Title: Staying Positive with Arthritis: A Program to Improve Quality of Life

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Abstract

Background: Osteoarthritis (OA) is a prevalent and disabling source of chronic pain for which African Americans (AAs) bear a disproportionate burden. The purpose of this study is to test a patient-centered, non-invasive intervention to improve pain outcomes and reduce disparities in AA and White Veterans with knee OA. The intervention is designed to increase positive affect (PA), that is, enjoyable feelings such as happiness or contentment, the health benefits of which are well-documented.

Objectives: The primary aim of this study is to evaluate the impact of a PA intervention on pain and physical functioning in AA and white Veterans with knee OA through a randomized, controlled, clinical trial. We hypothesize that patients randomized to a PA intervention will experience improved pain and functioning compared to patients randomized to an attention control (AC) program, and that these improvements will be larger for AAs than for whites. The secondary aim of this study is to identify variables that mediate the effects of the PA intervention on pain and functioning. We hypothesize that the effects of the PA intervention will be mediated by psychosocial variables known to be associated with OA outcomes or racial differences in OA outcomes (e.g., depression, self-efficacy, pain coping, perceived discrimination).

Methods: A randomized, controlled, 2-arm design will be used to compare the effects of a 6-week PA intervention with that of an AC program on pain and functioning at 1, 3, and 6-months post-intervention among AA and white Veterans with knee OA. Approximately 180 AA and 180 white primary care patients with knee pain symptoms consistent with OA will be recruited from participating VA medical centers following the original protocol. After the original patients have been recruited, approximately 240 additional primary care patients with knee pain symptoms consistent with OA will be recruited from participating VA medical centers using expanded inclusion criteria that take into account ICD-10 codes. Eligible participants will complete an in-person baseline assessment of study outcomes, mediators, and control variables and be randomized to a 6-week PA or AC program. The PA program consists of completing 6 at-home activities (1 per week) that have been shown to increase positivity. The AC program consists of 6 affectively neutral activities. Both groups will receive weekly telephone calls from trained interventionists to clarify instructions for the next week's activity and assess completion of the previous week's activity. Outcomes and proposed mediating variables will be assessed via telephone surveys at 1 month, 3 months, and 6 months post-intervention. Study outcomes include self-reported pain and physical functioning as measured by the Western Ontario MacMaster Index. Hypothesized mediators include depressive symptoms, positive/negative affect, satisfaction with life, arthritis self-efficacy, pain coping, pain catastrophizing, perceived discrimination, global stress, and social support. To assess intervention impact over time and by race (primary aim), we will fit linear mixed models that allow repeated measures on the

continuous outcomes for each participant and assess change in outcomes over time. To identify mediators (secondary aim), we will use a multiple mediator bootstrap approach to assess whether the effect of the intervention is mediated by the hypothesized mediators.

List of Abbreviations

Provide a list of all abbreviations used in the protocol and their associated meanings.

AA(s) – African American(s)

AC – Attention Control

CHERP – Center for Health Equity Research and Promotion

CIRB – Central Institutional Review Board

DSM-IV – Diagnostic and Statistical Manual of Mental Disorders, 4th edition

HSR&D – Health Services Research and Development

ICD-9 – International Classification of Diseases – 9th Revision

ICD-10 – International Classification of Diseases – 10th Revision

IRB – Institutional Review Board

LSI – Local Site Investigator

OA – Osteoarthritis

OARSI – OA Research Society International

PA – Positive Affect

PBRN – VA Women's Health Practice-Based Research Network

PHI – Protected Health Information

PHQ – Patient Health Questionnaire

PI – Principal Investigator

PKI – Public Key Infrastructure

PVAMC – Philadelphia VA Medical Center

TBN – To Be Named

TJR – Total Joint Replacement

US – United States

VHA – Veterans Health Administration

VA – Veterans Affairs

VAPHS – VA Pittsburgh Healthcare System

WH(s) – White(s)

WOMAC – Western Ontario MacMaster

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2.0 Introduction

2.1 Background and Study Rationale

2.1.1. Osteoarthritis causes substantial chronic pain and disability. Arthritis affects roughly 1 in 5 (46.4 million) adults in the United States (US) and half of US adults over age 65.[1] Arthritis affects 16% of Veterans Affairs (VA) patients, making it one of the most prevalent chronic conditions among VA patients.[2] Arthritis is the most common cause of disability and causes more functional limitations than heart disease or diabetes.[1] Osteoarthritis (OA), the most common form of arthritis, is associated with disability, high health care costs, and reduced quality of life.[3,4] People with OA are more likely to have physical and mental health comorbidities and receive more medications.[5] OA accounts for $185.5 billion in annual medical expenses; $36.1 billion are patient out-of-pocket expenses.[4] The current project focuses on improving OA-related pain and functioning to reduce the burden of this significant clinical condition.

2.1.2. There are racial disparities in the impact and management of OA. Radiographic knee OA has been found in 52% of African Americans (AAs) compared to 36% of whites (WHs).[6] Among people reporting physician-diagnosed arthritis, AAs are more likely than WHs to experience severe joint pain, daily activity limitations, and work limitations.[7] In Veteran patients with knee OA, AAs report more pain and functional impairment than WHs.[8,9] Treatments used to manage OA also differ between AAs and WHs. Compared to WHs with OA, AAs are prescribed lower doses of drugs for OA and are less likely to adhere to OA drug regimens.[10] Our research found that AAs, more so than WHs, prefer less invasive and non-traditional OA treatments over more aggressive treatments.[11,12] AAs are more likely to use massage, prayer, creams, and over-the-counter medications to treat OA symptoms,[13] whereas WHs are more willing to undergo total joint replacement (TJR), the only effective option for advanced OA.[14] Our work suggests that treatment preferences are a major factor driving racial disparities in TJR utilization.[12] The current project is designed to reduce racial disparities in OA using a novel intervention that is aligned with African American (AA) preferences for less invasive and non-traditional treatments and targets mechanisms that underlie racial disparities in OA pain and functioning.[9,15]

2.1.3. More effective treatments for managing OA are needed. There is no known cure for OA and no drug is available to stop the progression of the disease. The goals of treatment are to alleviate symptoms, maintain and improve physical functioning, reduce disability, improve quality of life, and provide patient education.[16] Over 50 treatments for OA exist, including non-pharmacological (e.g., self-management, exercise, acupuncture), pharmacological (e.g., analgesics, intra-articular corticosteroids, topical creams), and surgical (e.g., arthroscopy, TJR) treatments.[17] Existing treatments yield only small to moderate improvements in pain.[17] A review found that the combined effect size (Cohen's d) of all non-pharmacological treatments was 0.25, with self-management/patient education having the smallest effect on pain (Cohen's d = 0.06).[17] Pharmacological treatments were only slightly more effective (combined Cohen's d = 0.39), and all were associated with major adverse side effects.[17] There is clearly a need for more effective treatments for OA with minimal side effects or complications.

2.1.4. OA treatments that can reduce racial disparities in OA pain and functioning are needed. A review of randomized, controlled trials of non-pharmacological OA interventions found that only 3 of 25 studies included AA participants.[18] Only 2 studies reported on racial differences and both found no racial difference in intervention efficacy.[18] Two studies, including one by our research team, focused on improving the acceptability of TJR among AAs, with some success.[19,20] Given that TJR is reserved for advanced cases of OA and that some AA patients with advanced OA still prefer non-surgical management, non-invasive interventions that can reduce disparities in pain and functioning across all disease stages are critical. A review of OA interventions targeting disadvantaged populations (e.g., AAs, low-literacy patients) found only 3 that focused on AAs with OA and only 1 included a white (WH) comparison group so that the effect of the intervention on disparities could be examined.[21] Most interventions involved patient education using culturally tailored self-management programs. Overall, self-management/education programs showed small and short-lived benefits.[21] Given that existing interventions have done little to reduce OA racial disparities, we propose a new approach to improve pain and reduce pain disparities in patients with OA.

2.1.5. Positive affect improves health through biological, psychological, and social pathways. The proposed intervention is from the field of psychology and is designed to increase positive affect (PA). PA is defined as feelings that are experienced when one is pleasurably engaged with the environment (e.g., joy, excitement, contentment).[22] PA is associated with reduced mortality and other positive physical and mental health

outcomes.[22,23] PA impacts health through biological processes, such as the release of endogenous opioids and stress hormones.[22,24] PA also promotes health through psychosocial pathways by increasing creativity, curiosity, openness to new information, and the desire to connect with others.[25] This can promote health by improving our ability to overcome barriers to positive health behaviors, increasing openness to health recommendations, and strengthening social ties.

2.1.6. Increasing PA can improve OA pain management and reduce OA disparities through psychosocial mechanisms. The conceptual model in

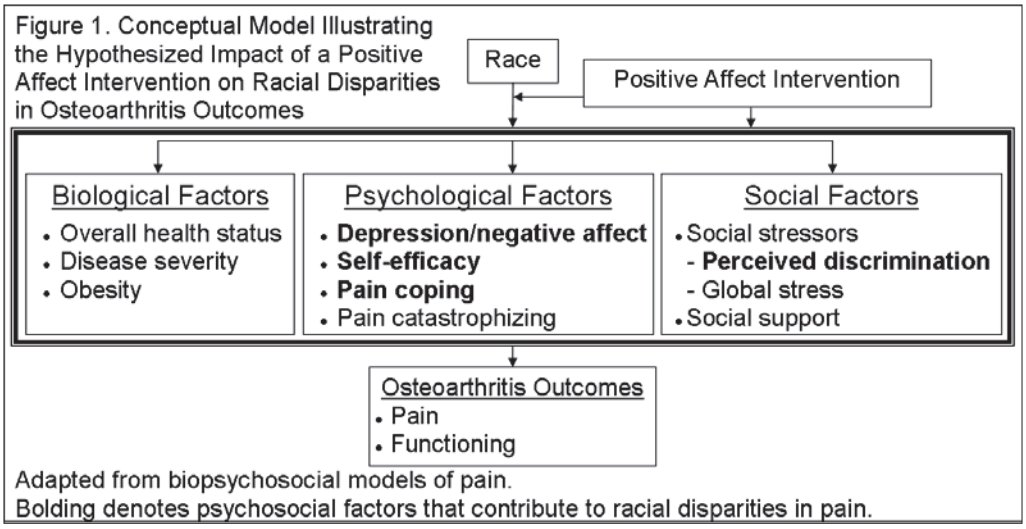

Figure 1 illustrates how PA can reduce racial disparities in OA outcomes. We developed this model by adapting biopsychosocial models of pain and arthritis[26,27] to incorporate factors underlying racial differences in pain and functioning.[15,28] The biopsychosocial model is featured in the VHA's National Pain Management Strategy and in the Institute of Medicine's call for a cultural transformation for pain treatment.[29,30] According to the model, pain is determined by biological, psychological, and social factors.[26,27] Because psychosocial factors can cause pain to be more or less extreme than one would expect based on biological indicators, targeting psychosocial factors may help reduce pain.

Our conceptual model highlights psychosocial factors that are associated with OA outcomes (Figure 1).[15,27] Depression often co-occurs with OA and is associated with worse pain and functioning and worse outcomes following TJR.[31-33] Pain-related cognitions, including self-efficacy, pain coping strategies, and pain catastrophizing (i.e., magnifying pain symptoms), are associated with OA pain severity and functional impairment.[27] Social factors such as stress and the availability of social support are also associated with OA outcomes.[27] Factors in bold contribute to racial disparities in pain related

to OA and other chronic conditions.[15,28] Allen et al. found that negative affect, poor self-efficacy, and emotion-focused coping accounted for worse OA pain and functioning among AAs than WHs, with negative affect being the strongest mediator.[15] Other studies show that perceived racial discrimination, a social stressor frequently encountered by AAs, is associated with greater bodily pain.[28]

2.1.7. Increasing PA may improve OA outcomes and reduce racial disparities in OA. Evidence indicates that PA has clinically meaningful positive effects on pain, OA outcomes, and several psychosocial factors in Figure 1. Our work shows that teaching people activities to increase PA is associated with a long-term reduction in self-reported bodily pain equivalent to a medium effect size.[34] Research by others also demonstrates that, whether inherently present or induced experimentally, PA is associated with reduced pain and greater pain tolerance.[22] Observational studies show that naturally occurring levels of PA predict less pain in subsequent weeks in women with OA or fibromyalgia[35] and better functioning two years following a hip fracture (e.g., Cohen's d effect sizes comparing those with high PA vs. those with depression at 2, 6, 12, 18, and 24 months following a hip fracture ranged from 0.29 to 0.44 for usual walking speed and 0.29 to 0.44 for chair stand speed).[36] Among people with OA knee pain, those with high PA also walk an average of 8.5% more steps per day than those with low PA.[37]

Experimental studies show that inducing PA in a controlled setting has short-term effects on pain. For example, watching a funny movie was associated with decreased self-reported pain and decreased pain medication in adults with chronic pain in a long-term care facility.[38] A study in an experimental setting also demonstrated that inducing optimism using a well-established PA activity caused lower ratings of pain intensity in response to a pain induction task (mean pain intensity rating of 57.55 vs. 68.10 on a scale of 0 to 100; Cohen's d = 0.55).[39] PA also affects psychosocial factors that contribute to OA outcomes and racial disparities in OA outcomes. For instance, it is well-established that PA interventions significantly reduce depressive symptoms (medium effect size [Cohen's d = 0.65, converted from r = 0.31], on average).[40] In addition, PA increases creativity, curiosity, and openness to new information,[25] which could improve OA through several of the psychosocial factors in Figure 1. For example, increasing PA may result in better coping strategies, more self-efficacy, and less pain catastrophizing. We will collect data in the proposed study to determine whether PA improves OA outcomes through these mechanisms.

Finally, a PA intervention is likely to be particularly beneficial to racial minority patients by guarding against the negative impact of race-based social

stress.[41,42] Disproportionate exposure to social stress, especially in the form of discrimination, is believed to be at the heart of racial disparities in health.[43] As part of her VHA HSR&D Career Development Award (RCD 06-287), Dr. Hausmann conducted several studies showing that perceived discrimination is associated with poorer health in a variety of patient populations.[44-46] Her work showed that discrimination impacts health by taking a negative toll on emotional wellbeing and one's overall outlook on life. In AA, Asian American, and Hispanic/Latino patients with hypertension, Dr. Hausmann and colleagues found that depression, anxiety, and cynical hostility mediated the negative effect of perceived discrimination on overall health.[46] Dr. Hausmann's work also shows that perceived discrimination among AA Veterans with OA is associated with less PA during encounters with orthopedic surgeons.[47] These studies suggest that guarding against the psychological and emotional impact of perceived discrimination should reduce its negative effects on health. In fact, studies show that naturally-occurring PA reduces the association between perceived discrimination and depressive symptoms, and experimentally inducing PA using a self-affirmation activity reduces perceptions of discrimination.[41,42] The proposed study tests an intervention that can potentially ameliorate the negative health effects of perceived discrimination by increasing PA, a natural buffer against psychosocial stressors like discrimination.

2.1.8. PA can be increased using simple, evidence-based activities. Studies show that PA can be increased through a variety of simple, evidence-based activities.[23,40,48] The commonality across techniques is that they increase one or more of the three core components of subjective wellbeing: pleasure, engagement, and/or meaning in one's life.[23] Strategies shown to improve wellbeing through one of these routes include activities involving gratitude, kindness, optimism, mindfulness, self-affirmation, identifying and using personal strengths, reflecting on good things, forgiveness, or some combination thereof.[40,48] PA interventions range in complexity from single-episode events carried out independently to multi-faceted, 12-week programs administered by trained clinicians. A meta-analysis found that PA interventions increased wellbeing and reduced depressive symptoms, with interventions consisting of multiple PA activities and of longer durations producing the largest effects.[40] We propose to test a 6-week PA intervention consisting of multiple evidence-based activities.

2.1.9. PA interventions have been translated for use in clinical patient populations. Most PA intervention studies focus on outcomes such as wellbeing or depressive symptoms and report improvements in these

outcomes in both depressed and non-depressed populations.[40] Recent studies also examine PA interventions tailored for use in clinical populations.[49-53] Randomized trials testing the effects of PA activities over and above disease-specific patient education and behavioral contracts found that PA increased positive health behaviors.[51,52] Compared to control groups that received educational materials and completed behavioral contracts, the addition of PA activities increased physical activity at 12 months in patients with coronary artery disease (PA group walked an average of 3.4 miles per week more)[51] and improved medication adherence in AA patients with hypertension (42% in PA group vs. 36% in control group adhered).[52] These studies demonstrate that PA can be used to increase desired health behaviors beyond the effects of standard approaches, such as patient education and behavioral contracts. PA interventions have also been developed for patients with acute cardiovascular disease, newly-diagnosed HIV, and schizophrenia.[49,50,54] Feasibility trials show that PA activities are acceptable in these patient populations and show promising preliminary benefits for outcomes such as optimism, depressive symptoms, anxiety, subjective wellbeing, health-related quality of life, overall psychological wellbeing, and hope.[49,50,54]

2.1.10. Summary of Background. OA is a painful and disabling condition that disproportionately affects AAs. Existing OA treatments yield only small to moderate improvements in pain and are not effective at reducing racial disparities in OA pain. Novel interventions aligned with the biopsychosocial model of pain and that target psychosocial factors associated with OA outcomes and disparities in OA outcomes are needed. A PA intervention has the potential to improve pain and functioning and reduce racial disparities in patients with OA through multiple psychosocial mechanisms. PA interventions have been developed for clinical patient populations but have not yet been fully tested in patients with OA or in Veterans, nor have their effects on racial differences in clinical outcomes been examined. This study will address these gaps by testing the impact of an evidence-based PA intervention on pain and functioning in AA and WH Veterans with OA.

3.0 Objectives

Our team conducted extensive pilot work to design a psychosocial intervention for Veterans with OA that incorporates evidence-based strategies for producing meaningful and sustainable increases in PA. The short-term objective of the current study is to test the impact of this PA intervention on pain and functioning in AA and WH Veteran patients with knee OA. Veterans

will be assigned to a 6-week PA intervention consisting of weekly PA at-home activities (PA intervention) or a 6-week program consisting of affectively neutral activities previously used in the control groups of other PA intervention studies (attention control). We hypothesize that the PA intervention will improve pain and functioning in Veterans with OA through its impact on psychosocial factors associated with OA outcomes (e.g., affective state, self-efficacy).[22,27] Given that psychosocial factors account for racial differences in OA, we further expect the benefits of the PA intervention to be larger for AAs than for WHs. This study therefore contributes to the long-term objective of reducing racial disparities in OA pain management among Veterans. The aims of this randomized, controlled trial are:

Primary Aim: To evaluate the impact of a PA intervention on pain and physical functioning in a sample of AA and WH Veterans with knee OA.

Hypothesis 1: Patients who are randomized to complete the PA intervention will experience improved pain and functioning compared to patients who are randomized to complete an attention control program.

Hypothesis 2: Improvements in pain and functioning associated with the PA intervention will be larger for AAs than for WHs.

Secondary Aim: To identify psychosocial variables that mediate the effects of the PA intervention on pain and functioning.

Hypothesis 3: The effects of the PA intervention on pain and functioning will be mediated by psychosocial variables known to be associated with OA outcomes or racial differences in OA outcomes (e.g., depression, self-efficacy, pain coping).

Exploratory Aim: Although there will not be adequate power to conduct formal tests to determine whether intervention effects are moderated by patient characteristics other than race, we will conduct exploratory analyses to examine sex as an additional moderator.

4.0 Resources and Personnel

This multi-site study will be led by **Principal Investigator (PI) Leslie Hausmann, PhD**. Dr. Hausmann is a core investigator at the Center for Health Equity Research and Promotion (CHERP), a national VA HSR&D Center of Innovation co-located at the VA Pittsburgh Healthcare System (VAPHS) and the Philadelphia VA Medical Center (PVAMC). As PI, Dr. Hausmann will oversee the conduct and execution of all phases of this project

and will serve as the Local Site Investigator (LSI) for the VAPHS site. She will supervise the hiring and training of research staff at VAPHS; monitor patient recruitment, administration of the intervention, and follow-up assessments at VAPHS; ensure quality of data management, analysis, and interpretation; prepare all project reports; manage the project budget; and lead efforts to disseminate study findings. She will also lead future implementation efforts to extend the benefits of PA activities to as many Veterans as possible.

Dr. Ibrahim will serve as a **Co-Investigator** and **LSI at PVAMC**. He will oversee the hiring and the training of the PVAMC staff. He will work with Dr. Hausmann to assure successful conduct of all the study components at the PVAMC site. Dr. Ibrahim will participate in weekly or as-needed conference calls with Dr. Hausmann and the study staff from participating sites to review study progress and discuss issues of recruitment, enrollment, and data collection. He will also participate in bi-weekly or as-needed conference calls with the full investigative team to discuss study progress in meeting participant recruitment and other study goals and to review emerging data.

As a Co-Investigator, Dr. Rollin M. Gallagher will participate in regular investigative team meetings to advance the goals of the study and maximize the future impact of this work by situating it in the broader context of VHA pain management efforts.

As a Co-Investigator, Dr. C. Kent Kwoh will participate in regular conference calls with the investigative team to provide expertise on racial disparities in the treatment of OA and to assist with the interpretation and dissemination of findings.

As a Co-Investigator, Dr. Acacia Parks will guide the content, format, and delivery of the study intervention; train research staff members to administer the intervention; and work with the team to ensure consistency in the delivery of the intervention throughout the recruitment period. She will participate in conference calls with the study team and will assist in interpreting results within the larger literature on positive psychology. She will also contribute to presentations, manuscripts, and the development of future projects.

As a Co-Investigator, Dr. Ernest Vina will provide input on the design and conduct of the project, participate in regular conference calls with the investigative team, and aid in the interpretation and dissemination of findings.

As a Co-Investigator, Dr. Debra Weiner will provide clinical expertise in pain management, assistance with patient recruitment through her affiliation with the VAPHS pain clinic, and methodological guidance regarding outcome measurement. Dr. Weiner will also participate in investigative team meetings to advance the goals of the study.

As a Co-Investigator and the senior biostatistician, Dr. Youk will design, direct, and supervise randomization procedures and all data analyses for the study. She will coordinate and supervise the activities of the Programmer

Analyst and ensure the integrity, verification, and documentation of all preliminary and final analyses. She will participate in regular meetings of the investigative team and assist in data interpretation and writing of manuscripts.

One or more **Programmer Analysts** will be responsible for the creation and maintenance of all project databases and tracking systems. S/he will coordinate data tracking, data entry, data verification, and data documentation across study sites and will train Research Assistants regarding data entry and tracking procedures. S/he will be responsible for extracting data from electronic medical records to identify potential participants. S/he will generate and distribute data and tracking reports as requested by the PI. S/he will perform data verification and quality assurance activities, prepare analytic datasets, and conduct preliminary study analyses under the supervision of the lead biostatistician, Dr. Youk.

A **Project Coordinator** will assist with interviewing, hiring, training and supervising VAPHS project staff. S/he will be involved in the daily management of the project activities and budget including coordination of communication with study investigators and research staff, preparation of Institutional Review Board (IRB) submissions, preparation of progress reports, materials for presentation at scientific meetings, and the final report, as well as manuscripts and correspondence related to the project. She will directly supervise the VAPHS Research Assistants. S/he will also serve as an Interventionist at VAPHS. S/he will be responsible for recruitment and administering all aspects of the study intervention, including the delivery of the randomly assigned intervention or control activity booklets to participants at the baseline visit, orienting participants to their assigned booklet, reviewing instructions for the first activity at the baseline visit, and conducting weekly telephone calls with each patient to ask about their experience with the prior week's activity, review the next week's activity, and help participants trouble-shoot anticipated barriers to completing activities.

Additional Interventionists, Research Assistants, and Local Project Coordinators will be hired as needed at participating sites and will be responsible for administering all aspects of the study intervention, including the delivery of the randomly assigned intervention or control activity booklets to participants at the baseline visit, orienting participants to their assigned booklet, reviewing instructions for the first activity at the baseline visit, and conducting weekly telephone calls with each patient to ask about their experience with the prior week's activity, review the next week's activity, and help participants trouble-shoot anticipated barriers to completing activities. Interventionists will not be directly involved in the collection of post-intervention follow-up data. They may assist with identifying and screening patients, completing and documenting the informed consent process, scheduling patients for study appointments, administering in-person baseline patient surveys, abstracting clinical data from electronic medical records, and entering data into project databases. Research Assistants will assist with study recruitment, data collection, and data entry. They will assist with

identifying and screening patients, completing and documenting the informed consent process, and scheduling patients for study appointments. They will also be responsible for conducting all telephone post-intervention follow-up surveys. Research Assistants responsible for collecting follow-up surveys will remain blind to whether participants have been randomization to the intervention or control arm of the study.

As a Collaborator, Diane Carney, MA, will serve as an advisor to the PI and study team to ensure that approved recruitment strategies used by the study team are designed so that they effectively reach women Veterans. Ms. Carney is Program Manager for the VA Women's Health Practice-Based Research Network (PBRN) at the VA Palo Alto Healthcare System. Ms. Carney will provide the PI with general guidance regarding strategies for recruiting women Veterans and strategies for clinic-based research (e.g., how to build relationships with PBRN clinic staff, via the local PBRN Site Leads). She will also serve as a liaison between the PI and LSIs and the PBRN site leads at participating study sites to maximize enrollment of women in the study.

PHI will be accessible to all personnel described in this section except for Diane Carney.

5.0 Study Procedures

5.1 Study Design

5.1.1. Experimental Design.

A randomized 2-arm design will be used to compare the effects of a 6-week PA intervention with that of an Attention Control (AC) condition on pain and functioning at 1, 3, and 6-months post-intervention among AA and WH Veterans with knee OA. We will recruit from participating sites approximately 180 AA and 180 WH primary care patients with symptomatic knee OA following the original protocol. After the initial 360 patients have been recruited using the originally proposed criteria, up to approximately 240 additional patients (including some men and some women, as resources allow) will be recruited to increase power to detect sex differences. Eligible participants will complete an in-person baseline assessment and be randomized to a 6-week PA or AC program. The PA program includes at-home activities (1 per week) shown to increase PA. The AC program includes affectively neutral activities. Both groups will receive weekly telephone calls from study interventionists to assess adherence and review the next week's activity. Participants will be telephoned 1, 3, and 6 months post-intervention to complete follow-up assessments. Those who cannot complete study

assessments over the phone will be permitted to complete them in person if necessary.

5.1.2. Randomization and intervention procedures.

5.1.2.1. Randomization of participants. We will randomize enrolled participants to one of two study arms (PA intervention or AC) using permuted block randomization at the patient level, stratified by study site and patient race. The study statistician will develop the randomization schedule using standard randomization procedures. Once a patient has enrolled and completed the baseline assessment, a study interventionist will open a sealed envelope containing the patient's random assignment. Randomized patients will be included in intent-to-treat analyses.

5.1.2.2. Masking. Participants will not be told whether they have been assigned to the PA or AC arm. Interventionists who deliver the PA and AC programs cannot be blinded to assignment. However, research assistants responsible for all post-intervention assessments will be blinded to treatment assignments.

5.1.2.3. PA intervention program. The PA intervention is based on empirical research regarding how to implement PA interventions to provide maximum and sustained benefits.[55] PA interventions that are administered individually (vs. in a group), are of longer duration (e.g., over multiple weeks vs. 1-time events), and combine multiple activities yield the largest effects.[40] For our PA intervention, we selected the following PA activities, all of which have sustained benefits for wellbeing and had the greatest potential for use in Veterans with OA.

Three Good Things: Participants write down three positive events that happen each day, completing the exercise at the end of each day for 1 week. This activity focuses attention on positive events to overcome our natural predisposition to remember negative events.[56] It has been shown to increase subjective wellbeing and reduce depressive symptoms, with effects lasting for 6 months.[23]

Expressing Thanks: Participants write a thank-you letter to someone who has been kind to them but was never thanked.[23] Writing a letter of thanks provides an immediate and intense increase in gratitude.[57] Reading thank-you letters to the intended recipient produces increases in subjective wellbeing and decreases in depressive symptoms of greater magnitude than the Three Good Things activity.[23]

Making Good Moments Last: Participants practice prolonging the experience of 1 positive moment each day for a week. This cultivates mindfulness, which leads to more frequent positive emotion and enhanced

self-regulation.[58] Research on Mindfulness-Based Stress Reduction demonstrates that mindfulness has numerous physical and psychological benefits.[59] While a full mindfulness meditation practice can be time-consuming to learn and difficult to maintain, this activity is a brief and easy way to enhance mindfulness in everyday life.

Acts of Kindness: Practicing kindness is associated with increased subjective wellbeing.[60] Based on evidence that completing 5 acts of kindness in a single day produces larger improvements in wellbeing than distributing 5 kind acts over a week,[60] participants complete 5 kind acts in 1 day for this activity.

Increasing Pleasant Activity: Participants identify from a list of pleasant activities those that give them a sense of enjoyment or achievement, or bring them closer to others. They then engage in at least 4 pleasant activities per day for a week and record them in an activity diary. Increasing pleasant activities is one of the most well-researched intervention strategies for reducing depression.[48] We include it in our PA intervention based on its effectiveness across different populations and its ease of administration.

Practicing Your Favorite(s): For the first 5 weeks, participants will complete one new activity each week. In week 6, participants will select an activity from previous weeks to complete again. Repeating an activity serves to engage participants in identifying PA activities that appeal to them, and to give them additional practice building PA activities into their daily lives.

5.1.2.4. AC program. The only difference between the PA and AC programs is that patients randomized to the AC arm will receive an activities booklet that contains affectively neutral activities used in control conditions in previous studies testing the impact of PA activities (**Appendix A**).[23,57,61,62] Using AC activities established as structurally similar, yet affectively neutral in previous PA studies assures that any increases in PA or improvement in other variables among participants in the AC arm would be due to placebo effects. This provides the strongest possible comparison condition to achieve our primary study aim, which is to evaluate the impact of a PA intervention on pain and physical functioning. It is important to show that improvements in the PA intervention arm are not simply due to expectations and/or motivation, given that patients who are particularly motivated to be positive may self-select into the study.

5.1.2.5. PA and AC program delivery. PA and AC activities will be delivered using a combination of activity booklets and oral instructions provided during weekly telephone calls from trained interventionists. Interventionist will orient

participants to the booklets and review the first activity at the end of the baseline visit. The booklet contains all instructions patients need to complete the full program. However, the interventionist will conduct weekly telephone calls to provide any additional support patients may need. During these calls, the interventionist will assess whether participants completed the previous week's activity, review instructions for the next week's activity, and help participants trouble-shoot anticipated barriers to completing the next activity. At the conclusion of week 6, the interventionist will encourage participants to continue using activities in the booklet. Introducing a single new activity each week, trouble-shooting barriers to completing each activity, and providing the opportunity to identify and practice activities they find most beneficial are features of efficacious PA interventions.[56] Those who cannot complete study assessments over the phone will be permitted to complete them in person if necessary.

5.1.2.6. Program fidelity. Prior to the start of enrollment, interventionists, research assistants, and LSIs from participating sites will be trained on how to deliver the PA and AC programs in a consistent manor. Those attending the training will learn how to describe each activity accurately and systematically, anticipate and respond to resistance or barriers to completing activities, and provide encouragement when necessary. Once enrollment begins, conference calls will be held from those administering the intervention at participating sites to discuss delivery of the intervention and address questions as they arise. Once frequent conference calls are no longer needed, refresher training sessions via telephone or video-conferencing will be held as needed to maintain treatment integrity for the remainder of enrollment.

5.1.3. Follow up procedures.

Research staff will telephone Veterans to assess outcomes and proposed mediating variables at 1- month (+ or - 1 week), at 3 months (+ or - 1 week), and at 6 months (+ or - 1 week) post-intervention. To maximize study retention, Veterans will receive a card at the baseline visit to help them keep track of upcoming appointments and will be mailed reminder letters prior to the 1, 3, and 6-month follow-up calls. A blank survey will be mailed with the reminder letters for Veterans to refer to during the telephone call. Veterans who cannot complete the follow-up surveys by telephone will also be permitted to complete the surveys in person, if that is more feasible for them. To maintain blinding of staff to randomization assignment, a study staff member at one site may make follow-up calls for participants recruited at another site.

5.1.4. Study population. The target population will be AA and WH Veterans who have symptomatic knee OA. Vulnerable populations will not be recruited in this study. Biological specimens are not a part of this study.

5.1.5. Risks and benefits. There is a possible risk that some participants will experience psychological discomfort while disclosing information about themselves during the surveys. To protect against this risk, study participants will be assured that participation is completely voluntary, that they can refuse to answer any of the study questions, and that they have the right to withdraw from the study at any time without penalty. There is also a risk of breach of confidentiality. To protect against this risk, all data collected from participants will be maintained separately from identifiable information and will be stored in locked filing cabinets and in databases on secure servers located behind the VA firewall to which only the study investigators and designated research staff will have access through the use of VA login and password permissions.

Participants may directly benefit from participating in this study. Research has shown that doing activities such as the ones in the PA intervention in this study reduces pain and increases overall well-being for some people. While it is hopeful that participation in this study will reduce pain and increase well-being of participants assigned to the PA intervention arm, this outcome cannot be guaranteed.

This study will lead to knowledge that will help others and society in general by adding to the scientific knowledge available regarding methods to reduce pain and increase well-being.

Given the minimal nature of the study risks and the potential benefits to be gained from this research, the benefits outweigh the risks for this study.

5.2 Recruitment Methods

5.2.1. Identification and recruitment of participants. We have requested a waiver or alteration of the informed consent process for screening purposes only (CIRB Form 112a). We will use data from the Corporate Data Warehouse (CDW), accessed through the VA Informatics and Computing Infrastructure (VINCI), to identify potential participants meeting eligibility criteria that can be ascertained from administrative data. Specifically, a VINCI programmer will be assigned to the study to help identify Veterans who are non-deceased; are non-Hispanic WH or AA; are 50 years or older; have had a primary care appointment at a participating site in the past 12 months; have

ICD-9 codes indicating a diagnosis of OA; and do not have ICD-9 codes indicating a diagnosis of inflammatory arthritis (rheumatoid arthritis, lupus, psoriatic arthritis, or ankylosing spondylitis), Alzheimer's disease, or dementia. [Note: Diagnoses based on ICD-10 codes will be incorporated after the original study sample size has been met.] The VINCI programmer will create data views that study staff will use to determine potential participants. Staff will then request information about patients meeting the above criteria: names, addresses, telephone numbers, site of care, patientICN, gender, race, ethnicity, age, and date and location of most recent outpatient visit. We will request this data at the beginning of study recruitment and may request updates of potential participants as needed until recruitment targets have been met. A research staff member will download the data provided by VINCI into designated subfolders accessible only to authorized study personnel through the use of VA login and password permissions. Data transfers between CDW and VINCI, and between VINCI and approved study staff, take place entirely behind the VA firewall, so data will remain behind the VA firewall at all times.

Study staff will inform patients in the files provided by VINCI about the study by mail. Mailings will be made in batches throughout the recruitment period until recruitment goals have been met. Mailings to potential participants will include a letter describing the study, a study brochure, and reply card (see Appendix B). The study brochure will provide potential participants with a number they can call to verify the validity of the study. Potential participants will be asked to contact the research team via telephone or postage-paid reply card to express interest in the study or to indicate that they are not interested in participating.

Potential participants who do not opt-out of future contact about the study within 2 weeks following the mailing will be telephoned by research staff to complete a more in-depth screening. In the event that patient contact information provided by VINCI is incomplete or incorrect (e.g., telephone number no longer in service), research staff may access electronic medical records through CPRS to update the contact information obtained from VINCI. For potential participants who cannot be reached after 2 messages have been left at their available telephone numbers, no additional call attempts will be made unless they contact the study staff to indicate that they are interested in being contacted further. In the event that recruitment goals are unable to be met using this calling plan, potential participants who were unable to be reached after the first mailing may be mailed a second time, followed by up to 2 additional telephone messages.

We will supplement this recruitment strategy by placing study brochures in waiting areas of clinics at participating sites. When possible and with permission of the clinic staff, study staff may also be stationed in clinic reception areas so that interested patients may approach our staff to learn about the study and be screened. Depending on the physical layout of reception areas, research staff may set up a table or booth that patients may approach for information about the study.

5.2.2. Participant payments. Enrolled participants will be reimbursed up to $110. Participants will receive $20 after completing the in-person visit baseline visit and each of the 1-month, 3-month, and 6-month follow-up telephone surveys. Participants will also receive $5 after the completion of each of the weekly assessments during the 6-week program. Payments will be delivered in the form of cash, mailed checks, or direct deposit, per local payment policies at participating sites.

5.3 Informed Consent Procedures

Patients who meet the study's eligibility criteria will meet in person with a research team member, who will explain the details of the study and obtain written informed consent. Participants will be advised that they are free to withdraw from the study at any time, and that the information provided by them will be kept strictly confidential.

Eligible patients will be considered to be enrolled in the study after they provide written documentation of informed consent but prior to initiation of the baseline interview or randomization to the PA or AC study arm.

The PI, LSIs, and the project coordinators, Interventionists, and Research Assistants at participating sites will be authorized to obtain informed consent.

All study personnel will have current VA Human Subjects Protections and Good Clinical Practices CITI training and will be trained by the PI or LSIs on the elements of informed consent and the correct process for obtaining informed consent for this study.

5.4 Inclusion/Exclusion Criteria

Inclusion criteria

The target population will be AA and WH Veterans with symptomatic knee OA. Specific inclusion criteria include:

- Age 50 years or older
- Receive primary care at a participating site
- Self-report as non-Hispanic black/AA or non-Hispanic WH
- Frequent, symptomatic knee pain identified using questions from the OA Initiative[63]
- Pain level of 4 or higher on a 0-10 numeric rating scale
- Can speak, read, and write in English

Exclusion criteria

Patients will be excluded if they:

- Report serious problems with hearing, eyesight, or memory
- Report having been diagnosed any type of arthritis other than osteoarthritis or degenerative arthritis
- Report that they are currently being treated or followed for recent cancer
- Report having had a steroid injection into one or both knees in the past 3 months

- Report having had a knee replacement into one or both knees in the past 3 months
- Report having plans to have a knee replacement in one or both knees in the next 6 months
- Report that there is a reason they cannot complete the study procedures, which include telephone calls and program activities that involve reading and writing
- Do not have a telephone number where they can receive telephone calls from research staff
- Screen positive for cognitive impairment on the Six-Item Screener to Identify Cognitive Impairment[64]

5.5 Study Evaluations

5.5.1. Data collection. Outcomes, mediating variables, and covariates will be assessed using validated instruments with strong psychometric properties (refer to cited references below for psychometric information; see **Appendix C** for model study questionnaires).

5.5.1.1. Study outcomes: OA pain and functioning (baseline, 1 month, 3 months, and 6 months post-intervention). The OA Research Society International (OARSI) Standing Committee for Clinical Trials Response Criteria Initiative and the Outcome Measures in Rheumatology Committee recommend a core set of three outcomes to be used in clinical trials of OA treatments: pain, physical function, and patient global assessment.[65] We will measure all three in this study, with the study being powered to detect race differences in the effect of the intervention on pain. We will assess pain and physical functioning using the pain and functioning subscales of the Western Ontario MacMaster (WOMAC) Index.[66] Designed to assess lower extremity pain and function in patients with OA, the WOMAC consists of pain, stiffness, and physical function subscales and can be used to compute an overall measure of OA severity. Although we will focus on the pain and functioning subscales, we will administer the full WOMAC so we can also compute an overall score. We will measure Patient Global Assessment of pain in the last week using an 11-point numeric rating scale.[65]

Although the main study outcomes are OA pain and functioning, increasing PA may also make patients more open to considering TJR as a treatment option. We will assess willingness to undergo TJR at each time point for exploratory purposes using the willingness to consider TJR item used in prior studies.[12]

5.5.1.2. Hypothesized mediators (baseline, 1 month, 3 months, and 6 months post-intervention). Depressive symptoms will be assessed by the 8-item Patient Health Questionnaire (PHQ-8), which assesses the 9 DSM-IV

criteria for the diagnosis of depressive disorders, with the exception of suicidality.[67] PHQ-8 has psychometric properties comparable to the PHQ-9 and is recommended for studies such as ours where a) there is low risk of suicidality among participants, b) depression is not an inclusion criterion or a primary outcome, and c) research staff are unable to provide adequate intervention if suicidal thoughts are reported by participants (e.g., because staff are communicating with participants by telephone).[67] **Positive and negative affect** will be assessed using the positive and negative affect subscales of the International Positive and Negative Affect Schedule Short Form.[68] **Satisfaction with life** will be assessed by the Satisfaction With Life Scale.[69] **Arthritis self-efficacy** will be measured using the 20-item Arthritis Self-Efficacy Scale, which assesses patients' perceived ability to cope with consequences of chronic arthritis.[70] **Pain coping** will be assessed by the Daily Coping Inventory adapted for pain coping, which assesses patients' use of emotion-focused (e.g., sought or found spiritual support or comfort) or problem-focused (e.g., did something to help you relax) pain coping strategies.[71] **Pain catastrophizing** will be assessed by the Pain Catastrophizing Scale, which measures the degree to which patients magnify the unpleasantness of pain experiences, ruminate on pain-related thoughts, and feel helpless in response to pain.[72] **Perceived discrimination** will be assessed by the Everyday Discrimination measure, which assesses how often one has encountered day-to-day unfair treatment (e.g., treated with less respect than other people) and the attributed reason for the treatment (e.g., one's race or sex).[73] **Global stress** will be measured using the Perceived Stress Scale, which assesses the extent to which people appraise their life as stressful.[74] **Social support** will be assessed by an abbreviated version of the Medical Outcomes Study Social Support Survey.[75]

5.5.1.3. Demographic and clinical covariates (baseline only, except for OA treatments): OA treatments participants are using will be assessed at all time points (baseline, 1 month, 3 months, and 6 months post-intervention) by a comprehensive list of treatment options based on those assessed in the OA Initiative.[63] All other demographic and clinical covariates will be assessed only at baseline. A demographic survey will be used to assess participants' **sex, age, income, education, employment, marital status**, and **general health status**. **Health literacy** will be assessed by the item, "How confident are you filling out medical forms by yourself?" This was the best single-item measure for detecting inadequate literacy in a study of VA outpatients, demonstrating high specificity and sensitivity.[76] **Physical comorbid medical conditions** will be assessed using an interviewer-administered version of the Charlson Comorbidity Index.[77] **Mental comorbidity** will be assessed using items from

the 2010 Behavioral Risk Factor Surveillance System Questionnaire to assess diagnoses and treatment of depression or anxiety.[78]

Comorbidity will be further assessed by having research staff conduct chart reviews to extract medical diagnoses that are recorded in enrolled participants' electronic medical records. **Obesity** will also be determined through chart reviews by extracting the most recent height and weight measurements available in patients' electronic medical records at baseline, which will be used to calculate body mass index. For participants who have a knee x-ray or MRI available in their medical record, we will assess **biologic disease severity** by looking at the x-ray and MRI reports for signs of OA. Reports documenting osteophytes with joint space narrowing, bony sclerosis, or possible deformity of bone ends or simply osteoarthritis will be considered radiographic confirmation of OA.

5.5.1.4. Intervention adherence and engagement (6 weekly surveys after baseline). Adherence to and engagement with PA and AC activities will be assessed during weekly surveys. Participants will be asked if they completed the previous week's activity.[79] In addition, participants will rate how much they felt they benefited, how much they enjoyed, and how difficult they found each exercise using a 7-point Likert-type scale.[79]

5.6 Data Analysis

5.6.1. General approach. Analyses will be performed using SAS or Stata. We will check the outcomes for normality and use transformations if necessary. We will compute descriptive statistics to determine central tendency, data sparseness, and the existence of outliers for all other continuous variables. For categorical variables, we will generate frequency and percentage distributions to identify data sparseness, and categories with small frequencies will be merged when appropriate. Differences in baseline variables by study arm and by race will be tested using chi-square statistics for categorical variables and t-tests for continuous variables. We will test study hypotheses using linear mixed models that account for repeated measures, assess change over time (baseline, 1 month, 3 months, and 6 months), and allow for missing data if data are missing at random. Demographic and clinical variables (see **5.5.1.3**) with a univariate association with the outcome ($p<0.10$) will be considered for inclusion as covariates. Covariates will be retained in final multivariable models if significant at $p<0.05$ and all models will be adjusted for study site. All tests will be two-sided.

We will conduct intent-to-treat analyses[80] that include all patients in the groups to which they were randomized, regardless of adherence and/or

subsequent withdrawal. We will also perform exploratory analyses to examine whether there is a dose-response effect of the intervention.

5.6.2. Missing data. While we will attempt to minimize missing data, it is likely that there will be some incomplete data from missing assessments, lost-to-follow-up, or withdrawal. We will attempt to assess the missing data mechanism for data missing due to lost-to-follow-up or withdrawal. If there are significant differences in baseline variables between participants that have complete outcome data and those that do not, we will adjust for those covariates in the models.[81] If no systematic differences are found or if the missing data is intermittent, the missingness will be handled as part of the regression modeling. Using linear mixed linear models allows the use of all available data, including data from those who are missing one or more of the assessments. We will also assess sensitivity to the missingness by performing completers-only analyses.

5.6.3. Analyses for primary aim, hypothesis 1: Patients who are randomized to complete the PA intervention will experience improved pain and functioning compared to patients who are randomized to complete an attention control program. Intervention effects will be assessed using separate models for pain and functioning that include fixed effects for study arm (PA intervention vs. control), time, and the interaction between study arm and time.

5.6.4. Analyses for primary aim, hypothesis 2: Improvements in pain and functioning associated with the PA intervention will be larger for AAs than for WHs. Whether intervention effects differ by race will be assessed by adding to the Hypothesis 1 model fixed effects for race, the study arm and race interaction, the time and race interaction, and the 3-way interaction between study arm, race, and time.

5.6.5. Analyses for secondary aim, hypothesis 3: The effects of the PA intervention on pain and functioning will be mediated by psychosocial variables known to be associated with OA outcomes or racial differences in OA outcomes (e.g., depression, self-efficacy, pain coping). We will assess whether intervention effects are mediated by proposed mediators (see **5.5.1.2.**) using a multiple mediation bootstrap approach that allows indirect effects of each potential mediating variable to be examined while controlling for the effects of other mediators.[82] We will fit race-specific mediation models to assess whether mediating effects are different among WH and AA patients.

5.6.6. Analyses for exploratory aim. Although there will not be adequate power to conduct formal tests to determine whether intervention effects are moderated by patient characteristics other than race, we will conduct exploratory analyses to examine sex as an additional moderator. We will plot each outcome separately for men and women to evaluate whether response to the intervention varies by patient sex. We will also run models testing the

effect of the intervention over time (Primary Aim, Hypothesis 1) separately for men and women.

5.6.7. Power calculations. This study uses a repeated measures design with 2 intervention groups (PA, AC), 2 race groups (WH, AA), and 4 time periods (baseline, 1 month, 3 months, and 6 months post-intervention). We computed sample size estimates that were powered to detect a racial difference in WOMAC pain subscale scores for the intervention effect over time (80% power). Interaction effects between study arm, race, and time were taken into account in the sample size computations. A 30% change in baseline pain scores is widely accepted as a clinically meaningful improvement, although changes on the WOMAC as small as 12% are also meaningful.[83,84] We therefore estimated the sample sizes needed to detect race differences in response to the intervention, assuming the intervention will produce a 12% to 30% improvement for our target population. As seen in Table 1, 360 Veterans (180 in each study arm split equally for each race), would be needed to detect a 20% change in baseline WOMAC pain subscale scores (effect size = 0.26) for 80% power. We therefore set the initial target sample size at 360, which ensures adequate statistical power to detect a clinically meaningful effect of 20-30% change from baseline. The initial target sample size of 360 also allows for possible attrition over the course of the study, as a 25% change from baseline would still be detectable with as few as 232 participants.

Table 1: Sample Size Estimates for 80% Power to Detect a Range of Clinically Meaningful Effects

Change from Baseline	Effect Size	Sample Size
12%	0.16	804
15%	0.20	516
20%	0.26	360
25%	0.33	232
30%	0.39	164

After the initial target sample at each participating site is reached for the study using the original protocol, we will continue recruitment as resources allow to support analyses of the exploratory aim examining sex as a potential moderator. Specifically, we will attempt to enroll up to approximately 240 additional Veterans (including some men and some women, as resources allow) using expanded criteria that includes individuals with OA codes using ICD-10, which was not in use at the time the study was initiated. All other inclusion criteria and recruitment procedures will remain the same. Taking ICD-10 codes into account is necessary to identify patients who have been diagnosed with relevant diagnoses since October of 2015, when the ICD-10 system began being used in the VA. It is essential to enroll both men and women using the expanded criteria because there may be systematic differences between patients who are more recently diagnosed and those who were identified using ICD-9 codes. If we only enroll women using the expanded criteria, then we will not be able to determine whether sex differences in outcomes are due to more women participants being more recently diagnosed with arthritis. Therefore, we will attempt to recruit both men and women using the expanded criteria. To maximize the inclusion of women, however, we will plan to invite all women who meet the expanded inclusion criteria to participate; we expect this will be approximately 5% of the

overall number of patients identified, based on the proportion of women who met the original study criteria based on ICD9 codes.

The expanded cohort will potentially allow comparison by sex. Using the same logic that was used to generate the power calculations for the number of participants needed to detect meaningful Race X Intervention X Time interactions (Table 1), we need an overall sample size ranging from 164 to 360 (approximately half white and half black) to detect 30% to 20% changes in baseline. To have the same power to detect Sex X Intervention X Time interactions, we would need 82 to 180 women in the final sample. Thus we will attempt to increase our overall target sample size, as resources allow, by 240 participants.

5.7 Withdrawal of Subjects

Study participants will be assured that participation is completely voluntary, that they can refuse to answer any of the study questions, and that they have the right to withdraw from the study at any time. There will be no penalty or consequences should a participant choose to withdraw from this research study. To withdraw from the study, participants may tell the PI, LSI, or study personnel that they no longer wish to participate. If participants express interest in withdrawing during the intervention phase of the study, they will be given the option of discontinuing the intervention but still completing the follow up surveys. There will be no penalty if participants choose not to complete these surveys and withdraw completely from the study.

The PI can withdraw participants from the study without their consent for reasons, such as it is in their best interest to discontinue the study protocol, they do not follow the study plan, or they experience a study-related injury.

Withdrawal of participants will be documented using a study withdrawal form (Appendix D) that indicates the participant study id number, the date the participant was withdrawn, whether the participant withdrew or was withdrawn by the PI, and the reason for the withdrawal (when available).

6.0 Reporting

All current applicable federal and state laws and CIRB procedures for reporting unanticipated problems, serious adverse events, and protocol deviations will be followed.

A data and safety monitoring plan will be implemented to ensure that there are no changes in the risk/benefit ratio during the study and that confidentiality of research data is maintained. LSIs and study personnel at each participating site will meet regularly to discuss issues like study progress, modifications, documentation, recruitment, retention, data analysis, and confidentiality and to address any local issues or concerns as they emerge. These meetings will be overseen by the LSI, who will be responsible

for assuring that activities at their site are conducted according to the IRB-approved protocol. LSIs will report to the CIRB and the study PI all instances of adverse events, protocol deviations, or other problems identified during the meetings within the required reporting timeframes using the standard forms and/or procedures set forth by the CIRB (i.e., Unanticipated Serious Adverse Events, Unanticipated Problems and Deviations that meet certain reporting criteria will be reported to the VA Central IRB within 5 business days, and all other events will be reported at time of continuing review). The PI will also communicate with LSIs through regular conference calls and by email to inform engaged sites of changes to the study or any serious adverse events or unanticipated problems that may impact the conduct of the study.

7.0 Privacy and Confidentiality

The study requires use of subjects' Protected Health Information (PHI).

Privacy of participants will be protected by allowing patients to opt out of future contact about the study, conducting in-person interviews in private settings, and allowing participants to refuse to answer any questions they do not wish to answer.

Data management policies described in the VA Information Resource Center Data Security Statement will be used to maximize data security and minimize risk of breach of confidentiality. Electronic data will be stored on computer systems within the VA computing network that is protected by a VA firewall and accessible only to authorized study personnel through the use of VA login and password permissions. Paper files will be locked in filing cabinets. Only project staff will have access to electronic and paper data. Data from screening forms will be entered into a database so that information may be summarized on patients who do not meet eligibility criteria or decline to enroll. Enrolled participants will be assigned a unique study identifier and included in a study cohort tracking system. Survey responses will be recorded in writing by research staff and double-entered by hand into study databases.

All staff will undergo training modules on maintaining patient privacy and confidentiality that are required for all VHA employees. All staff will also have current PKI email encryption.

8.0 Communication Plan

Prior to starting study activities at participating sites, the PI will review all LSI applications to assure they are aligned with the model procedures and study materials approved by the CIRB. LSIs will notify the study PI, as well as all others who need to be notified at their site, when local site approval has been granted.

As the study is conducted, LSIs and study personnel at each participating site will meet regularly to discuss issues like study progress, modifications, documentation, recruitment, retention, data analysis, and confidentiality and to address any local issues or concerns as they emerge. These meetings will be overseen by the LSI, who will be responsible for assuring that activities at their site are conducted according to the IRB-approved protocol. LSIs will report to the CIRB and the study PI all instances of adverse events, protocol deviations, or other problems identified during the meetings within the required reporting timeframes using the standard forms and/or procedures set forth by the CIRB. The PI will also communicate with LSIs through regular conference calls and/or by email to inform engaged sites of changes to the study or any serious adverse events or unanticipated problems that may impact the conduct of the study.

The PI will notify the LSIs when the study reaches the point that it no longer requires engagement of the local facility. LSIs will be responsible for completing all locally-required notifications that the site is no longer engaged in the study.

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List of Amendments to Staying Positive with Arthritis Study Protocol

Amendment 01 – October 17, 2014, approved December 23, 2014

- Change in the study team staff
- Revised the protocol, waiver of informed consent, and waiver of HIPAA authorization to reflect a change in the source data for sending recruitment mailings to potential participants

Amendment 02 – June 8, 2015, approved July 29, 2015

- Changed recruitment materials to correct typos and grammatical errors and added a study brochure and flier
- Modified the surveys and correct answer options
- Modified phone screening instruments to make it easier for interviewers to clearly see eligibility criteria, make answer options consistent on the whole instrument, and make questions clearer.

Amendment 03 – June 26, 2015, approved July 2, 2015

- Changed the format of the mailing postcard

Amendment 04 – August 20, 2015, approved September 14, 2015

- Changed the protocol to include exclusion criteria and to give Veterans the option to complete assessments over the phone or in person
- Modified the phone screening instrument to include skip patterns and to include additional exclusion questions
- Modified surveys to include checkboxes for the manner in which the survey was completed
- Modified telephone scripts to include clarifying language for the study

Amendment 06 – June 15, 2016, approved June 21, 2016

- Changed the protocol, informed consent form, waiver of HIPAA authorization, and waiver of informed consent to increase the number of participants enrolled in the study, as allowed by the existing study budget and timeline