assessment is the same for both substudies.

All participants will complete approximately three hours of testing at each testing time point. All testing will occur in the on medication state. Testing will consist of biomechanical, non-motor features and disease severity data from each individual. The following are the specific assessment components for each time point:

Baseline assessment (or Pre-test for those assigned to the normal care control group)

A. Intake and review of forms
    a. Review Screening measures (completed prior to arrival)
    b. Consent form
    c. Demographic data
    d. Review medical history (completed prior to arrival)
B. General Questionnaires
    a. Review current medication list (completed prior to arrival)
    b. Physical Activity Scale for the Elderly (Washburn et al., 1993)
    c. Fall history questions
    d. Activity Specific Balance Confidence Index (Powell & Myers 1995).
    e. The MacArthur Scale of Subjective Social Status (Adler, Epel, Castellazzo, & Ickovics, 2000)
C. Clinical measures
    a. Review Patient Questionnaire section of the UPDRS (completed prior to arrival)
    b. Movement Disorder Society Unified Parkinson Disease Rating Scale (MDS-UPDRS) (Goetz et al., 2008)
    c. New Freezing of Gait Questionnaire (Nieuwboer et al., 2009)
    d. PASS iADL assessment (Chisholm, Toto, Raina, Holm, & Rogers, 2014)
    e. Canadian Occupational Performance Measure (Law et al, 1998)
D. Measures of motor function
    a. Timed Up and Go test (Posiadlo & Richardson, 1991)
    b. Four square step test (Dite & Temple, 2002)
    c. Mini-Balance Evaluation Systems Test (mini-BESTest) (Franchignoni, F., et al, 2010)
    d. Standardized gait analysis – computerized mat (Pilgram, Earhart, & Pickett, 2016)
    e. Gait Analysis – free locomotion.
E. Measures of non-motor function
    a. Review the Pittsburgh Sleep Quality Index (completed prior to arrival) (Buysse, 1989)
    b. Beck Depression Inventory-II (Beck et al, 1996)
    c. UCLA Loneliness Scale V3 (Russell 1996)
    d. Perceived Isolation Scale (Chisholm et at, 2014)

All selected assessment tools are valid and reliable and have been previously used to assess individuals over the age of 65 years and/or individuals with PD.

General Questionnaires:

Demographic, medical history, PD history and current medication data will be collected from each individual. The demographic form will be sent to the individual's home with the welcome letter and the participant will be asked to complete the form and bring it with them to their visit. This information is necessary for the study as it allows for proper categorization of levadopa equivalent dosage levels which may impact symptom presentation and medical history information which may help to inform if the individual is healthy enough for exercise.

The Physical Activity Scale for the Elderly allows for quantification of current exercise and sedentary behaviors.

As falls are one of the primary variable of interest for the larger study, the Fall history questionnaire will provide data on falls in the previous 6 months as well as the most common mechanisms for falls. During the study falls will be logged weekly. Additionally, the Activity Specific Balance Confidence Index will provide data about how fearful individuals are about falling and how this level of confidence changes with various tasks that are common to everyday living.

The effect of socioeconomic status on exercise practices for individuals with PD in rural and metropolitan underserved communities is one of the primary aims of this study. The MacArthur Scale of Subjective Social Status will be used to assess how perceived status and income related to exercise practices.

Clinical measures:
The MDS-UPDRS is the gold standard in clinical rating of disease severity for individuals with PD. All individuals in study 1 will complete this assessment at all assessment points. The assessment will be administered by a trained investigator. Additionally, all UPDRS subsection III components will be recorded for blinded rating by a study team member blinded to the testing session.

New Freezing of Gait Questionnaire – is a valid and reliable tool for rating the presences of motor freezing during gait for individuals with PD. All individuals in study 1 will complete this assessment at all assessment points.

The Performance Assessment of Self-care Skills (PASS) assessment (Chisholm, Toto, Raina, Holm, & Rogers, 2014) will be administered to examine changes in performance of activities of daily living. The PASS consists of 26 activities of daily living and is designed to allow for a client-centered, performance-based means of objectively assessing occupation-based interventions. Additionally, this kitchen component of the PASS assessment will be performed in an instrumented environment (SMIL kitchen) to allow for quantification of kinetic and kinematic measures relative to the performance of these tasks.

The Canadian Occupational Performance Measure (COPM) will be administered to assess the participant's self-report of performance and satisfaction of self-selected occupational tasks.

Measures of motor function:
The Timed Up and Go test and Four Square Step Test are common clinical measures of motor function. Both tests have been used in elderly populations and individuals with PD to examine the effects of interventions and have been found to have a high degree of reliability and validly when used in the listed population groups.

The mini-BESTest will be used to assess balance. This 14-item, clinical battery is used to assess balance in four component areas (anticipatory transitions, postural response, sensory orientation and dynamic gait) and provides a single number summary of balance performance (maximum possible score = 30). This is relatively commonly used balance assessment battery. Mini-BESTest performance will also be video recorded for rating by a blinded rater.

Standardized gait analysis – Using the GaitRite® System, we will capture the temporal and spatial parameters of each participant during walking. The GaitRite® mat is a 14 foot portable electronic walkway, embedded with sensors to enable the measurement spatiotemporal variables of gait such as cadence, normalized velocity, stride length, base of support, and percent of cycle in double support. Participants will begin at a starting point two meters from the mat, then walk toward and step onto the mat to continue walking until they achieve the stop line located two meters off of the opposite side of the mat. Data will be collected for forward preferred speed, backward preferred speed, forward fast, tandem and dual task gait. Each participant will complete five trials for each condition.

Free locomotion gait analysis - Additional gait data will be collected during free locomotion, that is walking that is not constrained by a specific task or area. Participants will be asked to walk throughout the laboratory space and through nearby ground-floor hallways outside the laboratory, while wearing miniature wearable sensors to record their motion. These sensors are approximately 50mm square by 20mm thick. They are mounted with straps to the tops of the shoes, and optionally the ankles, thighs, waist, upper arms and lower arms. Sensors record time, acceleration, angular velocity, magnetic field, air pressure (altitude), and optionally relative distance. Sensors will be worn throughout the duration of each lab visit, to measure movements beyond the range of other instruments. Data obtained concurrently with the in-lab assessments listed above will be used to quantify foot motion with improved detail relative to the other instrumentation.

Measures of non-motor function:
Measures of sleepiness and depression will be collected as these are known confounds in both elderly individuals and individuals with PD. The two selected batteries, the Pittsburgh Sleep Quality Index and the Beck Depression Inventory-II are questionnaires that the participants will complete prior to the end of each session.

As depression can significantly impact performance on the outcome measures, influence the extent to which exercise benefits an individual and be improved via exercise, the Beck Depression Inventory will be administered to all individuals. As this tool or the health history form may identify depression or suicidality, a follow-up plan has been established to address both contingencies. The questions that address suicidality will be viewed by the PI within minutes of the completion of the survey tool. However, as little to no evidence exists to suggest that suicide are rates differ systematically from the general population, we will not have a clinical psychologist or psychiatrist on the research team.

Follow-up Plan (Suicidality): In the event that a participant is identified as being at imminent risk of harm (e.g., suicidal), the PI will immediately assign a study team member to call 911 while the PI remains with the individual. The participant will be notified by the PI that a confidentiality breach has occurred.

Follow-up Plan (clinically concerning depression): In the event that a participant scores at or above a 3 on the depression index question that specifically refers to suicide, the PI will notify the study participant of the potential concern and will make a recommendation for further clinical care. This notification will occur in a private area designated for confidential communication such as consent procedures. Only the PI and the participant will be present.

During all testing sessions:

1. **Rest breaks** – Participants will be frequently prompted and given rest breaks regularly and as needed.

2. **Adherence to medication schedules –** As medication management can significantly impact the safety of the individual as well as the outcomes of the data collection sessions, individuals will be instructed to maintain their medication schedules during testing procedures.

3. **Safety protocol during testing -** To minimize risks to participants during evaluation sessions, a spotter to assist in preventing falls will be present as needed and a gait belt can be donned as necessary. Testing staff will also be prepared to provide first aid for minor injuries and to contact emergency healthcare personnel in the event of a more serious injury. In the event of a more serious, life-threatening emergency, the emergency protocol described below will be implemented.

Study 1 Intervention

Qualifying participants will stratified by age and motor symptom severity as assessed by the UPDRS (UPDRS Motor score (+/- 4 points) and then randomly assigned to either the in-home cycling group or the waitlist control group.

For individual assigned to the control group, pre-testing will occur six-months before the baseline measures are collected (figure 1). This period will allow us to collect normal care control data from each participant prior to their six months in the active phase of the study. During this period, each individual will be contacted weekly by the study team to complete a falls questionnaire. Baseline testing will occur within two weeks of the start of the Intervention. Post-test data will be collected following the 6-month intervention and will occur within 1 week of the last calendar day of the intervention.

Participants will be asked to not begin any new exercise programs once enrolled in the study, but will not be asked to discontinue any current physical activity. Information about current physical activity level will be collected at all time points.

Activity monitors (Garmin VívoSmart 3) will be donned by all study participants throughout the duration of the study starting at the time of either pre-test or baseline assessment depending on group assignment and continuing through the 3-month follow-up. These devices allow for activity monitoring as well as online monitoring of heartrate. Participants will be asked to wear the activity monitors at all times once enrolled in the study. Number of steps taken daily and amount of aerobic activity will be used to compare changes in activity level.

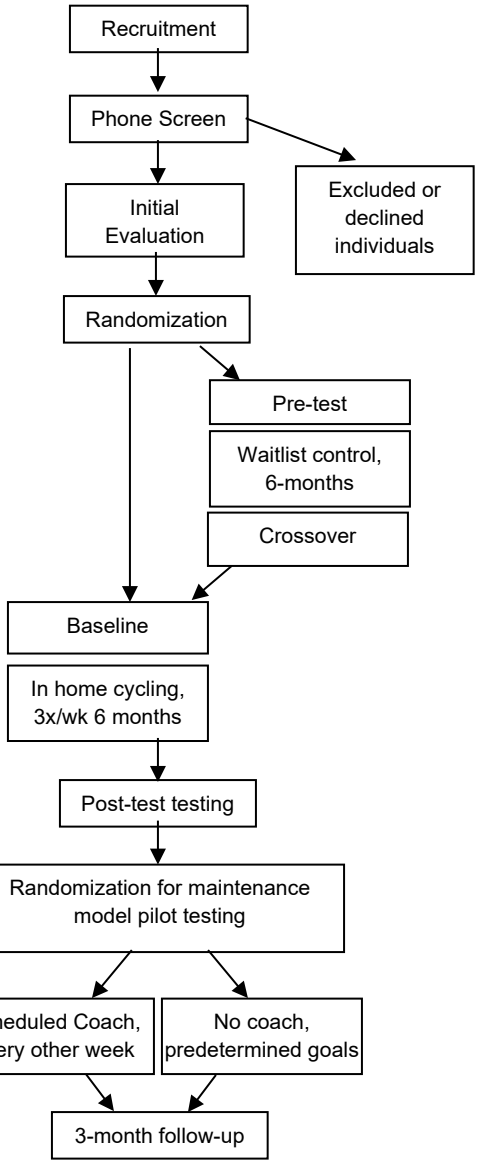

Figure 1. Movement of participants through the study.

Cycling -The initial cycling session will occur in the participant's home within 2-weeks of the baseline assessment. Two members of the testing team will be present. The team will set-up the bike and properly fit it to the individual rider. Additionally, the team will ensure the stationary bike is set-up in a safe and secure manner and in an area free of clutter and dangerous obstacles. Study team member will also set-up and establish a secure connection using the MiFi device at this time. Both groups will be provided with a MiFi wireless internet connection if needed to allow for data collection of cycling and activity monitor data.

A tablet will be installed and mounted to the recumbent bike. A remote connection will be made to an individual at the UW to test the Skype connection and show the participant how to use the technology. This testing will lessen the likelihood of study dropout due to frustration with the technology component. An additional failsafe has been built into the computer system which allows us to remotely control the software and assist the participant if necessary. For privacy, we will not be able to access the machine without the participant clicking the allow button on the screen.

The selected recumbent bike has been chosen based on a number of factors which make it safe, user friendly and allow for the tracking of the desired speed and duration data. The bike weighs over 100 pounds and has a wide footprint to prevent tipping as well as a low ground clearance step through to allow individuals with PD to get on and off the bike without falling. The saddle is a wide padded seat with a fully supportive backrest to promote comfort but also maximize rider safety. Pulse sensors are located on the display mount

and seat handles and pulse readings are incorporated into the software which allows for real-time tracking of the speed and resistance settings of the cycle. Additionally, this bike comes with a large digital display and preprogrammed cycling sessions that will allow a programmed and progressive exercise plan to be implemented after the 6-month group cycling program ends.

Scheduled training sessions will occur in the individual's home with digital display connecting the individual with PD to a member of the research team. Training sessions will occur three times per week for 6 months. Each training session will consist of up to 30 minutes of cycling at a target speed with a 2-minute warm-up session, and a 2-minute cool down at the end of the session. Actual intervention times will be based on the individual's endurance level and will increase over the sessions. The initial target speed will be at 110% of the average pace established by the individuals during the first testing session (10% above the self-selected velocity). Target velocities for future training sessions will be based upon the average of the previous week's training sessions. It will be the job of the research assistant to help the individual attain and maintain their target velocity during testing.

When beginning the cycling sessions, participants will have their maximum and target heart rate calculated. The calculation for target heartrate is 220 – participant age. Target heartrate will be calculated using a span of 50-85% of the calculated maximum (50 to 70% of maximum = moderate and 70 to 85% of maximum = vigorous exercise). Individuals will be provided with a printout of these calculations as well as the weekly exercise goals established by the Centers for Disease Control and Prevention and the American Heart Association (see Appendix I and II). Participants will not be instructed to cycle on the days without scheduled cycling sessions, but they will be informed of the CDC and American Heart Association recommendations and told that they are invited to use the bike outside of the scheduled sessions. All participants will be asked to complete a daily exercise log (Appendix III). Logbooks entries will be collected from all participants at four-week intervals and reviewed by the study team.

Participants will be provided with an information sheet to describe the cycling sessions, their target heart rate, perceived exertion and the exercise journal (appendix V, "In-Home Cycling Program – Partnered Cycling - ") and the one page "How much physical activity do you need" document from the American Heart Association. For those in the partnered cycling group, we will gradually increase the duration of the cycling sessions for the first 12 weeks while verbally coaching them to keep their heart rate between 50 and 70% of their calculated maximum. The sessions during the first week will last 5 minutes. As the individual exercises, it will take a greater speed to attain the desired heart rate. For the second twelve weeks, the research assistant will help the participants to monitor the average speed of the final session of the previous week and suggest an increase in the target speed to increase the individual's heart rate. The research assistant will also assist the individual in monitoring their heart rate to stay in the upper end of the target intensity range. The goal durations and intensities for each week are listed in table 1.

Week	Target Duration	Target Intensity
1	5 mins	50 – 70% of max heart rate
2	10 mins	50 – 70% of max heart rate
3	12 mins	50 – 70% of max heart rate
4	15 mins	50 – 70% of max heart rate
5	17 mins	50 – 70% of max heart rate
6	20 mins	50 – 70% of max heart rate
7	20 mins	50 – 70% of max heart rate
8	22 mins	50 – 70% of max heart rate
9	25 mins	50 – 70% of max heart rate
10	25 mins	60 – 70% of max heart rate
11	30 mins	50 – 70% of max heart rate
12	30 mins	60 – 70% of max heart rate
13	30 mins	60 – 70% of max heart rate
14	30 mins	60 – 70% of max heart rate
15	30 mins	60 – 70% of max heart rate
16	30 mins	60 – 70% of max heart rate
17	30 mins	60 – 70% of max heart rate
18	30 mins	60 – 70% of max heart rate

19	30 mins	60 – 70% of max heart rate
20	30 mins	60 – 70% of max heart rate
21	30 mins	60 – 70% of max heart rate
22	30 mins	60 – 70% of max heart rate
23	30 mins	60 – 70% of max heart rate
24	30 mins	60 – 70% of max heart rate

During the first testing session of each week a study team member will complete a falls assessment with each individual.

Normal Care Control - Individual assigned to the control group will be advised to continue their daily routines during the first 6-months. Following this period, they will complete a baseline assessment and crossover into the cycling group. This period will allow us to collect normal care control data from a randomly assigned, age and disease severity (+/-4 points) matched individual. During this period, each individual will be contacted weekly by the study team to complete a falls questionnaire.

Health Coach: Following completion of the 6-month in-home cycling program, participants will be asked to continue their training program following the same training regime. Half of the individuals in the study will have been randomly assigned within their strata to a health coach mediated maintenance program while the remaining individuals in the strata will be assigned to the self-motivated program. Individuals in the health coach group will be introduced to their assigned health coach during the final week of the 6-month intervention and a schedule of meeting times will be determined. Individuals will meet with their health coach once every other week for 15-minutes during their cycling sessions. Individuals in both groups will be taught how to access the built-in programming options on the bike which allow for use of customized training programs. We will set-up the training program for each individual and make sure that they are fully able access the module. During this period, each individual will continue to be contacted weekly by the study team to complete a falls questionnaire.

Improved Future Implementation

At the completion of the 6-month cycling intervention and again following the 3-month maintenance period, all participants will complete an interview with the study team during the last cycling session. This interview is designed to inform the research team about the effectiveness and delivery of the intervention from the participant's perspective. The questionnaire has been developed from the Center for Disease Control's Evaluation Framework. The following questions will be asked:

1. Why did you join this program? (posttest only)
2. As you became involved, did you discover other reasons for participating that you did not initially anticipate? (posttest only)
3. In what way(s) has the program met your expectations and/or needs?
4. In what way(s) has the program failed to meet your expectations and/or needs?
5. In your opinion, what are the most important outcomes or benefits that have resulted from your participation? (posttest only)
6. How would you rate the overall success of (the in-home cycling program or follow-up period) using a scale from one to ten, where one is a complete failure and ten is a total success? Why?
7. Are there other factors or circumstances that you think contributed to the success (or failure) of the program? Please explain.
8. Did you experience any challenges or barriers (e.g., competing priorities, organizational challenges, job role changes, technological challenges) that kept you from participating in the program at the level that you would have liked to participate?
    a. Were you able to participate in as many sessions as you wanted to participate in? If not, why?
9. Can you think of anything the team could do differently to address the challenges or barriers that might keep people from participating fully?

Posttest assessment
All measures listed in the Pre-test assessment protocol will be included at posttest except those measures listed under “Intake and review of forms” and “Screening measures”

3-month follow-up assessment
All measures listed in the Pre-test assessment protocol will be included at 3-month follow-up except those measures listed under “Intake and review of forms” and “Screening measures”

During all testing sessions:

1. **Rest breaks** – Participants will be frequently prompted and given rest breaks regularly and as needed.

2. **Adherence to medication schedules –** As medication management can significantly impact the safety of the individual as well as the outcomes of the data collection sessions, individuals will be instructed to maintain their medication schedules during testing procedures.

3. **Safety protocol during testing -** To minimize risks to participants during evaluation sessions, a spotter to assist in preventing falls will be present as needed and a gait belt can be donned as necessary. Testing staff will also be prepared to provide first aid for minor injuries and to contact emergency healthcare personnel in the event of a more serious injury. In the event of a more serious, life-threatening emergency, the emergency protocol described below will be implemented.

Study 2 Intervention

Qualifying participants will stratified by age and motor symptom severity as assessed by the UPDRS (UPDRS Motor score (+/- 4 points) and then randomly assigned to either the social or solo in-home cycling group.

The initial cycling session for both groups will occur in the participant's home with two members of the testing team. The team will set up the bike and properly fit it to the individual rider. Additionally, the team will ensure the stationary bike is safe, secure and in an area free of clutter and dangerous obstacles. Study team members will set-up and establish a secure connection using the MiFi device, if necessary, at this time. Both groups will be provided with a MiFi wireless internet connection if needed to allow for data collection of cycling and activity monitor data.

For those in the social cycling group, a tablet will be installed and mounted to the recumbent bike. A remote connection will be made to an individual at the UW to test the Skype connection and show the participant how to use the technology. This testing will lessen the likelihood of study dropout due to frustration with the technology component. An additional failsafe has been built into the computer system which allows us to remotely control the software and assist the participant if necessary. For privacy, we will not be able to access the machine without the participant clicking the allow button on the screen.

The selected recumbent bike has been chosen based on a number of factors which make it safe, user friendly and allow for the tracking of the desired speed and duration data. The bike weighs over 100 pounds and has a wide footprint to prevent tipping as well as a low ground clearance step through to allow individuals with PD to get on and off the bike without falling. The saddle is a wide padded seat with a fully supportive backrest to promote comfort but also maximize rider safety. Pulse sensors are located on the display mount and seat handles and pulse readings are incorporated into the software which allows for real-time tracking of the speed and resistance settings of the cycle. Additionally, this bike comes with a large digital display and preprogrammed cycling sessions that will allow a programmed and progressive exercise plan to be implemented after the 6-month group cycling program ends.

Scheduled training sessions will occur in the individual's home with digital display connecting the individual with PD to a member of the research team. Training sessions will occur three times per week for 6 months. Each training session will consist of up to 30 minutes of cycling at a target speed with a 2-minute warm-up session, and a 2-minute cool down at the end of the session. Actual intervention times will be based on the individual's endurance level and will increase over the sessions.

When beginning the cycling sessions, participants will have their maximum and target heartrate calculated. The calculation for target heartrate is 220 – participant age. Target heartrate will be calculated using a span of 50-85% of the calculated maximum (50 to 70% of maximum = moderate and 70 to 85% of maximum = vigorous exercise). Individuals will be provided with a printout of these calculations as well as the weekly exercise goals established by the Centers for Disease Control and Prevention and the American Heart Association (see Appendix I and II). Participants will not be instructed to cycle on the days without scheduled cycling sessions, but they will be informed of the CDC and American Heart Association recommendations and told that they are invited to use the bike outside of the scheduled sessions. All participants will be asked to complete a daily exercise log (Appendix III). Logbooks entries will be collected from all participants at four-week intervals and reviewed by the study team. During the first testing session of each week a study team member will complete a falls assessment with each individual.

Participants will be provided with an information sheet to describe the cycling sessions, their target heart rate, perceived exertion and the exercise journal (appendix V, "In-Home Cycling Program – Partnered Cycling - ") and the one page "How much physical activity do you need" document from the American Heart Association. For those in the partnered cycling group, we will gradually increase the duration of the cycling sessions for the first 12 weeks while verbally coaching them to keep their heart rate between 50 and 70% of their calculated maximum. The sessions during the first week will last 5 minutes. As the individual exercises, it will take a greater speed to attain the desired heart rate. For the second twelve weeks, the research assistant will help the participants to monitor the average speed of the final session of the previous week and suggest an increase in the target speed to increase the individual's heart rate. The research assistant will also assist the individual in monitoring their heart rate to stay in the upper end of the target intensity range. The goal durations and intensities for each week are listed in table 1.

Week	Target Duration	Target Intensity

1	5 mins	50 – 70% of max heart rate
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8	22 mins	50 – 70% of max heart rate
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11	30 mins	50 – 70% of max heart rate
12	30 mins	60 – 70% of max heart rate
13	30 mins	60 – 70% of max heart rate
14	30 mins	60 – 70% of max heart rate
15	30 mins	60 – 70% of max heart rate
16	30 mins	60 – 70% of max heart rate
17	30 mins	60 – 70% of max heart rate
18	30 mins	60 – 70% of max heart rate
19	30 mins	60 – 70% of max heart rate
20	30 mins	60 – 70% of max heart rate
21	30 mins	60 – 70% of max heart rate
22	30 mins	60 – 70% of max heart rate
23	30 mins	60 – 70% of max heart rate
24	30 mins	60 – 70% of max heart rate

For those assigned to the solo cycling group, three sessions will be scheduled during the first week of the program. A study team member will call the individual 10 minutes after the scheduled completion time during the first week to see if the individual needs any extra assistance with the bike or the journal. Each individual will be provided an information sheet to describe the cycling sessions, their target heart rate, perceived exertion and the exercise journal (appendix VI, “In-Home Cycling Program – Independent Cycling -”) and the one page “How much physical activity do you need” document from the American Heart Association. Sessions will be self-directed by the participant; however, a suggested progression is provided on page 4 of the “In-Home Cycling Program” document. All individuals in the solo group will be asked to complete the daily exercise journal. At the end of each week, a study team member will contact the individuals in the solo cycling group via a telephone call to ask about falls and provide the individual with their average speed of the final session of the previous week.

All participants will be asked to not begin any new exercise programs once enrolled in the study, but will not be asked to discontinue any current physical activity. Information about current physical activity level will be collected at all time points including the exercise journal.

Activity monitors (Garmin VívoSmart 3) will be donned by all study participants throughout the duration of the study starting at the time of either pre-test or baseline assessment depending on group assignment and continuing through the 3-month follow-up. These devices allow for activity monitoring as well as online monitoring of heartrate. Participants will be asked to wear the activity monitors at all times once enrolled in the study. Number of steps taken daily and amount of aerobic activity will be used to compare changes in activity level. During the exercise sessions, heartrate will be monitored via the heartrate monitor on the bike and the heartrate monitor on the activity monitors.

At the time of enrollment, all participants will have their maximum and target heartrate calculated. The calculation for target heartrate is 220 – participant age. Target heartrate will be calculated using a span of 50-85% of the calculated maximum (50 to 70% of maximum = moderate and 70 to 85% of maximum = vigorous exercise). Individuals will be provided with a printout of these calculations as well as the weekly exercise goals

established by the Centers for Disease Control and Prevention and the American Heart Association (see Appendix I and II).

Posttest assessment
All measures listed in the Pre-test assessment protocol will be included at posttest except those measures listed under “Intake and review of forms” and “Screening measures”

3-month follow-up assessment
All measures listed in the Pre-test assessment protocol will be included at 3-month follow-up except those measures listed under “Intake and review of forms” and “Screening measures”
During all testing sessions:

1. **Rest breaks** – Participants will be frequently prompted and given rest breaks regularly and as needed.

2. **Adherence to medication schedules –** As medication management can significantly impact the safety of the individual as well as the outcomes of the data collection sessions, individuals will be instructed to maintain their medication schedules during testing procedures.

3. **Safety protocol during testing -** To minimize risks to participants during evaluation sessions, a spotter to assist in preventing falls will be present as needed and a gait belt can be donned as necessary. Testing staff will also be prepared to provide first aid for minor injuries and to contact emergency healthcare personnel in the event of a more serious injury. In the event of a more serious, life-threatening emergency, the emergency protocol described below will be implemented.

Participant Renumeration
At the conclusion of the study, participants will be offered the option of keeping the bike and tablet or returning the bike and tablet and receiving $400. All participants will be allowed to keep the VívoSmart 3 they were given at the beginning of the study. If the individual was also asked to participate in the normal care control wait-list group they will be eligible for an additional $50.

The prorated payment schedule for those not in a wait-list group:
Baseline assessment only - $50
Baseline assessment plus 2 months –$100
Baseline assessment plus 4 month – $200
Baseline assessment plus 6 month – $300
Baseline, 6 months and posttest – Fitbit + $300
Baseline, 6 months exercise, posttest and 3-mo follow-up - $400 + VívoSmart 3 or
Bike, tablet and VívoSmart 3

The prorated payment schedule for wait-list group:
Initial assessment only - $50
Initial and baseline assessment - $100
Initial and baseline assessment plus 2 months - $150
Initial and baseline assessment plus 4 month - $250
Initial and baseline assessment plus 6 month - $350
Initial and baseline assessment, 6 months and posttest - VívoSmart 3 + $350
Initial and baseline assessment, 6 months exercise, posttest and 3-mo follow-up - $450 + VívoSmart 3 or
Bike, tablet and VívoSmart 3
+ $50.

Safety Monitoring Plan:

A detailed Data and Safety Monitoring Plan has been established following the guidelines of the UW-Madison ICTR Data Monitoring Committee. The DSMP is included as Appendix IV.

Steps to Minimize Risks during data collection

To minimize the risks to participants during the data collection sessions, the following risks have been identified and precautions will be taken.

a. Physical Risks: Fatigue is the most common or frequent physical risk as some of the participants may currently be relatively sedative. Additionally, there is a possibility of a fall and injury during the assessment.

    a. Steps to Physical Risks: Fatigue: frequent breaks are schedule in the protocol. Additionally, participants will be informed that they may request a break at any time.

    Falls: All participants will be closely spotted by trained study personnel during data collection sessions. Those individuals who are older or who have indicated a recent fall will asked to wear a gait belt.

Steps to Minimize Risks during Exercise, and the Safety/Emergency Protocols

To minimize the risks to participants during the exercise intervention, a number of measures and precautions will be taken. All participants will be asked during the phone screen if they have ever been told that they should not exercise or if they have any reason to believe that they should not exercise. Each individual will complete a medical and health history form covering musculoskeletal, cardiovascular, respiratory, and other health conditions and provide a thorough list of prescription medications. If any contraindications for exercise are reported, the individual will be instructed to review the exercise protocol with their physician prior to study enrollment and provide documentation asserting that the individual is cleared for exercise. Financial assistance for a necessary screening visit to a medical provider is available. Prior to beginning all legs of the study that involve the cycling intervention, all individuals will have their maximum and target heartrate calculated and will be provided with their individual results. This table will be posted on the bike so that it is visible at all times. During scheduled exercise sessions, a study team member will monitor the participant's heart rate and perceived exertion (Borg Rating of Perceived Exertion (RPE) (Borg, 1970); appendix II) for the duration of the session. Outside of these scheduled sessions and in the solo cycling group, participants can make use of the reference card to monitor their heartrate and RPE, both of which have target ranges which are highlighted in the information sheet (appendix V and VI). All participants will be asked to complete a daily exercise log (Appendix III). Logbooks entries will be collected from all participants at four week intervals and reviewed by the study team. Any indication of significant discomfort, exercise intolerance, a desire to stop or a medical emergency will result in termination of the session. All research staff will be familiarized with the main signs and symptoms of adverse events and will know to follow the emergency and non-emergency protocols described below.

B. Physical Risk: Common physical risks include muscle soreness, fatigue and shortness of breath. Less common physical risks include falls, heat intolerance, and skin irritation from the activity monitor. Rare but possible risks include cardio-vascular related events (sudden cardiac arrest, myocardial infarction, and stroke).
    a. Steps to decrease physical risks –To minimize the risks of muscle soreness, we will follow appropriate guidelines for exercise by including a warm-up prior to the start of each training period, and ending with a cool-down period. We will also recommend participants keep a towel nearby and we will encourage hydration, before, during, and after exercise.

    To minimize excessive fatigue and shortness of breath, the intensity of the cycling session will be gradually increased and based upon the participant's previous results and anecdotal reports of fatigue before, during, and after exercise. Additionally, we will use the Borg Rating of Perceived Exertion (RPE) (Borg, 1970) and the maximum and target heartrate formulas described above to monitor participants' exercise response as well as to help individuals monitor their target and

maximum heartrate values on their own throughout the sessions. Participants may terminate a session at any time.

To minimize skin irritation due to the wearing of the Garmin VivoSmart activity tracker, participants will be instructed to wear the monitor snuggly, but not too tight on their preferred wrist. Participants will be told to remove the device and place it in a pocket if it cannot be donned comfortably.

To minimize the risk of falls, we will utilize a customized recumbent bike, specifically fit to the individual rider, with a wider seat for more stability, handlebars on the seat, and a lower ground profile that allows participants easy entry and exit without necessitating a step over a central support. Two members of the research team will set-up the bike and properly fit it to the individual rider. Additionally, the team will ensure the stationary bike is set-up in a safe and secure manner and in an area free of clutter and dangerous obstacles.

For heat intolerance, we will encourage participants to exercise in either an air-conditioned room, or in front of a fan. And as previously mentioned, the Borg Scale and HRR will be used to monitor exertion, and target heart rate intensities. Participants may terminate a session at any time.

Given that the proposed intervention is an aerobic protocol, there is the risk for cardio-vascular related events (sudden cardiac arrest, myocardial infarction, and stroke). To minimize these risks, all participants will be asked if they have ever been told that they should not exercise or if they have any reason to believe that they should not exercise during the phone screen. Further, all participants will complete a medical and health history form covering musculoskeletal, cardiovascular, respiratory, and other health conditions and provide a thorough list of prescription medications. If any contraindications for exercise are reported, the individual will be instructed to review the exercise protocol with their physician prior to study enrollment and provide documentation asserting that the individual is cleared for exercise. Financial assistance for a necessary screening visit to a medical provider is available.

TAge-defined heart rate targets will be calculated and each individual in all groups will be informed of their target heart rate zones. To continuously monitor HR, each participant will don a Garmin VívoSmart 3 which provides beats per minute heartrate data and each bike includes a handlebar sensor for participants to grasp and receive a read-out of current HR. An informational sheet has been provided to instruct the participants about the use of heart rate zone calculations and perceived exertion levels (appendix V and VI). All individuals regardless of assigned group will be instructed to target a moderate exercise level. Moderate heart rate values are individual specific. Moderate RPE values are between 3 and 5. During monitored sessions, the research assistant will continuously monitor heart rate and will enquire about RPE at 5 minute intervals. These values will be compared to his/her target HR and RPE. **All participants will be informed that any sessions can/will be terminated by the researcher or participant at any time. The emergency protocol (detailed below) will be implemented if necessary.**

C. Psychosocial Risks: Loss of confidentiality – One potential risk of participating in this study is that confidential information about the participants may be accidentally disclosed. If a participant's current diagnosis of PD is not known to others, the potential to cause damage to their psychological well-being as well as to their reputation exists.

Frustration: Participants may become frustrated with the assessments as the complete battery may take up to 3 hours to complete.

Embarrassment: Individuals may be embarrassed if they are unable to perform a task or if they stumble of fall during the performance of a task.

Suicidality: The identification of suicidal thoughts is possible due to the depression questionnaire. In the case of identified suicide risk, the study team will immediately call 911. This will compromise the confidentiality of the participant and the participant will be notified of this breach of confidentiality.

a. Steps to Psychosocial Risks: *Confidentiality*: All possible care will be taken to maintain confidentiality. No subject will be identified in any report or publication. All data will be coded at the time of data collection. All participants will be assigned an identification number prior to data collection and all documents and files will be named using this ID. All data will be stored on computers which will be kept in the SMIL. All data analysis will be performed on computers in the SMIL or in the faculty office of the PI. A password is necessary for access to the computers and they all are equipped with automatic log off. Data being moved from one location to another will be moved via UW Box or the College of Education's secure network. Only members performing research have access to these computers, therefore identification of any subjects or data is unlikely. Coded data will be kept indefinitely.

Data will be stored/banked for future research projects in a double secured location. In a locked filing cabinet or a password protected computer within a locked room. Coded data will be stored on the School of Education servers indefinitely. It will be used for future research related to exercise studies in the lab. Data may be shared with researchers outside the UW. Dr. Pickett will be responsible for deciding when/to whom to disseminate coded data, and will work with other researchers if necessary to confirm that they have proper IRB approval/etc., as necessary. Required UW-Madison IRB approval would be obtained prior to the release of any data.

Contact information: Each participant will have a sealed folder which contains their emergency contact information including instructions for the local 911 operator and contact information for an identified contact person. During the scheduled sessions, the research team member will be given access to the participant folder for the duration of the session. The sealed folders marked with the participant names will be kept locked in the PI's research office. These folders are to be unsealed only in the case of an emergency. All folders and their contents will be destroyed once the individual completes the three-month follow-up or if they withdraw from the study.

Personal privacy during testing sessions will be maintained by testing in a private room and limiting the people within the research lab to current employees or students associated with the lab.

Frustration: To minimize the risk of frustration with the data collection sessions frequent breaks will be provided as will snacks and water during the testing sessions. Additionally, the testing sequence provides a variety of tasks to complete. If it appears that an individual is becoming frustrated with the given task, that task can be stopped or paused and a different task can be completed without disruption of the data collection session.

Embarrassment: The PI and her team all have experience working with individuals at an increased risk of falls. The study team will also talk with the individual to minimize the extent to which they feel embarrassed. We will minimize the likelihood of falling by using proper spotting techniques.

Depression: The risk associated with learning that you are depressed or suicidal based on the Beck Depression Inventory score is difficult to minimize. The study team will follow the developed protocol

Protocol in the Event of an Emergency During Data Collection Sessions in the UW – Natatorium
In the case of a medical emergency, a study team member will call 911, while a second team member stays with the participant. Standard lab operating procedure requires two individuals to be present in the lab during data collection sessions.

Protocol in the Event of an Emergency During Monitored Cycling Sessions – Call 911

a. Emergency preparedness – All research staff involved in the proposed intervention will be familiarized with the signs and symptoms of a medical emergency. As part of each participant's information folder, we will also have an emergency preparedness plan, which will include the following information:

   - The 10-digit telephone number to contact emergency services (the equivalent of 911) in the participant's local area
   - Special instructions to be given to emergency providers to access the individual in their home setting (i.e. gate codes or entrance locations).
   - Contact information for the participant's caregiver or emergency contact person

b. Emergency response – The researcher will call 911 immediately if a participant presents with signs of a medical emergency or is unable to verbally respond. We will also call 911 if the participant falls and hits his/her head with or without loss of consciousness, or is unable to get up or move limbs. Once 911 has been contacted, the researcher will continue to monitor the situation via the bike's digital interface, while simultaneously contacting the participant's emergency contact. When emergency responders arrive, the researcher will provide any known details of the event, along with any requested information as noted in the preparedness plan. This information can be conveyed via the Skype connection or to the 911 operator during the call.

Follow-up Protocol

a. Termination of session – In the event a participant ends the session early, or reports "not feeling right," "not feeling well", "feeling tired," or any comment that might cause concern, or the participant greatly exceeds their maximum heart rate for an extended period, the researcher will discontinue the session. If the participant's heart rate is within an acceptable exercise recovery range and they are not in distress, a follow-up call will be made to the individual 1 hour later. The participant's emergency contact will be called to advise him/her of the situation if the individual has not recovered by the 1 hour phone call.
b. Initiation of follow up phone calls (1 hr, 4-6 hrs, and 24 hrs) – The researcher will follow up with the participant and/or his/her emergency contact one hour after an exercise session in which the individual reports not feeling well and once again the following day (24-hour period). The emergency procedure noted above will be initiated if necessary.

Outside of monitored sessions, individuals are instructed to call 911, if they feel a medical emergency is occurring. For non-emergency medical situations, it is recommended that individuals consult their regular physician.

Power and Statistical Analysis

As this is a pilot study, we have not proposed a recruitment level that will properly power the outcome measures for a desired effect size. Previous work by Dr. Pickett during her post-doctoral training under the guidance of Dr. Gammon Earhart at Washington University in St. Louis indicate that approximately 27 individuals per group are needed to provide 89% power to detect differences in a similar intervention at a significance level of 0.05. This estimate uses gait velocity as the primary variable of interest and relies on a previous measured average forward gait velocity of 1.2 +/- 0.1m/s and an average backward gait velocity of 0.6+/- 0.1 m/s for 60 individuals with PD. The estimate is designed to detect a difference of 1 SD or 0.1 m/s, which is equivalent to an effect size of 0.4. Additionally, an attrition rate of approximately 15-20% should be expected. As the future RCT will likely focus on spatiotemporal measures collected during ADL task performance, this estimate provides some guidance for future work, but ideally future proposals will be powered from pilot data on the aims proposed herein. The proposed study of 40 individuals (20 per group) will provide pilot data which will be used to estimate effect size for the subsequent proposal (study 1).

To examine the reach of the project into the lower SES Parkinson disease community, we will analyze questions 6 and 7 of the MacArthur Scale of Subjective Social Status. A descriptive analysis of these data and subsequent comparison to income data for the state of WI will allow us to assess if individuals with PD in lower SES communities were optimally targeted.

To examine the qualitative effectiveness of the cycling intervention as well as the health coach intervention we will code the responses from the survey, assess common themes and use these data to inform the development of a larger RCT.

For both studies, we will employ a 2x2 repeated measures ANOVA with time and intervention as the factors, to determine the outcomes of the cycling intervention effectiveness aims. Additionally, we will use a time (posttest to 3-month follow-up) by group to examine the effectiveness of the health coach maintenance model. Variables of interest include: total number of completed sessions and session duration; PASS scores, walking velocity, stride length, base of support; gait variables (velocity, stride length, base of support and % of time in double support) and MiniBESTest scores as well as number of falls; and mean daily step count.

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Appendix I

Example of printout provided to participants to remind them of their maximim and target heart rate as well as their weekly exercise goals. The example is for an 80 yearold participant.

Maximum heartrate: **140 beats/minute**

Target heartrate: **moderate = 70 to 98 beats/min**
vigorous = 98 to 119 beats/min

Weekly goal: 150 minutes of moderate exercise
or
75 minutes of vigorous exercise

Overexerting Yourself
Beware of pushing yourself too hard too soon or too often. If you are short of breath, are in pain or cannot work out as long as you'd planned, your exercise intensity may be too high for your fitness level. Build intensity gradually.

Appendix II

Rating of Percieved Exertion (RPE) scale. This will be attached to the top visable surface of the bike display.

Rating	Description
0	Nothing At All
0.5	Very, Very Light
1	Very Light
2	Fairly Light
3	Moderate
4	Somewhat Hard
5	Hard
6	
7	Very Hard
8	
9	
10	Very, Very Hard (Maximal)

Appendix III

Exercise Log

Start Date:_____

Week:____1_____

	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
Did you bike today							
Minutes of cycling							
Estimated Average Speed							
RPE during activity							
RPE 5 minutes after							
Highest Heartrate							
Did you have any discomfort during the session?							

Did you do any additional physical activity this week?

Do you have any concerns about this weeks cycling sessions?

Did you fall this week? If yes, please describe the falls.

Appendix IV

DATA AND SAFETY MONITORING PLAN

Protocol Title: Examining the reach, effectiveness and maintenance of social engagement on exercise outcomes: in-home cycling for individuals with Parkinson disease

Principal Investigator: Kristen A. Pickett, PhD
IRB Number: [IRB #]

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1. Summary

The benefits of exercise for individuals with Parkinson disease (PD) have been well documented; however, individuals with PD living in rural and underserved urban settings are largely unable or unwilling to participate in group exercise programs due in large part to their distance from such programs and financial considerations. Additionally, community based programs which provide social support and engagement have been shown to benefit elderly individuals as well as individuals with pathology, but are equally unattainable to this group. Taking the exercise to these individual via telemedicine or tele-exercise may be an ideal means of delivering this type of intervention.

The long-term goal of this project is to improve outcomes for underserved populations of individuals with Parkinson disease (PD) by providing access to in-home physical activity via a telehealth approach. Approximately one million Americans currently live with a diagnosis of PD and it has been estimated that delaying the progression by 20% would result in a $75,891 savings per individual based on reduced health care costs, income maintenance, increased duration of life and improved quality of life. However, individuals with PD of lower socioeconomic status, people of color and rural dwelling seniors have been critically underserved by clinical and academic programming resulting in poorer health outcomes.

These two studies will examine: 1) the Reach, Effectiveness, Implementation and Maintenance and 2) the optimal delivery method for an in-home exercise intervention program for individuals with PD living in underserved communities. We will deliver a managed and meaningful exercise intervention that not only addresses the benefits of physical activity for individuals with PD, but also offers a social connection to research staff outside of the participant's typical caregiver(s).

Study 1
Examine the reach, effectiveness and maintenance of an in-home, partnered cycling program for underserved individuals with PD.

Study 2
Examine the effects of social engagement during in-home exercise on a small sample of individuals with Parkinson Disease (PD). This pilot investigation will directly measure the effect of social support and engagement for rural dwelling individuals with PD.

2. Safety Contact Information

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3. Participants Safety

3.1 Potential Risks and Benefits for Participants

Potential Risks:

Physical: Common physical risks include muscle soreness, fatigue and shortness of breath. Less common physical risks include falls, heat intolerance, and skin irritation from the activity monitor. Rare but possible risks include cardio-vascular related events (sudden cardiac arrest, myocardial infarction, and stroke).

Psychosocial: Potential psychosocial risks include loss of confidentiality, frustration, embarrassment, depression or identification of suicidal thoughts.

Potential Benefits:

We do not yet know the full extent to which exercise may benefit individuals with Parkinson disease. Recent evidence suggests that exercise is beneficial to some individuals with PD in some cases. Some of the possible benefits may include improvements in physical function, quality of life, number of falls, balance, psychological factors including depression and non-motor features of PD.

3.2 Adverse Event (AE) Definition

Adverse event (AE) means any untoward or unfavorable medical occurrence in a human subject or others that happens during or after participation in a research study.

An abnormal heartrate, perceived exertion rating, fall or other data point will not be assessed as an AE unless that value leads to therapeutic intervention, emergency medical service or is considered by the investigator to be a clinically significant change from baseline. These AEs will be entered into the study database.

3.3 Serious Adverse Event (SAE) Definition

An adverse event is considered "serious" if, in the view of either the investigator or sponsor, meets any of the following criteria:

- Result in death
- Are life-threatening
    - (Refers to an AE in which the participant was at risk of death at the time of the event. It does not refer to an event, which hypothetically, might have caused death if it were more severe.)
- Requires an inpatient hospitalization or prolongation of an existing hospitalization
- Result in persistent or significant disability or incapacity.
    - (Disability is defined as a substantial disruption of a person's ability to conduct normal life functions.)
- Result in a congenital anomaly/birth defect.
- Constitute, based upon appropriate medical judgment, an event that may jeopardize the participant's health and may require medical or surgical intervention to prevent one of the other outcomes listed above.

3.4 Unanticipated Problem (UP) Definition

The Office for Human Research Protections (OHRP) considers unanticipated problems involving risks to participants or others to include, in general, any incident, experience, or outcome that meets all of the following criteria:

- The incidence, experience, or outcome is unexpected given the research procedures described in protocol-related documents (e.g., the study protocol, the consent documents) and the characteristics of the subject population being studied. An event may be considered unexpected if it exceeds the nature, severity, or frequency described in the study-related documents.
- The incidence, experience, or outcome is related or probably related to participation in the research study. Probably related means the incidence, experience, or outcome is more likely than not to be caused by the research study procedures.
- The occurrence of the incidence, experience, or outcome suggests that the research places participants or others at a greater risk of harm (physical, psychological, economic, or social) than was previously known or recognized.

3.5 Classification of an Adverse Event

3.5.1 Severity of Event

All AEs will be assessed by the PI using the Common Terminology Criteria for Adverse Events (CTCAE) Version 5., each event is searchable using the Safety Profiler website (https://safetyprofiler-ctep.nci.nih.gov/CTC/CTC.aspx). For AEs not included in the protocol defined grading system, the following guidelines will be used to describe severity.

- **Mild** – Events require minimal or no treatment and do not interfere with the participant's daily activities.
- **Moderate** – Events result in a low level of inconvenience or concern with the therapeutic measures. Moderate events may cause some interference with functioning.
- **Severe** – Events interrupt a participant's usual daily activity and may require systemic drug therapy or other treatment. Severe events are usually potentially life-threatening or incapacitating.
- **Life Threatening** – Places the patient or subject at immediate risk of death. It does not include an adverse event that, had it occurred in a more severe form, might have caused death.
- **Death**

3.5.2 Relationship to Study Intervention

For all collected AEs, the PI will determine the AE's causality based on temporal relationship and her judgment. The degree of certainty about causality will be graded using the categories below.

- **Definitely Related** – Clearly related to the study procedures and other possible contributing factors can be ruled out.
- **Probably Related** – Likely related to the study procedures and the influence of other factors is unlikely.
- **Possibly Related** – Possibly related to the study procedures and there are other factors that could be equally likely.
- **Unlikely to be related** – Doubtfully related to the study procedures and there is another likely cause.
- **Unrelated** – Clearly not related to the study procedures and/or evidence exists that the event is definitely related to another cause.

3.5.3 Expectedness to Study Intervention

The Principal Investigator (PI) will be responsible for determining whether an AE is expected or unexpected.

For studies not evaluating an investigational drug or device, an AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described in the protocol, the IRB application, or the informed consent document.

3.6 Collection and Reporting of AEs, SAEs & UPs

Study participants will be instructed to contact the PI if any serious or unexpected adverse event occurs. Reported AE's will be recorded in detail in an AE case report form.

Adverse events that occur or are discussed during monitored sessions will be recorded by the study team and the PI will be notified as soon as possible. Events occurring outside of the monitored sessions or by individuals assigned to the solo cycling group will be identified by weekly calls with the participants and review of the exercise logs every four weeks. Any adverse events will be discussed at weekly research team meetings and will be reviewed to determine whether a change in protocol is necessary.

AE/SAEs that meet the definition of an unanticipated problem will be reported to the IRB within 14 business days. Events that are immediately life threatening, severely debilitating to other current subjects or resulted in a death will be reported to the IRB Chair or IRB Director via telephone or email within 24 hours (1 business day) of site awareness.

3.7 Protection Against Study Risks

Informed Consent Process

Individuals completing the phone screening will provide verbal informed consent. For those who elect to participate in the study, all participants will provide written informed consent prior to being enrolled in the full study.

Protection Against Risks

A. Steps to Minimize Risks during data collection

To minimize the risks to participants during the data collection sessions, the following risks have been identified and precautions will be taken.

b. Physical Risks: Fatigue is the most common or frequent physical risk as some of the participants may currently be relatively sedative. Additionally, there is a possibility of a fall and injury during the assessment.

c. Steps to Physical Risks: Fatigue: frequent breaks are schedule in the protocol. Additionally, participants will be informed that they may request a break at any time.

Falls: All participants will be closely spotted by trained study personnel during data collection sessions. Those individuals who are older or who have indicated a recent fall will asked to wear a gait belt.

B. Steps to Minimize Risks during in-home exercise

To minimize the risks to participants during the exercise intervention, a number of measures and precautions will be taken. All participants will be asked during the phone screen if they have ever been told that they should not exercise or if they have any reason to believe that they should not exercise. Each individual will complete a medical and health history form covering musculoskeletal, cardiovascular, respiratory, and other health conditions and provide a thorough list of prescription medications. If any contraindications for exercise are reported, the individual will be instructed to review the exercise protocol with their physician prior to study enrollment and provide documentation asserting that the individual is cleared for exercise. Financial assistance for a necessary screening visit to a medical provider is available. Prior to beginning all legs of the study that involve the cycling intervention, all individuals will have their maximum and target heartrate calculated and will be provided with their individual results. This table will be posted on the bike so that it is visible at all times. During scheduled exercise sessions, a study team member will monitor the participant's heart rate and perceived exertion (Borg Rating of Perceived Exertion (RPE) (Borg, 1970)) for the duration of the

session. Outside of these scheduled sessions and in the solo cycling group, participants can make use of the reference card to monitor their heartrate. Any indication of significant discomfort, exercise intolerance, a desire to stop or a medical emergency will result in termination of the session. All research staff will be familiarized with the main signs and symptoms of adverse events and will know to follow the emergency and non-emergency protocols described below.

Physical Risk: Common physical risks include muscle soreness, fatigue and shortness of breath. Less common physical risks include falls, heat intolerance, and skin irritation from the activity monitor. Rare but possible risks include cardio-vascular related events (sudden cardiac arrest, myocardial infarction, and stroke).

a. Steps to decrease physical risks during exercise session –To minimize the risks of muscle soreness, we will follow appropriate guidelines for exercise by including a warm-up prior to the start of each training period, and ending with a cool-down period. We will also recommend participants keep a towel nearby and we will encourage hydration, before, during, and after exercise.

b. To minimize excessive fatigue and shortness of breath, the intensity of the cycling session will be gradually increased and based upon the participant's previous results and anecdotal reports of fatigue before, during, and after exercise. Additionally, we will use the Borg Rating of Perceived Exertion (RPE) (Borg, 1970) and the maximum and target heartrate formulas described above to monitor participants' exercise response as well as to help individuals monitor their target and maximum heartrate values on their own throughout the sessions. Participants may terminate a session at any time.

c. To minimize skin irritation due to the wearing of the Garmin VivoSmart activity tracker, participants will be instructed to wear the monitor snuggly, but not too tight on their preferred wrist. Participants will be told to remove the device and place it in a pocket if it cannot be donned comfortably.

d. To minimize the risk of falls, we will utilize a customized recumbent bike, specifically fit to the individual rider, with a wider seat for more stability, handlebars on the seat, and a lower ground profile that allows participants easy entry and exit without necessitating a step over a central support. Two members of the research team will set-up the bike and properly fit it to the individual rider. Additionally, the team will ensure the stationary bike is set-up in a safe and secure manner and in an area free of clutter and dangerous obstacles.

e. For heat intolerance, we will encourage participants to exercise in either an air-conditioned room, or in front of a fan. And as previously mentioned, the Borg Scale and HRR will be used to monitor exertion, and target heart rate intensities. Participants may terminate a session at any time.

f. Given that the proposed intervention is an aerobic protocol, there is the risk for cardio-vascular related events (sudden cardiac arrest, myocardial infarction, and stroke). To minimize these risks, all participants will be asked if they have ever been told that they should not exercise or if they have any reason to believe that they should not exercise during the phone screen. Further, all participants will complete a medical and health history form covering musculoskeletal, cardiovascular, respiratory, and other health conditions and provide a thorough list of prescription medications. If any contraindications for exercise are reported, the individual will be instructed to review the exercise protocol with their physician prior to study enrollment and provide documentation asserting that the individual is cleared for exercise. Financial assistance for a necessary screening visit to a medical provider is available.

Age-defined heart rate targets will be calculated and each individual in all groups will be informed of their target heart rate zones. To continuously monitor HR, each participant will

don a Garmin VívoSmart 3 which provides beats per minute heartrate data and each bike includes a handlebar sensor for participants to grasp and receive a read-out of current HR. An informational sheet has been provided to instruct the participants about the use of heart rate zone calculations and perceived exertion levels (appendix V and VI). All individuals, regardless of assigned group, will be instructed to target a moderate exercise level. Moderate heart rate values are individual specific. Moderate RPE values are between 3 and 5. During monitored sessions, the research assistant will continuously monitor heart rate and will enquire about RPE at 5 minute intervals. These values will be compared to his/her target HR and RPE. **All participants will be informed that any sessions can/will be terminated by the researcher or participant at any time.**

C. Psychosocial Risks: Loss of confidentiality – One potential risk of participating in this study is that confidential information about the participants may be accidentally disclosed. If a participant's current diagnosis of PD is not known to others, the potential to cause damage to their psychological well-being as well as to their reputation exists.

a. Frustration: Participants may become frustrated with the assessments as the complete battery may take up to 3 hours to complete.

b. Embarrassment: Individuals may be embarrassed if they are unable to perform a task or if they stumble of fall during the performance of a task.

c. Depression: As a depression screen is included in the study protocol an individual who does not know they are depressed may need to be notified. In the case of identified serious depression, the PI will notify the study participant of the potential concern and will make a recommendation for further clinical care.

d. Suicidality: The identification of suicidal thoughts is possible due to the depression questionnaire. In the case of identified suicide risk, the study team will immediately call 911. This will compromise the confidentiality of the participant and the participant will be notified of this breach of confidentiality.

e. *Confidentiality*: All possible care will be taken to maintain confidentiality. No subject will be identified in any report or publication. All data will be coded at the time of data collection. All participants will be assigned an identification number prior to data collection and all documents and files will be named using this ID. All data will be stored on computers which will be kept in the SMIL. All data analysis will be performed on computers in the SMIL or in the faculty office of the PI. A password is necessary for access to the computers and they all are equipped with automatic log off. Data being moved from one location to another will be moved via UW Box or the College of Education's secure network. Only members performing research have access to these computers, therefore identification of any subjects or data is unlikely. Coded data will be kept indefinitely.

Data will be stored/banked for future research projects in a double secured location. In a locked filing cabinet or a password protected computer within a locked room. Coded data will be stored on the School of Education servers indefinitely. It will be used for future research related to exercise studies in the lab. Data may be shared with researchers outside the UW. Dr. Pickett will be responsible for deciding when/to whom to disseminate coded data, and will work with other researchers if necessary to confirm that they have proper IRB approval/etc., as necessary. Required UW-Madison IRB approval would be obtained prior to the release of any data.

Contact information: Each participant will have a sealed folder which contains their emergency contact information including instructions for the local 911 operator and contact information for

an identified contact person. The sealed folders marked with the participant names will be kept locked in the PI's research office. These folders are to be unsealed only in the case of an emergency. All folders and their contents will be destroyed once the individual completes the three-month follow-up or if they withdraw from the study.

Personal privacy during testing sessions will be maintained by testing in a private room and limiting the people within the research lab to current employees or students associated with the lab.

Frustration: To minimize the risk of frustration with the data collection sessions frequent breaks will be provided as will snacks and water during the testing sessions. Additionally, the testing sequence provides a variety of tasks to complete. If it appears that an individual is becoming frustrated with the given task, that task can be stopped or paused and a different task can be completed without disruption of the data collection session.

Embarrassment: The PI and her team all have experience working with individuals at an increased risk of falls. The study team will also talk with the individual to minimize the extent to which they feel embarrassed. We will minimize the likelihood of falling by using proper spotting techniques.

Depression: The risk associated with learning that you are depressed or suicidal based on the Beck Depression Inventory score is difficult to minimize. The study team will follow the developed protocol

4. Interim Analysis

An interim analysis will not be performed.

5. Stopping Rules

5.1 Participant Stopping Rules

Participants will be informed that they have the right to withdraw from the study at any time for any reason, without prejudice to their medical care. The investigator also has the right to withdraw participants from the study for any of the following reasons:

- If study intervention is discontinued due to AE
- Protocol violation
- Lost to follow-up
- Study terminated
- Non-compliance

5.2 Study Stopping Rules

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party. If the study is prematurely terminated or suspended, the PI will promptly inform the IRB and will provide the reason(s) for the termination or suspension.

Circumstances that may warrant termination or suspension include, but are not limited to the following:

- Determination of unexpected, significant, or unacceptable risk to participants
- Demonstration of efficacy that would warrant stopping
- Insufficient compliance to protocol requirements
- Data that are not sufficiently complete and/or evaluable
- Determination of futility

Study may resume once concerns about safety, protocol compliance, data quality are addressed and satisfy the applicable federal and institutional regulatory authorities.

6. Data and Safety Monitoring

The PI will be responsible for ensuring participants' safety on a weekly basis.

6.1 Frequency of Data and Safety Monitoring

Exercise logs will be collected from participants every four weeks and reviewed by the PI for adverse events. The PI and the study team are required to document all adverse events, including serious adverse events and must be reported to the IRB in accordance with the Health Sciences IRB reporting guidelines.