**Physical Activity Pathway for Patients with Osteoarthritis in Primary Care (OA-PCP)**

**Protocol Number: 18-0877**

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**Principal Investigator: Kelli D. Allen, PhD**

**Sponsor: University of North Carolina at Chapel Hill**

**Grant Title: Physical Activity Pathway for Patients with Osteoarthritis in Primary Care**

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**Version Number: 5.0**

**01 July 2020**

**Summary of Changes from Previous Version:**

| Affected Section(s) | Summary of Revisions Made | Rationale |
|---|---|---|
| | Protocol re-formatted; revisions made on previous versions were related to preliminary activities in preparation for the single group pilot trial | For submission to Clinical Trials |
| | | |

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## STATEMENT OF COMPLIANCE

The trial will be carried out in accordance with International Council on Harmonisation Good Clinical Practice (ICH GCP) and the following:

- United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 312, and/or 21 CFR Part 812).

National Institutes of Health (NIH)-funded investigators and clinical trial site staff who are responsible for the conduct, management, or oversight of NIH-funded clinical trials have completed Human Subjects Protection and ICH GCP Training.

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the Institutional Review Board (IRB) for review and approval. Approval of both the protocol and the consent form(s) must be obtained before any participant is consented. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form(s) will be IRB approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

**INVESTIGATOR'S SIGNATURE**

The signature below constitutes the approval of this protocol and provides the necessary assurances that this study will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable US federal regulations and ICH guidelines.

Principal Investigator or Clinical Site Investigator:

Signed: _____ Date: _____

Name:

Title:

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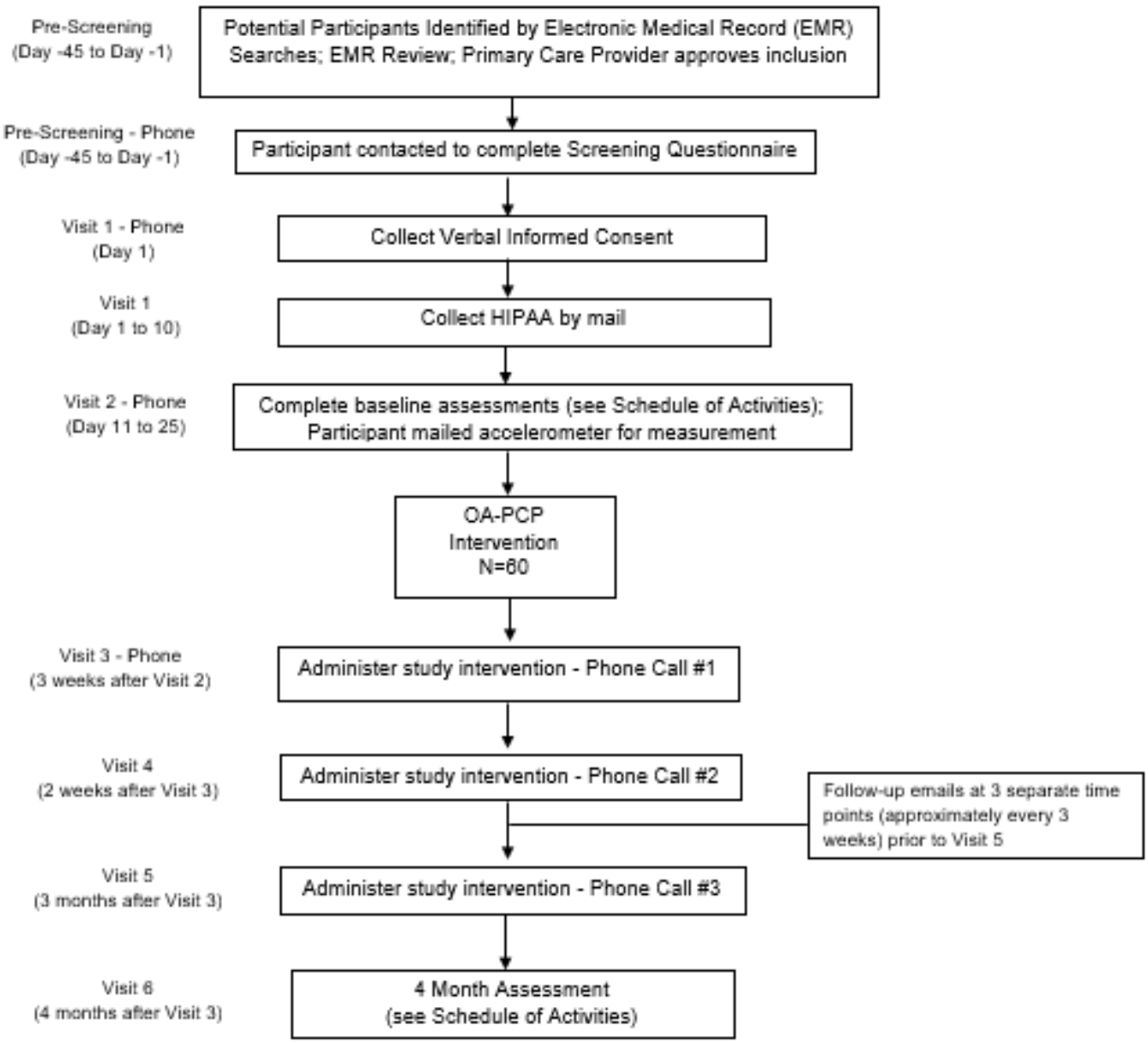
# 1 PROTOCOL SUMMARY

## 1.1 SYNOPSIS

| | |
|---|---|
| **Title:** | Physical Activity Pathway for Patients with Osteoarthritis in Primary Care |
| **Grant Number:** | 1-R21-AG056568-01A1 |
| **Study Description:** | The overall objective of this study is to gather preliminary evidence on the efficacy, feasibility and acceptability of the Osteoarthritis Physical activity Care Pathway (OA-PCP). |
| **Objectives:** | Obtain data on the efficacy, feasibility and acceptability of the OA-PCP program. |
| **Endpoints:** | Primary Endpoint:<br>Objectively assessed physical activity (PA), measured via accelerometer. The primary metric of interest is minutes of moderate to vigorous physical activity (MVPA). Other metrics will include light intensity PA, sedentary minutes and step counts. These will be assessed at baseline and 4-month follow-up time points.<br><br>Secondary Endpoints: Self-reported pain and function (Western Ontario and McMaster Universities Osteoarthritis Index; WOMAC). These will be assessed at baseline and 4-month follow-up time points. |
| **Study Population:** | N = 60 participants age ≥65 recruited from University of North Carolina (UNC) primary care. We will enroll both males and females from all racial and ethnic backgrounds. |
| **Phase or Stage:** | Based on the Obesity-Related Behavioral Intervention Trials (ORBIT) framework, this study is a Phase IIb trial. |
| **Description of Sites/Facilities Enrolling Participants:** | We will involve UNC primary care clinics. |

| | |
|---|---|
| **Description of Study Intervention/Experimental Manipulation:** | The OA-PCP will include four phases. Phase 1: Physical Activity Screening: This component of the OA-PCP will be completed as part of the enrollment process. Phase 2: Brief PA Counseling: This will be delivered via phone by a PA Coach, who will be trained in relevant aspects of PA and motivational interviewing. Phase 3: Linkage to PA Programs and Resources Phase 4: PA Coaching Follow-Up. The PA coach will call participants approximately 3 months following the initial call. The coaching calls will focus on PA goal-setting and identifying PA resources. The PA coach will also email at three separate time points (approximately every 3 weeks) prior to the 3-month follow-up call. |
| **Study Duration:** | 2 years |
| **Participant Duration:** | 4 months |

## 1.2 SCHEMA


Pre-Screening
(Day -45 to Day -1)
Potential Participants Identified by Electronic Medical Record (EMR) Searches; EMR Review; Primary Care Provider approves inclusion
Pre-Screening - Phone
(Day -45 to Day -1)
Participant contacted to complete Screening Questionnaire
Visit 1 - Phone
(Day 1)
Collect Verbal Informed Consent
Visit 1
(Day 1 to 10)
Collect HIPAA by mail
Visit 2 - Phone
(Day 11 to 25)
Complete baseline assessments (see Schedule of Activities); Participant mailed accelerometer for measurement
OA-PCP Intervention N=60
Visit 3 - Phone
(3 weeks after Visit 2)
Administer study intervention - Phone Call #1
Visit 4
(2 weeks after Visit 3)
Administer study intervention - Phone Call #2
Follow-up emails at 3 separate time points (approximately every 3 weeks) prior to Visit 5
Visit 5
(3 months after Visit 3)
Administer study intervention - Phone Call #3
Visit 6
(4 months after Visit 3)
4 Month Assessment
(see Schedule of Activities)

## 1.3 SCHEDULE OF ACTIVITIES

| | Pre-screening (Pre-consent) | Visit 1 Day 1 to 10 | Visit 2 Day 11 to 25 | Visit 3 (3 weeks after Visit 2) | Visit 4 (2 weeks after Visit 3) | Follow-up emails at 3 separate time points | Visit 5 (3 months after Visit 3) | Visit 6 (4 months after Visit 3) |
|---|---|---|---|---|---|---|---|---|
| EMR Review Eligibility | X | | | | | | | |
| Screening Phone Call | X | | | | | | | |
| Informed Consent & HIPAA | | X | | | | | | |
| Outcome Measures | | | | | | | | |
| Objectively Assessed Physical Activity (accelerometer) | | | X | | | | | X |
| Patient Reported Measures: | | | | | | | | |
| -Physical Function (WOMAC) | | | X | | | | | X |
| -Pain (WOMAC) | | | X | | | | | X |
| Participant Characteristics | | | X | | | | | |
| Acceptability | | | | | | | | X |
| OA-PCP Intervention | | | | X | X | X | X | |
| Adverse Event Reporting | | | X | X | X | X | X | X |

# 2 INTRODUCTION

## 2.1 STUDY RATIONALE AND BACKGROUND

### 2.1.1. CLINICAL SIGNIFICANCE

Osteoarthritis (OA) is a Major Cause of Pain and Disability among Older Adults

OA is one of the most prevalent chronic conditions in the U.S. Lifetime risks of symptomatic knee and hip OA are 45% and 25%, respectively [1,2], and the prevalence of OA is expected to rise dramatically over the next several decades [3]. The incidence of OA begins to rise around age 50 years, and OA affects about 1/3 of adults age ≥65 years [4,5]. OA is associated with significant pain, functional limitations, and poorer health-related quality of life [6]. Among older adults, the risk of disability attributable to knee OA is as great as that due to cardiovascular disease and greater than any other medical condition [7]. In addition, studies show that arthritis is a significant barrier to engagement in physical activity (PA) among individuals who are overweight and those who have diabetes and cardiovascular disease [8-10]; therefore addressing OA symptoms is also critical for management of common comorbid health conditions.

Physical Activity is Essential for OA Management, But Most Patients are Inactive

Guidelines consistently include PA as a core component of managing knee and hip OA [11-13], based on its strong evidence for effectiveness [14]. A meta-analysis of trials of PA for knee OA found that effect sizes for aerobic exercise were 0.52 and 0.46 for pain and disability, respectively; for strengthening exercises, effect sizes were 0.39 and 0.32[15]. These are moderate to large effect sizes and are comparable to those observed for pharmacological treatment of OA [16]. Among patients with hip OA, meta-analysis also showed that land-based exercise substantially reduced pain and improved physical function – providing 28% and 24% improvement from baseline, respectively [17]. Despite strong evidence for PA in managing OA symptoms, it is substantially under-utilized [18,19]. For example, in a study of adults who had or were at risk for knee OA, only 2% of African Americans and 13% of Caucasians were currently meeting PA recommendations [19]. *There is an urgent need to improve PA levels among older adults with OA, particularly to reduce risk for downstream functional limitations and disability.*

Primary Care is a Key But Under-Utilized Setting for Promoting PA

The vast majority of patients with OA are seen in primary care, which therefore represents a key opportunity to integrate PA into a comprehensive OA management approach [20]. Yet evidence shows that we are failing to bring PA into the conversation about OA management [21]. For example, in one study less than half of inactive patients with arthritis (primarily OA) reported that a doctor had ever suggested PA as a strategy to help manage joint symptoms [22], despite the fact that exercise is included as a first-line therapy in OA treatment guidelines [23]. This is in contrast to the overwhelming majority of patients who take pain medications to help manage OA symptoms [24]. Other data show that only 1/3 of patients overall receive advice to increase PA from a primary care provider [25]. There are a number of reasons that health care providers infrequently recommend or counsel patients about PA, including include lack of routine PA screening, lack of time within clinic visits, and lack of provider confidence in skills to deliver PA counseling [20]. These challenges are addressed in our proposed intervention approach.

Evidence supports the effectiveness of PA interventions within primary care settings [20,26-28]. *However, we have failed to move this evidence toward implementation, as PA is still not incorporated into health care delivery models.* The following are critical gaps that must be addressed in order to successfully integrate PA interventions into primary care, each of which will be addressed by this study:

- *Approach for Regular PA Screening*: Prior studies suggest that incorporation of routine PA screening into health care settings can facilitate clinician-patient conversations about PA [29,30]. However, studies have not examined models that systematically follow up on PA screening with an intervention for those who are inactive.
- *Approach to Sustainable Intervention Delivery:* A key reason that PA interventions have not been integrated into clinical settings is the lack of feasible delivery models, both in terms of organization and financial support. This project will develop and test an intervention that can be delivered within the context of the Center for Medicare and Medicaid Services (CMS) Chronic Care Management (CCM) services, as described below. This provides a practical model for both reimbursement and intervention delivery personnel.

- *Implementation Science-Based Approach to Development*: Models for PA interventions in primary care must have input from key stakeholders throughout all phases of the development and testing processes [31]. These stakeholders include patients and their supportive partners, primary care personnel, and representatives of clinical and community-based PA programs

### 2.1.2. PREMISE

Developing an OA Physical activity Care Pathway (OA-PCP) for Primary Care Settings

We initially developed the OA-PCP model based on: 1) key recommendations for PA interventions in primary care, 2) the "Let's Get Moving" intervention, 3) the Socioecological Model of Health Behavior, and 4) CMS guidelines for delivering CCM services:

*Key recommendations for PA interventions in primary care*, based on prior studies, include: use of trained coaches to deliver the PA intervention, engagement of patients as active participants who select goals and identify strategies to overcome barriers, inclusion of follow-up contacts and tailored feedback, and integration with community-based and other PA resources [20,27].

*The "Let's Get Moving" intervention* is a systematic approach to integrating PA into primary care that was implemented in United Kingdom general practices based on research evidence [32-34]. This model involves four phases: 1.) Screening for physical inactivity in a primary care setting, 2.) Brief PA counseling intervention, 3.) Connection with community and other PA resources, 4.) Follow-up to assess progress and promote maintenance. The OA-PCP mirrors these four phases.

*The Social Ecological Model of Health Behavior* has been applied to many interventions and emphasizes the unique and complementary strengths of intervention components at different levels [35,36]. As shown in Figure 1, OA-PCP components address the *individual* and *interpersonal* levels though PA counseling, the *organizational* level via systematic PA screening and intervention initiation in primary care, and the *community* level by linking patients with programs and resources. The ultimate goal of this research is to provide a strong evidence base that will lead to *public policy* level initiatives such as systematic, widespread roll-out and quality measures related to PA screening and intervention in health care systems.

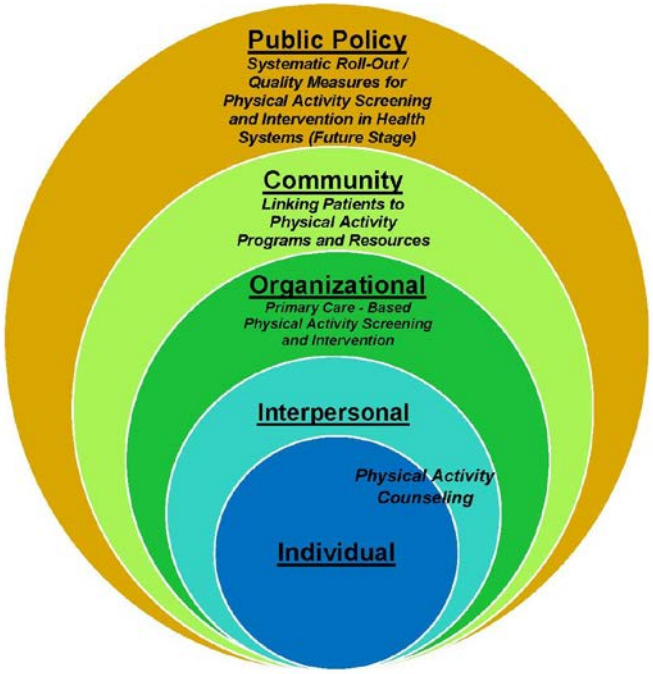



Figure 1: Social Ecological Model of Health Behavior Applied to OA-PCP

*CCM services* were initiated by the CMS in 2015, and provision of these services has been growing under this model and reimbursement structure; CMS is actively promoting delivery of these services. Briefly, these services provide "at least 20 minutes of clinical staff time, directed by a physician or other qualified health care professional, per calendar month," for patients with two or more chronic health conditions. OA is one of the qualifying chronic conditions, and many conditions that commonly co-occur with OA also qualify (e.g. diabetes, depression, hypertension, cardiovascular disease). Therefore, a large proportion of patients with Medicare coverage who have OA are eligible for these services. PA counseling could be delivered as a component of CCM services, since these include addressing patients' functional needs, referrals to other clinicians and community-based services, patient education, motivational counseling and self-management support. Embedding PA counseling within the context of CCM services is appealing because it integrates PA within the broader disease management process. Importantly for the structure of the OA-PCP, CCM services do not need to be delivered by the billing practitioner; they may be delivered by other clinic staff under the direction of the billing practitioner.

Some primary care clinics at our institution (University of North Carolina at Chapel Hill (UNC)) are currently delivering these services using a model that involves "care assistants" (typically individuals with Bachelor Degree level of education in an appropriate field who are given training in CCM) who are supervised by billing practitioners. Also importantly for the OA-PCP, CCM services can be delivered via telephone, which is a typical delivery model at UNC. This project focuses on patients who are eligible for CMS CCM services, since this is a currently active reimbursement model and since many patients with OA are age 65 or older.

### 2.1.3. PRIOR STUDIES AND RATIONALE FOR DEVELOPMENT

Overall Experience of the Research Team

This project builds on the collective experience of our study team in OA management, PA interventions, and primary care-based studies. Dr. Allen's has led 8 clinical trials of behavioral and health services interventions among individuals with OA [37-43]. Of high relevance to this project were two randomized clinical trials of patient and provider based interventions for managing OA in primary care [37,44]. These studies directly interfaced with primary care clinics, showing the feasibility of this approach and our experience with these types of interventions. Dr. Callahan is an international leader in evidence-based PA programs for OA, particularly community-based and self-directed interventions. She led the evaluation of the Arthritis Foundation Walk With Ease program and 5 other PA intervention trials [45-52]. She participated in development of the National Public Health Agenda for OA and directs the Osteoarthritis Action Alliance (OAAA), a coalition of more than 95 organizations committed to increasing PA among individuals with OA [53]. Dr. Golightly is a physical therapist and epidemiologist with expertise in the clinical aspects of OA and PA intervention approaches for OA [54]. She serves as the Grants Program Manager for the OAAA, partnering with communities and healthcare systems nationwide to implement evidence-based PA programs for people with OA. Dr. Nelson is a rheumatologist with expertise in OA diagnosis, clinical care and epidemiology. She is also the medical advisor for the OAAA and leads an OAAA workgroup focused on health systems and OA management. Dr. Cleveland is an epidemiologist and statistician with extensive expertise in conducting analyses related to OA and PA, as well as other outcomes. Dr. Powell is an implementation scientist who has expertise in understanding strategies to implement effective health services interventions [55-57]. Dr. Vu is a qualitative methodologist who has contributed to many studies that conduct formative assessments of multi-level and health system based interventions [58-60]. Dr. Hales is an expert in use of accelerometers to measure PA [61,62] and is currently collaborating with Dr. Callahan on a study of partner-focused PA among individuals with arthritis.

## 2.2 RISK/BENEFIT ASSESSMENT

### 2.2.1 KNOWN POTENTIAL RISKS

Emotional distress: it is unlikely that the types of questions participants will be asked in this study will result in emotional distress, but we understand that participants may be uncomfortable with answering questions about some aspect of their health or other things about them. To minimize this risk, we will let participants know they may choose not to answer any study questions and can still be involved in the study.

Breach of confidentiality: we will be collecting some elements of personal health information necessary for the study. To minimize breaches of confidentiality, all data will be stored on a secure UNC server and paper information will be stored in locked filing cabinets in the office of a study team member, and only approved study personnel will have access to those data.

Risks of Exercise: The physical activity coach will give participants information on exercise programs appropriate for people with OA. This information follows guidelines recommended by physicians and researchers. However, exercise programs may be associated with risk of injury, muscle soreness, and joint pain. The risk of sudden death during physical activity is about 1 death per 656,000 hours of physical activity. In general, the risk of these events with moderate physical activity is very low.

### 2.2.2. KNOWN POTENTIAL BENEFITS

Participants may experience improvements in pain, physical function or other symptoms related to OA, from participating in the OA-PCP program. It is possible that this study may not benefit participants directly, but participation in this study may lead to information that can benefit other patients with knee and hip OA, as well as their health care providers.

### 2.2.3 ASSESSMENT OF POTENTIAL RISKS AND BENEFITS

This is a minimal risk study with physical risks that are comparable to those that would be encountered with exercise programs in clinical or community settings. Furthermore, we do not anticipate any significant psychological, social, financial, or legal risks to be associated with participation in this study. Given the high and increasing rate of OA, the persistent deficits of physical inactivity, and the lack of a standard, evidence-based approach to address these deficits in primary care settings, we believe the value of the information to be gained outweighs the risks of participation in the study.

## 3 STUDY OBJECTIVES AND ENDPOINTS

| OBJECTIVES | ENDPOINTS | JUSTIFICATION FOR ENDPOINTS |
|---|---|---|
| **Primary** | | |
| **Obtain data on the efficacy of the OA-PCP program on objectively assessed PA, measured via accelerometer.** | MVPA (primary metric), light intensity activity, sedentary minutes, step counts and other PA metrics, assessed at baseline and 4 months. | MVPA was chosen as the primary metric because it corresponds to Department of Health and Human Services (DHHS) PA recommendations. Other complementary PA metrics are also important for describing the overall activity patterns of participants. The 4-month time point corresponds to the end of OA-PCP calls. |
| **Secondary** | | |
| **Obtain data on the efficacy of the OA-PCP program with respect to improvement in self-reported physical function and pain**. | Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain and function subscales, assessed at baseline and 4 months. | These secondary metrics will be assessed because they are key outcomes in OA and can be improved with regular PA. The 4-month time point corresponds to the end of OA-PCP calls |

## 4 STUDY DESIGN

### 4.1 OVERALL DESIGN

**This study will be a single group pilot trial of the refined OA-PCP among n=60 patients with knee and/or hip OA in primary care clinics.**

We will conduct this pilot trial in primary care clinics that differ in terms of practice size and urban / rural location, with advisement on clinic selection from the North Carolina Network Consortium (NCNC) Core Team. Study patients will complete assessments at baseline and 4 months, with the latter allowing about a one-month period

following completion of one PA counseling follow-up call. This will allow a sufficient initial assessment of the feasibility and acceptability of the OA-PCP.

## 4.2 SCIENTIFIC RATIONALE FOR STUDY DESIGN

See section 2.1

## 4.3 JUSTIFICATION FOR INTERVENTION

The Scientific Premise and Prior Studies sections above describe the prior literature, recommendations and preliminary studies that have informed development and refinement of the OA-PCP components. The number, frequency and types of contacts were selected based on feasibility to deliver within CMS CCM services. Content of each PA counseling contact is based on scientific evidence related to behavior change and successful strategies for increasing PA [20,27,35,63].

## 4.4 END-OF-STUDY DEFINITION

A participant is considered to have completed the study if he or she has completed 4-month follow-up assessment.

# 5 STUDY POPULATION

## 5.1 INCLUSION CRITERIA

Participants need to be age 65 or older, and have, in addition to OA, one other chronic health condition that qualified under CCM guidelines, including: diabetes, depression, hypertension, hyperlipidemia, heart failure, atrial fibrillation, ischemic heart disease, stroke/TIA, peripheral vascular disease, COPD, bronchiectasis, asthma, rheumatoid arthritis, osteoarthritis, HIV/AIDS, chronic kidney disease, hepatitis (chronic & viral B & C) and osteoporosis. Other inclusion criteria are: 1) Self-reported current symptoms in a joint with OA, using the following validated item: “Do you have pain, aching or stiffness in your knees/hips on most days?” [64]. Patients also had to self-report a pain score of ≥3 on a 0-10 numeric scale (0=no pain, 10=extreme pain), which is an approach recommended by the Osteoarthritis Research Society International Clinical Trial Guidelines [65]. 2) Self-reported physical activity <150 minutes per week, which aligns with public health recommendations. We will use the Physical Activity Vital Sign (PAVS) [29,66-68], which includes the following two questions: 1. “On average, how many days a week do you engage in moderate to strenuous exercise (like a brisk walk)?” 2. “On average, how many minutes do you exercise at this level?” The PAVS has been implemented in a large health care system, showing good face and discriminant validity [29,30]. We also selected this physical activity screening approach because it would be feasible to administer in primary care settings as part of implementing OA-PCP.

## 5.2 EXCLUSION CRITERIA

| **Exclusion Criteria and Sources of Information** | | |
|---|---|---|
| Criterion | EMR | Phone Screening |
| Pain in chest when performing physical activity | | X |
| Pain in chest when not performing physical activity | | X |
| Loss of balance because of dizziness or loss of consciousness | | X |
| Recommendation from doctor to only perform physical activity under medical supervision | | X |

| | | |
|---|---|---|
| No documented diagnosis of knee or hip OA | X | |
| Dementia | X | X |
| Psychosis | X | X |
| Active Substance abuse disorder | X | X |
| Total knee or hip replacement surgery, meniscus tear, ligament tear, or other significant lower extremity injury or surgery in the last 6 months | X | X |
| Severe hearing or visual impairment | X | X |
| Serious/terminal illness as indicated by referral to hospice or palliative care | X | X |
| Unstable angina | X | X |
| Hospitalization for cardiovascular event in last 6 months | X | X |
| History of ventricular tachycardia | X | X |
| Unstable chronic obstructive pulmonary disease (2 hospitalizations within the previous 6 months and/or on oxygen) | X | X |
| Stroke with moderate to severe aphasia | X | X |
| Recent history (last 6 months) of three or more falls | | X |
| Planning total joint replacement in next 6 months | | X |
| Other health problem that would prohibit safe physical activity participation | | X |
| Current participation in other study related to knee or hip osteoarthritis or physical activity | | X |
| Unable to speak English | X | X |

## 5.3 LIFESTYLE CONSIDERATIONS

N/A

## 5.4 SCREEN FAILURES

Screen failures are defined as participants who consent to participate in this study but are not subsequently assigned to the study intervention or entered in the study. Individuals who do not meet the criteria for participation in this trial (screen failure) because of meeting one or more exclusion criteria (e.g., development of an exclusionary health condition) will not be rescreened.

## 5.5. STRATEGIES FOR RECRUITMENT AND RETENTION

Potential participants will first be identified from among patients of participating primary care providers in UNC clinics, using the electronic medical record (EMR). Specifically, we will identify patients age 65 and older with diagnosis codes for knee or hip OA (M17.0, M17.10, M17.11, M17.12, M17.2, M17.30, M17.31, M17.32, M17.4, M17.5, M17.9, M16.0, M16.10, M16.11, M16.12, M16.2, M16.30, M16.31, M16.32, M16.4, M16.50, M16.51, M16.52, M16.6, M16.7, M16.9, M19.90, M19.91, M19.92, M19.93, M15.0 (primary, generalized OA)), a diagnosis code for at least one qualifying comorbid health condition under CCM guidelines listed above, and no diagnosis codes for exclusionary health conditions. Primary care providers will be asked to review lists of patients eligible

based on the EMR and approve a final list of patients to contact. These patients will be mailed an introductory letter, signed by their primary care provider (to illustrate providers' endorsement and support), and then called by a study team to further assess eligibility. Patients who are eligible and interested in participating will complete a verbal consent process and be mailed or emailed a HIPAA wavier form to sign and return. Then participants will complete baseline assessments via telephone and be mailed an accelerometer for physical activity assessment. Participants will be paid $25 for completing each phone-based assessment and $15 for returning the accelerometer at each time point.

All participants will receive the OA-PCP intervention. Participants will have regular contact with an interventionist throughout the study period. Based on our prior studies, we believe this will enhance retention. In addition, we believe that the lack of requirement for any in-person study visits will enhance both recruitment and retention. To facilitate completion of recruitment calls, as well as baseline and follow-up assessment calls, we will call participants on different times of day and different days, across multiple weeks. We have used this strategy successfully in prior studies to reach participants at times convenient to them.

## 6.0 STUDY INTERVENTIONS

## 6.1 STUDY INTERVENTION ADMINISTRATION

As summarized in Figure 2, the OA- PCP will include four phases.

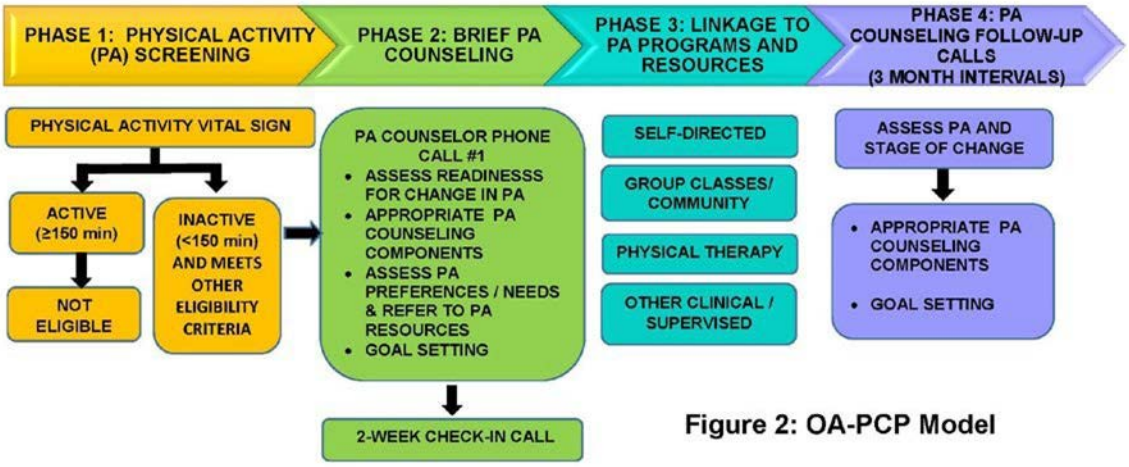



**Figure 2: OA-PCP Model**

*Phase 1: Physical Activity Screening:* This component of the OA-PCP will be completed as described above for the enrollment process.

*Phase 2: Brief PA Counseling:* This will be delivered via phone by the PA Counselor (akin to "care assistant" in the CCM model), who will be trained in relevant aspects of PA and motivational interviewing. The content for the initial call is designed to be brief enough that it can be embedded within a routine CCM call; future calls are even shorter. We have developed detailed scripts for all OA-PCP calls. At the beginning of the first call, the counselor will assess participants' Stage of Change for PA based on previously developed definitions: pre-contemplation (not ready to increase PA right now), contemplation (getting ready to increase PA, intend to within the next 6 months), preparation (ready to increase PA within the next month), action (have been increasing PA during the past 6 months) and maintenance (have been regularly active for at least 6 months, focused on avoiding setbacks). The content of the remainder of the call will be tailored to participants' Stage of Change. This is a patient-centered approach and also allows the calls to be briefer, since only relevant components are delivered. There are 4 potential components for the first counseling call (depending on Stage of Change); these are based on prior studies and recommendations for behavior change interventions. The following is a brief description of each:

1. *Description of the Benefits and Appropriateness of PA for OA*: Content includes a summary of benefits of

PA and basic information for safe, appropriate PA in the context of OA. In accordance with OA treatment guideless and DHHS recommendations[69,70], the PA counselor will recommend that participants incorporate aerobic, strengthening and stretching activities in a comprehensive approach to PA. With regard to aerobic activity, the PA counselor will encourage participants that a good long-term goal is to do 150 minutes of moderate intensity activity per week, per DHHS recommendations [70]. However, the counselor will also stress the value and health benefits of interim goals when increasing amount of weekly aerobic activity. With respect to strengthening exercises, participants will be encouraged to perform these at least twice per week on non-consecutive days. Lower extremity strengthening exercises will be emphasized. Participants will be encouraged to perform stretching exercises daily. Instructions and example strengthening and stretching exercises are included in the Arthritis Foundation brochure described below.

2. *Discussion of Preferences for PA and Identifying Appropriate PA Resources*: The counselor will ask participants brief questions to understand types of PA they enjoy most and are likely to engage in. Based on this information, the counselor will recommend specific PA programs resources; a summary of these resources will be mailed and / or emailed to the participant. This will lead directly to Phase 3 of the OA-PCP intervention, described below.
3. *PA Goal-Setting*: The counselor will work with participants to establish and document PA goals, with an initial focus on the next 2 weeks (before check-in call; Figure 2). The counselor will talk with participants about potential barriers and use a problem-solving approach to address each one.
4. *Discussion of Plans for Dealing with Setbacks*: For participants who are regularly active, having plans for dealing with setbacks helps to avoid discouragement and prolonged time away from PA. The counselor will give tips for identifying setbacks early and work with participants to identify strategies for dealing with these.

Motivational interviewing (MI) principles will be used throughout the phone call and will be a particular emphasis for individuals in the pre-contemplation and contemplation stages. These principles are woven into our phone scripts. MI is a key behavior change strategy that can elicit participants' own motivations and / or ambivalence toward PA [71]. This helps individuals to explore and resolve their own, sometimes conflicting attitudes toward changing PA behaviors, building autonomy and internal awareness that is essential for long-term behavior change. To support topics discussed during the first phone call, participants will be mailed and/ or emailed materials including: 1) handouts describing appropriate exercise for people with osteoarthritis, tips on PA for people with arthritis (including pain management), instructions for different types of exercise (aerobic, strengthening, stretching), and example exercises. 2) A list of PA programs and resources adapted for their locality. 3) A worksheet for documenting PA goals.

Approximately two weeks after the initial call, the PA counselor will contact participants to check in on whether they have successfully connected with PA programs or resources discussed, as well as review progress toward PA goals and set new goals. Content for this call will be tailored based on the first call. The PA counselor will be able to refer to notes from the prior call regarding initial PA goals. If participants have encountered any barriers since the first call, they will be addressed and other PA resources identified if needed. If participants were not ready to set a PA goal or identify PA resources of interest at the first call, they will be invited to do so at call #2.

*5. Follow-up emails:* At the first call, the counselor will ask participants to opt-in (or opt-out) to receive follow-up emails after the 2-week check in call. For those participants that agree to opt-in, the counselor will email the participant at three separate time points (approximately every 3 weeks) prior to the 3-month follow-up call. The content of the emails will be based on individual PA goals set during previous check in calls.

*Phase 3: Linkage to PA Programs and Resources*

There are a large number of OA-appropriate, evidence-based PA resources, and a collection of these resources has been developed (and is updated on an ongoing basis) by the OAAA at UNC; a key source for informing this collection is the CDC's Compendium of Arthritis Appropriate Physical Activity and Self-Management Education Interventions. Table 2 shows representative examples of these resources, which include tools to facilitate individual PA, as well as group-based classes. With regard to the latter, we will perform an environmental scan for programs available within the communities surrounding study clinics; this will be facilitated by the OAAA, the Arthritis Foundation's Online Resource Finder and the Evidence-Based Leadership Council. Based on our prior experience, there are many free, appropriate PA programs available in communities, including walking groups and classes in senior centers. Local resource information will be use to tailor patient handouts. Participants will be able to contact the PA counselor throughout the intervention period if they have questions about PA resources, or if they would like information on different resources. We will document the frequency and nature of the contacts to inform and refine the intervention.

**Table 2. Example OA-Appropriate PA Resources and Programs**

| | |
|---|---|
| **Self-Directed** | |
| Walk With Ease (Self-Directed) | Resources to help people with arthritis learn to walk safely and regularly. Tools include a guidebook, walking diary, example exercises, interactive online resources (starting point test, motivational tools, activity log) and a mobile app. COST: Free |
| Exercises for Chronic Conditions | Exercise CDs developed by Stanford University, appropriate for people with arthritis and other chronic health conditions. COST: $10 |
| Arthritis Foundation Online PA Tools | Resources including arthritis-friendly exercise videos, workouts, tips for people with arthritis. COST: Free |
| **Group-Based** | |
| Arthritis Foundation Exercise Program | Community-based exercise program; trained instructors cover a variety of range-of-motion and endurance-building activities and health education topics. COST: Free or low cost, varies by location |
| Walk with Ease (Group-Delivered) | Community-based walking program developed by the Arthritis Foundation with regular meetings, facilitated by trained leaders. COST: Typically free |
| Fit and Strong | Community-based PA and behavior change intervention offering stretching, balance, and aerobic exercises. COST: Typically free at Senior Centers |
| Tai Chi for Arthritis | Group classes available at many YMCAs and other community centers. COST: Varies from low cost to free |
| Arthritis Foundation Aquatic Program | Group classes led by a trained instructor, including joint range of motion, breathing, and light aerobic activities. Many community aquatic centers have similar, appropriate programs for older adults. COST: Varies based on location, some free |

*Phase 4: PA Counseling Follow-Up*

The PA counselor will call participants approximately three months following the initial call, again using our developed phone scripts and tailored based on earlier calls. For participants who previously set goals and identified PA resources to engage with, the counselor will assess progress, identify additional PA resources if needed, and work with the participants to set new, longer-term PA goals. If participants did not set goals or selected PA resources to try during calls 1 or 2, they will be invited to do so at this time.

## 6.2 FIDELITY

PA Coach will be trained by Dr. Allen and will conduct mock sessions of all OA-PCP calls prior to study initiation.

## 6.3 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND BLINDING

N/A – This is a single group, pre-post pilot trial of the OA-PCP.

## 6.4 STUDY INTERVENTION ADHERENCE

The study database will be used to track participants' completion of all assessment visits, as well as all intervention contacts. The coordinator will also maintain close communication with the PA coach regarding

intervention delivery. If participants miss intervention calls, a study team member may assist the PA coach in attempting to reach the participant.

## 6.5 CONCOMITANT THERAPY

Participants will be permitted to continue any other OA treatment during the course of the study.

# 7 STUDY INTERVENTION/ DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

## 7.1 DISCONTINUATION OF STUDY INTERVENTION

When a participant discontinues from the OA-PCP intervention but not the study, remaining study procedures (e.g., follow-up assessments) will be completed as indicated by the study protocol. If a clinically significant finding is identified after enrollment (e.g. health-related changes that may change the safety level of participating in an independent PA program), the investigator or qualified designee will determine if any change in participant management is needed. Any new clinically relevant finding will be reported as an adverse event (AE). The data to be collected at the time of study intervention discontinuation will include the reason(s) for discontinuing the participant from the intervention, and methods for determining the need to discontinue.

## 7.2 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

Participants are free to withdraw from participation in the study at any time upon request.
An investigator may discontinue a participant from the study for the following reasons:

- Lost-to-follow up; unable to contact subject
- Any event or medical condition or situation occurs such that continued collection of follow-up study data would not be in the best interest of the participant or might require an additional treatment that would confound the interpretation of the study
- The participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation

The reason for participant discontinuation or withdrawal from the study will be recorded in the study database. Participants who discontinue or are withdrawn will be replaced up to the point of randomization assignment being given to the participant. Once participants are given their randomization assignment, they will be counted toward the total study sample size and not replaced.

## 7.3 LOST TO FOLLOW-UP

A participant will be considered lost to follow-up if he or she fails to complete the 4-month follow-up assessment. If a participant misses intervention calls prior to the 4-month time point and cannot be contacted during the time frame, the study team will still attempt to contact the participant for remaining calls / assessments. The study team must attempt to contact a participant at least 3 times, on different days of the week, different times of day, and across at least 2 weeks, before they are considered to have missed a visit / assessment or be lost to follow-up. These contact attempts will be documented in the study database.

# 8 STUDY ASSESSMENTS AND PROCEDURES

## 8.1 ENDPOINT AND OTHER NON-SAFETY ASSESSMENTS

Measures will be collected at baseline and 4-months by a trained research assistant. Other than the accelerometer, measures will be administered via phone. Participants will be paid $25 for completing each phone-based measure and $15 for returning the accelerometer device at each time point.

**Primary Efficacy Outcome: Objectively Assessed Physical Activity.**
We selected this as the primary study outcome because PA is the target of the intervention, and objective assessment has advantages over self-report in terms of accuracy [72]. Our specific primary outcome of interest is minutes of moderate to vigorous intensity PA (MVPA) per week, since this corresponds to DHHS recommendations and is a known predictor of outcomes in patients with OA [73]. We will also examine step counts, minutes of sedentary activity and other complementary metrics, as these are also important for providing a broad picture of PA among participants [74,75]. Each participant will be asked to wear the Actigraph GT3X+ (Pensacola, FL), which allows for the collection and manipulation of raw actigraphy data to facilitate accurate assessment of PA [76]. Participants will be asked to wear the monitors during all waking hours for 7 days. Following previously established thresholds, outcomes will only be computed for participants who wear the accelerometer for 4+ days with 10+ hours of daytime wear. Monitors will be worn on the waist, using either an elastic belt or clip, over the right hip. We may ask a subset of participants to wear a wrist-worn monitor in addition to the waist-worn monitor, in order to assess acceptability and compare values obtained from monitors worn at the two different sites. Accelerometers will be mailed with instructions and a pre-stamped / addressed return envelope. Several days after the accelerometer has been mailed, a study team member will call the participant to review instructions. A phone number will be provided for problems or questions. A second call will be made toward the end of the 7 days to ask about wear and to remind participants to return the monitor. If participants have not worn the monitor enough, they will be asked to wear the monitor a few extra days. Drs. Hales, Callahan and Allen have been involved with projects that have successfully mailed accelerometers to and / or from study participants with OA. There have been high rates of adherence (4+ days with 10+ hours of wear); 93% in one study of adults and partners with OA and 89% in another of 140 patients with OA, with minimal loss of monitors (< 2%). In Aim 2 of this project, valid accelerometer data were available for 57 participants at baseline (95%) and 52 participants at follow-up (86%). Upon return, accelerometer data will be downloaded, compiled into 60s epochs, processed to identify wear, non-wear, and sleep periods using current algorithms [77,78], and summarized using cut-points developed by Troiano [77] and Mathews [79]. These cut-points will allow us to calculate minutes of MVPA, as well as sedentary time and step counts.

**Secondary Efficacy Outcomes:**

Self-Reported Physical Function. Physical function is a key outcome in OA and can be improved with regular PA [14,15]. We will assess physical function with the widely used Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) subscale [80,81]; it includes 17 items, rated on a Likert scale of 0 (no difficulty) to 4 (extreme difficulty), that assess difficulty with performing a range of daily activities commonly affected by lower extremity OA. The reliability and validity of the WOMAC total score and subscales have been confirmed [81]. In patients with hip or knee OA, Bellamy et al. reported internal consistency coefficients (Cronbach's alpha) between 0.86 and 0.95 on WOMAC subscales.

Pain (WOMAC). We will assess self-reported pain using the WOMAC subscale [14,15]; it includes 5 items, rated on a Likert scale of 0 (no pain) to 4 (extreme pain), that assess pain during a range of daily activities.

**Exploratory Outcomes:**

Stanford Numeric Rating Scale (NRS) for Fatigue: We will assess self-reported fatigue using the Stanford NRS Scale for Fatigue; it includes 1 item, rated on a Likert scale of 0 (no fatigue) to 10 (severe fatigue), that assesses fatigue in the past 2 weeks.

PROMIS Sleep Disturbance Short Form 4a: We will assess self-reported sleep quality, sleep depth and restoration associated with sleep using the PROMIS Sleep Disturbance instrument; it includes 4 items, with 5 response options ranging in value from 1 to 5.

International Physical Activity Questionnaire (IPAQ): We will assess self-reported physical activity in the last 7

days using the IPAQ(93); it includes 7 items, assessing PA in four life domains: job-related work done outside the home, recreation, transportation and house and yard work.

**Participant Characteristics:**
We will collect the following information to characterize the study sample: age, race / ethnicity, gender, education, works status, marital status, body mass index, comorbid illnesses [82], joints with arthritis symptoms, and duration of knee / hip OA symptoms.

**Feasibility and Acceptability:**
The following metrics will inform *feasibility* of a larger trial, as well as decisions regarding the number of clinics needed to meet recruitment goals and expected rates of retention:

- Proportion of screened patients who meet the PA eligibility criterion (<150 min per week)
- Proportion of screened patients who are eligible overall
- Proportion of patients who consent to participate, along with refusal reasons for those who do not
- Proportion of participants who complete each phase of the intervention and follow-up assessments

We have developed open-ended questions to assess *acceptability* of the intervention. Topics include acceptability of each intervention component, usefulness of options provided for PA programs / resources, and suggestions for increasing the patient-centeredness of the intervention.

## 8.2 SAFETY ASSESSMENTS

The study PA coach will be trained to deliver the interventions in adherence to and within the scope of the intervention. If a study team member learns of any adverse events (AEs) that occur in the course of participants' home exercise, this will be documented on the Adverse Events form, as described below.

## 8.3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

### 8.3.1 DEFINITION OF ADVERSE EVENTS

This protocol uses the definition of adverse event from DHHS Office for Human Research Protections (OHRP): Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research (modified from the definition of adverse events in the 1996 International Conference on Harmonization E-6 Guidelines for Good Clinical Practice).

### 8.3.2 DEFINITION OF SERIOUS ADVERSE EVENTS

This protocol uses the definition of serious adverse event from DHHS OHRP: any adverse event that results in death; is life-threatening (places the subject at immediate risk of death from the event as it occurred); results in inpatient hospitalization or prolongation of existing hospitalization; results in a persistent or significant disability/incapacity; results in a congenital anomaly/birth defect; or based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition (examples of such events include allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse).

### 8.3.3 CLASSIFICATION OF AN ADVERSE EVENT

#### 8.3.3.1 SEVERITY OF EVENT

All AEs will be assessed by the Principal Investigator (PI) or co-investigators, if the PI is not available. 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. Of note, the term "severe" does not necessarily equate to "serious".]

#### 8.3.3.2 RELATIONSHIP TO STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

All AEs will have their relationship to study procedures, including the intervention, assessed by the PI or co-investigators based on temporal relationship and his/her clinical judgment. The degree of certainty about causality will be graded using the categories below.

- **Related** – The AE is known to occur with the study procedures, there is a reasonable possibility that the study procedures caused the AE, or there is a temporal relationship between the study procedures and the event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study procedures and the AE.
- **Not Related** – There is not a reasonable possibility that the study procedures caused the event, there is no temporal relationship between the study procedures and event onset, or an alternate etiology has been established.

#### 8.3.3.3 EXPECTEDNESS

The PI or Dr. Nelson or Dr. Golightly (co-investigators on the study) will be responsible for determining whether an AE is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described for the study procedures.

### 8.3.4 TIME PERIOD AND FREQUENCY FOR EVENT ASSESSMENT AND FOLLOW-UP

The occurrence of an AE or serious adverse event (SAE) may come to the attention of study team members during study visits. All AEs, not otherwise precluded per the protocol, will be captured on the Adverse Event Form. Information to be collected includes event description, time of onset, PI or co-investigator's assessment of severity, relationship to study procedures (assessed only by those with the training and authority to make a diagnosis), and time of resolution/stabilization of the event. All AEs occurring while on study will be documented appropriately regardless of relationship. All AEs will be followed to adequate resolution.

Any medical or psychiatric condition that is present at the time that the participant is screened will be considered as baseline and not reported as an AE. However, if the study participant's condition deteriorates at any time during the study, it will be recorded as an AE.

Changes in the severity of an AE will be documented to allow an assessment of the duration of the event at each level of severity to be performed. Documentation of onset and duration of each episode will be maintained for AEs characterized as intermittent.

The Project Coordinator will record events with start dates occurring any time after informed consent is obtained until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation. Participants are identified in the EMR as a study participant and for each AE/SAE occurrence, research team members will receive an alert through EMR. AEs or SAEs may also be reported to study PA coach during the course of intervention visits. Events will be followed for outcome information until resolution or stabilization.

### 8.3.5 ADVERSE EVENT REPORTING

Once Dr. Allen (or a co-investigator) is contacted about the adverse event, she / he will make a determination about the reporting requirements in accordance with UNC IRB guidelines.

The PI will report all adverse events to the NIH and UNC IRB as soon as possible, but no later than 10 working days after the investigator first learns of the event. Additionally, the PI or a co-investigator will report any AEs that suggest new or increased risk to participants or others within 7 calendar days of when the PI became aware of the information. For AEs that are not related to participation in the research and do not suggest new or increased risks to the participant, these will be reported at continuing review.

### 8.3.6 SERIOUS ADVERSE EVENT REPORTING

Once Dr. Allen (or a co-investigator) is contacted about a serious adverse event, she / he will make a determination about the reporting requirements in accordance with UNC IRB guidelines. This will include

notification of the UNC IRB, as well as the NIH, within 24-hours if a study-related death and within 48 hours if another SAE.

#### 8.3.7 REPORTING EVENTS TO PARTICIPANTS

N/A

#### 8.3.8 EVENTS OF SPECIAL INTEREST

N/A

#### 8.3.9 REPORTING OF PREGNANCY

N/A

### 8.4. UNANTICIPATED PROBLEMS

#### 8.4.1 DEFINITION OF UNANTICIPATED PROBLEMS

This protocol uses the definition of Unanticipated Problems as defined by the Office for Human Research Protections (OHRP). 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:

(1) Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the IRB-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied;

(2) Related or possibly related to participation in the research. *Possibly related* means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and

(3) Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

OHRP recognizes that it may be difficult to determine whether a particular incident, experience, or outcome is unexpected and whether it is related or possibly related to participation in the research. OHRP notes that an incident, experience, or outcome that meets the three criteria above generally will warrant consideration of substantive changes in the research protocol or informed consent process/document or other corrective actions in order to protect the safety, welfare, or rights of participants or others.

The following corrective actions or substantive changes that could be considered in response to an unanticipated problem include:

- Changes to the research protocol initiated by the investigator prior to obtaining IRB approval to eliminate apparent immediate hazards to subjects;
- modification of inclusion or exclusion criteria to mitigate the newly identified risks;
- implementation of additional procedures for monitoring subjects; suspension of enrollment of new subjects;
- suspension of research procedures in currently enrolled subjects;
- modification of informed consent documents to include a description of newly recognized risks;
- provision of additional information about newly recognized risks to previously enrolled subjects.

Only a small subset of adverse events occurring in human subjects participating in research will meet these three criteria for an unanticipated problem. Furthermore, there are other types of incidents, experiences, and outcomes that occur during the conduct of human subjects research that represent unanticipated problems but are not considered adverse events. For example, some unanticipated problems involve social or economic harm instead of the physical or psychological harm associated with adverse events. In other cases, unanticipated problems place subjects or others at increased risk of harm, but no harm occurs.

### 8.4.2 UNANTICIPATED PROBLEMS REPORTING

All UPs will be reported to UNC IRB within 48 hours of the PI becoming aware of the event.

### 8.4.3 REPORTING UNANTICIPATED PROBLEMS TO PARTICIPANTS

Participants will be given any new information gained during the course of the study that might affect their willingness to continue participation in the study.

## 9 STATISTICAL CONSIDERATIONS

### 9.1 STATISTICAL HYPOTHESES

As this is an exploratory study, there is no hypothesis testing. Analyses will focus on descriptive comparison of baseline and follow-up scores on primary and secondary outcomes.

### 9.2 SAMPLE SIZE DETERMINATION

As this is an exploratory study, sample size will be determined on the feasibility of completion within the time period, as well as gathering sufficient data and experience to evaluate the feasibility of the intervention.

### 9.3 POPULATIONS FOR ANALYSES

The primary analyses will be conducted using an intent-to-treat approach. Supportive exploratory analyses may be conducted to consider samples with greater completion of study intervention visits. Since this is an exploratory trial, the nature of these supportive analyses will be based on observed patterns of intervention contacts.

### 9.4 STATISTICAL ANALYSES PLAN

Feasibility metrics (proportions) will be calculated as described above. Based on our prior OA trials and other studies (37, 39, 70), we expect that about 90% of patients will be eligible based on the PAVS, about

35% of those eligible based on EMR evidence will meet all eligibility criteria and enroll, and the retention rate will be about 90%. For measures of feasibility, appropriateness and acceptability administered to providers, we will calculate scores (median, range) for each domain, as well as proportions of those who agree vs. disagree with each item. For measures of efficacy, we will assess feasibility of administration, particularly the proportion of participants with complete accelerometer data. Means and standard deviations for continuous variables and percentages for categorical variables will be calculated, and paired t-tests assess differences between pre-test and post-test MVPA and secondary outcomes Statistical significance will be assessed at the p=0.05 level.

# 10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

## 10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

### 10.1.1 INFORMED CONSENT PROCESS

#### 10.1.1.1 CONSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS

Consent forms describing in detail the study intervention, study procedures, and risks will be given to the participant and verbal documentation of informed consent will be completed prior to starting the study intervention.

#### 10.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

Once a potential participant meets the medical record and telephone screening criteria for eligibility, and is interested in participating, the study team member will begin the verbal consenting process by phone. If the participant does not have time to complete the verbal consent, the study team member will arrange a date and time to call the participant back. No other study activities will occur until this process is completed.

We will use a UNC IRB approved consent form / script with included language that satisfies the HIPAA requirements and outlines the protection of health information utilized in the study.

Verbal informed consent will be obtained by a trained study team member. The study team member will read the IRB approved verbal consent script to the potential participant and provide an opportunity for him/her to ask any questions that they may have about the research study. We anticipate this process to take approximately 20 minutes, but this time will not be limited should a participant have additional questions or concerns regarding the study. During this phase of the consent process, it will be stressed that the participant is not obligated to participate in the study, that participation is completely voluntary, and that he/she may withdrawal from the study at any time without penalty. Also, potential risks from participating in the study will be outlined in the consent form, as are the measures taken to protect against study specific risks. Once the information in the consent form is fully reviewed and understood by the individual, he/she will be asked to decide at that time if they would like to voluntarily participate in the research study. If the individual does choose to participate in the study, the study team member will document in REDCap the date verbal consent is collected. Each enrolled participant will then be mailed a copy of the consent form to keep for their records.

If after review of the consent form, the potential participant is not sure they would like to participate in the study at this time, they may choose to consider the study further, and then contact the study team if they decide later that they would like to participate.

Once verbal informed consent has been collected, the study team member will mail the participant a HIPAA authorization, and no activities will commence until this is received by the study team.

Participants will only be included if they have capacity to give legally effective consent. Additionally, this study will only recruit participants whom are English speakers.

### 10.1.2 STUDY DISCONTINUATION AND CLOSURE

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 to study participants, investigator, funding agency, and regulatory authorities. If the study is prematurely terminated or suspended, the PI will promptly inform study participants, the IRB, and sponsor/funding agency and will provide the reason(s) for the termination or suspension. Study participants will be contacted, as applicable, and be informed of changes to study visit schedule.

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

- 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 that the primary endpoint has been met
- Determination of futility

The study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the funding agency, sponsor, IRB or other relevant regulatory or oversight bodies (OHRP, SO).

### 10.1.3 CONFIDENTIALITY AND PRIVACY

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, the safety and oversight monitor(s), and the sponsor(s) and funding agency. This confidentiality is extended to the data being collected as part of this study. Data that could be used to identify a specific study participant will be held in strict confidence within the research team. No personally-identifiable information from the study will be released to any unauthorized third party without prior written approval of the sponsor/funding agency.

All research activities will be conducted in as private a setting as possible.

The study monitor, other authorized representatives of the sponsor or funding agency, representatives of the IRB, regulatory agencies or representatives from companies or organizations supplying the product, may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the participants in this study.

The study participant’s contact information will be securely stored on a secure study database for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by the reviewing IRB, Institutional policies, or sponsor/funding agency requirements.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be stored on a secure UNC server. The study data entry and study management systems used by research staff will be secured and password protected. At the end of the study, all study databases will be de-identified and archived on a secure UNC server.

Measures Taken to Ensure Confidentiality of Data Shared per the NIH Data Sharing Policies

It is NIH policy that the results and accomplishments of the activities that it funds should be made available to the public (see *https://grants.nih.gov/policy/sharing.htm*). The PI will ensure all mechanisms used to share data will include proper plans and safeguards for the protection of privacy, confidentiality, and security for data dissemination and reuse (e.g., all data will be thoroughly de-identified and will not be traceable to a specific study participant). Plans for archiving and long-term preservation of the data will be implemented, as appropriate.

Certificate of Confidentiality

To further protect the privacy of study participants, the Secretary, Health and Human Services (HHS), has issued a Certificate of Confidentiality (CoC) to all researchers engaged in biomedical, behavioral, clinical or other human subjects research funded wholly or in part by the federal government. Recipients of NIH funding for human subjects research are required to protect identifiable research information from forced disclosure per the terms of the NIH Policy (see *https://humansubjects.nih.gov/coc/index*). As set forth in 45 CFR Part 75.303(a) and NIHGPS Chapter 8.3, recipients conducting NIH-supported research covered by this Policy are required to establish and maintain effective internal controls (e.g., policies and procedures) that provide reasonable assurance that the award is managed in compliance with Federal statutes, regulations, and the terms and conditions of award. It is the NIH policy that investigators and others who have access to research records will not disclose identifying information except when the participant consents or in certain instances when federal, state, or local law or regulation requires disclosure. NIH expects investigators to inform research participants of the protections and the limits to protections provided by a Certificate issued by this Policy.

### 10.1.4 FUTURE USE OF STORED DATA

Data collected for this study will be analyzed and stored on a secure UNC server. After the study is completed, the de-identified data will be made available to other researchers, available by request to the PI. Investigators requesting study data must adhere to regulatory requirements for data use (e.g., IRB approvals, data use agreements). No biological samples are collected for this study.

### 10.1.5 KEY ROLES AND STUDY GOVERNANCE

| **Principal Investigator** |
|---|
| Kelli D. Allen, PhD |
| University of North Carolina at Chapel Hill |
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| 919-966-0558 |
| kdallen@med.unc.edu |

### 10.1.6 SAFETY OVERSIGHT

Because this study involves only survey-based assessments and participation in mild / moderate physical activity programs, this is a minimal risk study we do not believe it requires a data safety monitoring board. However, we will appoint a board or independent safety monitor if advised by the NIH.

### 10.1.7 CLINICAL MONITORING

Since this is a single site study there will not be site visits conducted by the PI or co-investigators. However, we will monitor the fidelity of intervention delivery as described above.

### 10.1.8 QUALITY ASSURANCE AND QUALITY CONTROL

Quality control (QC) procedures will be implemented as follows:

**Informed consent ---** During the consenting process, the study team member will review the completed consent document to ensure the participant has signed and dated the consent form accurately prior to completing any other study activities.

**Source documents and the electronic data ---** No data will be captured on source documents; all data from study measures and study interventions will be entered directly into the study database.

**Intervention Fidelity** — Consistent delivery of the study interventions will be monitored throughout the intervention phase of the study. Procedures for ensuring fidelity of intervention delivery are described in **Section 6.2**

**Protocol Deviations** – The study team will review protocol deviations on an ongoing basis and will implement corrective actions when the quantity or nature of deviations are deemed to be at a level of concern.

Should independent monitoring become necessary, the PI will provide direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor/funding agency, and inspection by local and regulatory authorities.

### 10.1.9 DATA HANDLING AND RECORD KEEPING

#### 10.1.9.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

Study data will be stored on a secure UNC server in a folder accessible only to IRB-approved study team members. We will use REDCap to store all patient information and dispositions, responses to screening and outcome assessments. REDCap is a secure web application supported at UNC that can be used to build and manage case report forms, surveys, and other data capture mechanisms.

#### 10.1.9.2 STUDY RECORDS RETENTION

Research study records will be maintained for no less than 6 years following the completion of the study, after which time personal identifying information will be removed. Research information in a subject's medical record will be kept indefinitely. No records will be destroyed without the written consent of the sponsor/funding agency, if applicable. It is the responsibility of the sponsor/funding agency to inform the investigator when these documents no longer need to be retained.

### 10.1.10 PROTOCOL DEVIATIONS

This protocol defines a protocol deviation as any noncompliance with the clinical trial protocol, ICH GCP, or Manual of Procedures (MOP) requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions will be developed by the site and implemented promptly.

These practices are consistent with ICH GCP:

- Section 4.5 Compliance with Protocol, subsections 4.5.1, 4.5.2, and 4.5.3
- Section 5.1 Quality Assurance and Quality Control, subsection 5.1.1
- Section 5.20 Noncompliance, subsections 5.20.1, and 5.20.2.

It will be the responsibility of the site investigator to use continuous vigilance to identify and report deviations that impact participant safety to the UNC IRB within 7 business days of the time the PI becomes aware to the event, if the protocol deviation harmed participant(s) or others or placed participant(s) or others at increased risk of harm. Otherwise, protocol deviations/violations that occur but do not affect participant safety will be submitted with the routine safety reports as noted. Protocol deviations will be sent to the reviewing IRB per their policies. The site investigator will be responsible for knowing and adhering to the reviewing IRB requirements. Further details about the handling of protocol deviations will be included in the MOP.

### 10.1.11 PUBLICATION AND DATA SHARING POLICY

This study will be conducted in accordance with the following publication and data sharing policies and regulations:

- National Institutes of Health (NIH) Public Access Policy, which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central upon acceptance for publication.

This study will comply with the NIH Data Sharing Policy and Policy on the Dissemination of NIH-Funded Clinical Trial Information and the Clinical Trials Registration and Results Information Submission rule. As such, this trial will be registered at ClinicalTrials.gov, and results information from this trial will be submitted to ClinicalTrials.gov. In addition, every attempt will be made to publish results in peer-reviewed journals. Data from this study may be requested from other researchers after the completion of the primary endpoint by contacting the study PI. Considerations for ensuring confidentiality of these shared data are described in Section **Error! Reference source not found.**

### 10.1.12 CONFLICT OF INTEREST POLICY

The independence of this study from any actual or perceived influence is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the design and conduct of this trial. The study leadership in conjunction with the National Institute on Aging has established policies and procedures for all study group members to disclose all conflicts of interest and will establish a mechanism for the management of all reported dualities of interest.

## 10.2 ADDITIONAL CONSIDERATIONS

N/A

## 10.3 ABBREVIATIONS

| | |
|---|---|
| AE | Adverse Event |
| CCM | Chronic Care Management |
| CMS | Center for Medicare and Medicaid Services |
| CoC | Certificate of Confidentiality |
| CFR | Code of Federal Regulations |
| DHHS | Department of Health and Human Services |
| EMR | Electronic Medical Record |
| GCP | Good Clinical Practice |
| HIPAA | Health Insurance Portability and Accountability Act of 1996 |
| ICH | International Council on Harmonisation |
| IPAQ | International Physical Activity Questionnaire |
| IRB | Institutional Review Board |
| MOP | Manual of Procedures |
| MI | Motivational Interviewing |
| MVPA | Moderate to Vigorous Intensity Physical Activity |
| NCNC | North Carolina Network Consortium |
| NIH | National Institutes of Health |
| OA | Osteoarthritis |
| OAAA | Osteoarthritis Action Alliance |
| OARSI | Osteoarthritis Research Society International |
| OA-PCP | Osteoarthritis Physical activity Care Pathway |
| OHRP | Office for Human Research Protections |
| ORBIT | Obesity-Related Behavioral Intervention Trials |
| PA | Physical Activity |
| PI | Principal Investigator |
| PROMIS | Patient-Reported Outcomes Information System |
| QC | Quality Control |
| SAE | Serious Adverse Event |
| NRS | Stanford Numeric Rating Scale (NRS) for Fatigue |
| UNC | University of North Carolina |
| WOMAC | Western Ontario and McMaster Universities Osteoarthritis Index |

## 10.4 PROTOCOL AMENDMENT HISTORY

| Version | Date | Description of Change | Brief Rationale |
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