TAI CHI STUDY PROTOCOL

R34AT009052
Tai Chi for Chronic Low Back Pain in Older Adults: A Feasibility Randomized Clinical Trial (Back Tai Chi)

Karen J Sherman, PhD, Principal Investigator
Kaiser Permanente Washington Health Research Institute
Kaiser Permanente Washington
1730 Minor Avenue, Suite 1600
Seattle, Washington 98101
Telephone: (206) 287-2426
Fax: (206) 287-2871

Sponsored by:

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TITLE	**Tai Chi for Chronic Low Back Pain in Older Adults**
INVESTIGATORS	Karen Sherman, PhD, Principal Investigator Kaiser Permanente Washington Health Research Institute, Seattle Elizabeth Phalen, MD Co-Investigator University of Washington, Seattle Manu Thakral, NP, PhD, Co-Investigator Kaiser Permanente Washington Health Research Institute, Seattle Judith Turner, PhD, Co-Investigator University of Washington, Seattle
STUDY OBJECTIVES	This study is designed to determine the feasibility of conducting a full-scale randomized controlled trial (RCT) of Standard Tai Chi, Enhanced Tai Chi, an Attention Control and Usual Medical Care for chronic low back pain in older adults. In addition, we will consider the feasibility of an attention control. By collecting data on recruitment and randomization rates, Tai Chi class and home practice attendance, rate and severity of adverse events and follow-up rates at 12, 26, and 52 weeks as well as observations of acceptability of Tai Chi classes and adequacy of Tai Chi performed, qualitative comments by participants, study staff and the Tai Chi instructor as well as the acceptability of the Attention Control, we will be able to determine the feasibility of the full-scale RCT.
DESIGN AND OUTCOMES	This is a feasibility RCT designed to test whether conducting an RCT of Tai Chi versus Attention Control versus Usual Medical Care to improve chronic low back pain in older adults is realistic. The feasibility of the full-scale study will be determined by assessing the feasibility of recruitment; acceptability and adherence of Tai Chi classes and home practice as well as the Attention Control; rate and severity of adverse events and adequate follow-uprates. Outcome measures for studies of back pain, including impact on back-related function and pain – primary outcomes for any RCTs of back pain, will be collected.

POPULATION/SITE	Persons who are at least 65 years of age, have had at least 3 months of non-specific (or degenerative) low back pain (and back pain on at least half the days over a 6 month period), and who rate their pain at least 4 on a 0 to 10 scale and have a score of at least 3 on a 0 to 10 Pain Interference Scale. Participants will be recruited from Kaiser Permanente Washington, an integrated healthcare system in the Puget Sound region of Washington State and from the general population of the region as necessary.
INTERVENTIONS	Participants will be randomized to one of two treatments: • Enhanced Tai Chi (TC) • Comprehensive Health Education Control • Usual Medical Care (UMC)
INTERVENTION SCHEDULE	Enhanced Tai Chi consists of Standard + Maintenance Tai Chi. Standard period: 12 weeks of 2x weekly classes of Tai Chi plus daily home practice on non-class days. Maintenance period: 24 weeks of maintenance Tai Chi (6 weeks of weekly Tai Chi classes; 6 weeks of every other week classes; 12 weeks of monthly classes). Home practice will be encouraged on all non-class days for the entire 52-week follow-up period. Attention Control consists of 12 weeks of 2x weekly classes about senior health with discussion. All Tai Chi participants have access to all care provided by their insurance. Usual Medical Care: participants are free to make any visits to their physicians and other health care providers and use other treatments.
SAMPLE SIZE	78 participants (39 Tai Chi, 15 Attention Control, 24 Usual Medical Care)
RECRUITMENT PERIOD	Participants will be recruited in 2 cohorts of 38 and 40 persons.
STUDY AIMS	1) To determine the feasibility of recruiting and randomizing older adults with cLBP into a trial of Tai Chi versus Attention Control versus Usual Medical Care. 2) To determine whether older adults with cLBP will come to classes in the primary 12 week period. To

	estimate home practice for tai chi (frequency and duration during this period). 3) To determine whether older adults with cLBP will come to maintenance classes, practice at home and find benefit from other strategies to enhance home practice. 4) To determine the rates of follow-up assessment of older adults with cLBP.
FEASIBILITY OUTCOMES	1) Recruitment yield and period of time to recruit and randomize one class cohort. Number of cohorts that could be recruited. 2) Class attendance and home practice adherence in primary treatment period 3) Class attendance and home practice adherence in secondary treatment period 4) Follow-up rates at 12, 26, and 52 weeks for outcome assessment. Primary outcome measures are back-related dysfunction and pain.
	These outcomes will be measured at baseline, 12 weeks (at the end of standard classes), 26 (during maintenance classes), and 52 weeks.
SAFETY OUTCOMES	Any adverse events identified during classes, on the follow-up interviews or through other means will be documented and reported on a regular basis to the Data Safety Monitoring Body (DSMB). Serious adverse events will be reported to the DSMB within 7 days. If attributable to the interventions, serious adverse events will also be reported to the IRB within 7 days.
MASKING	All persons collecting outcome information (i.e., assessors) will be masked to each participant's group assignment.

1. STUDY OBJECTIVES

This study is designed to determine the feasibility of conducting a full-scale randomized controlled trial (RCT) of Standard Tai Chi, Enhanced Tai Chi and Usual Medical Care for chronic low back pain in older adults. In the feasibility study, we will test our ability to recruit and randomize older adults with chronic low back pain, to determine whether the Enhanced Tai Chi intervention is feasible in terms of class attendance and home practice, and to determine follow-up rates at 12, 26 and 52 weeks.

2. BACKGROUND AND RATIONALE

2.1 Background on Back Pain

Back pain is the leading cause of disability worldwide, with both prevalence and burden increasing with age[1], with an estimated 12% of adults over age 65 suffer from impairing cLBP.[2] In the US, about $86 billion is spent annually on direct costs of medical care for back/neck pain[3]. Escalating costs of care for back pain are particularly marked for older Americans. While the Medicare population increased only 42% between 1991 and 2002, costs for back pain increased 387%.[4] In addition, during a recent 12-year period Medicare expenditures for epidural steroid injections increased 629%, expenditures for opioids for back pain increased 423%, while the number of lumbar magnetic resonance images increased 307% and the number of spinal fusion surgeries increased 220%.[5] Despite these large investments in medical care for back pain, the health and functional status of persons suffering from back pain in the U.S. has deteriorated.[3] Moreover, the rapid projected growth of older adults ensures that back pain in older adults will assume an increasingly greater clinical burden in the years to come.

Determining the cause of chronic low back pain (cLBP) is often difficult because of the numerous structures in the back that can give rise to pain. Moreover, virtually all older adults have radiographic evidence of spinal osteoarthritis, even though most are asymptomatic.[6] Even among older adults with back pain, the severity of their symptoms is poorly correlated with the severity of the imaging findings. Moderate to severe spinal stenosis is as common in older adults with and without chronic back pain.[6] Thus, imaging is not a good method to discern the cause of back pain in most circumstances.

2.2 Study Rationale

Identifying safe and effective treatments for cLBP in older adults remains a major challenge for clinicians, researchers, payers, and patients. Clinical guidelines for back pain in older adults are not available and many older adults have yet to find adequate relief. Older adults commonly have more disabling back pain,[7] more comorbidities with attendant polypharmacy[8] and are at higher risk of adverse effects of commonly used medication and non-pharmacological treatments.[2,9-11] They have substantially increased risks for: 1) gastric bleeding and renal insufficiency from use of NSAID drugs, 2) falls with use of muscle relaxants (which affect the central nervous system), and 3) falls, fractures, and cognitive impairment with use of narcotic analgesics. Because many older adults already take multiple medications for other chronic conditions, using medications for back pain increases their risk of drug-drug interactions. Surgical risks

also increase with age. Safety concerns are not limited to the use of conventional medical care. Even normally low risk complementary and integrative medical treatments such as high velocity spinal manipulation techniques may be contraindicated for older adults with osteoporosis, compression fractures, and other degenerative conditions. This may explain why older adults receive less treatment of any type for their back pain, despite reporting similar pain intensity and more disability.[12]

Given the expected aging of the US population in the coming decades, finding safer treatments for them is imperative. The 2007 back pain guidelines found 8 treatments effective for chronic low back pain. [13] These included exercise programs as well as three mind body therapies (wherein the mind is used to affect physical function and improve health[14] -- yoga, cognitive behavioral therapy, and progressive muscle relaxation. The most effective exercise programs included supervision of participants and encouraged adherence to achieve high dosage.[15] Stretching exercises were found to be best for reducing pain and muscle strengthening exercises were best for improving function. While some mind-body complementary and integrative health treatments such as meditation focus primarily on the mind, others including yoga and Tai Chi, promote movement as well as mental focus.

Tai Chi, a mind-body exercise from China that has grown in popularity in the US,[16] looks to be an excellent candidate as a treatment for chronic low back pain in older adults. Tai Chi has been found effective for younger adults with chronic low back pain.[17,18] Both studies measured pain intensity and found improvements, while the Hall study also measured back-treatments function and found improvements in it as well.[17] It contains numerous elements that are likely accessible to older adults that may be therapeutic. First, Tai Chi features gentle and progressive stretching movements within a moderate range of motion. It is likely to be relatively safe because it avoids putting the body into full extension or contraction as other exercise and yoga sometimes do. Of roughly 50 RCTs of Tai Chi (mostly of older adults) that monitored adverse effects, none reported any severe adverse effects.[19] Second, Tai Chi focuses on enhancing the body's capacity to integrate core and leg muscles rather than focusing on single muscle groups. Third, Tai Chi includes key characteristics of other exercise programs that have been found effective for cLBP (i.e., stretching and strengthening exercises delivered in supervised programs.[20] Fourth, Tai Chi incorporates focused breathing, mindful attention, visualization, and other components that are known to be beneficial for chronic pain.[16] Fifth, Tai Chi classes provide a venue for personal and social connection for persons who are socially isolated. Finally, baby boomers, who are now reaching age 65 in large numbers, have embraced a wide variety of CIM treatments[21] and may be less enthusiastic about participating in the types of exercise programs popular among the preceding generation.

In addition, Tai chi appears to have benefits for numerous health concerns and conditions[22-25] that are more common in the elderly, including balance and falls prevention,[26,27] cardiorespiratory fitness,[28,29] cognitive performance,[30] congestive heart failure,[29,31] bone health,[32] and osteoarthritis.[33,34]

In summary, we think Tai Chi is an ideal therapy for cLBP in older adults because it is safe, promotes active engagement in gentle exercise, includes a variety of potentially therapeutic elements, has been found effective for younger adults, and has been found helpful for a variety of comorbidities affecting many older adults. We are unaware of studies evaluating Tai Chi in older adults with chronic back pain. However, our 2001 survey of older adults with back pain in Seattle[35] found that a majority reported interest in Tai Chi training if it were offered for free and was recommended by their physician.

This study is proposed as a feasibility study comparing an "Enhanced Tai Chi" group to "Comprehensive Health Education" to "Usual Medical Care", which, if successful, would pave the way for a full-scale trial to evaluate Tai Chi as a treatment for older adults with chronic low back pain. Section 2.2a describes this goal, which is important for understanding the context of the feasibility trial, which is further described and justified in Section 3.

2.2a. Long Term Goal of Research

Our ultimate goal is to conduct an RCT to answer the practical question of whether Tai Chi is effective for relieving cLBP in older adults ***when added to*** Usual Medical Care. Our Standard dose of Tai Chi would be 12-week 2x/weekly series of Tai Chi classes (see Section 5 for further details and justification).Because Tai Chi requires ongoing practice, maintaining the practice is critical and so we would investigate the value of including and Enhanced Tai Chi group that receives Standard Tai Chi plus a 24 week maintenance period of progressively fewer classes: 6 weeks of weekly classes, 6 weeks of every other week classes and 12 weeks of monthly classes). All classes would be 60 minutes long. Participants would be asked to practice 15 minutes at home on all non-class days. The anticipated design of our full-scale trial is depicted on the next page (note that Usual Medical Care will be available to all study groups). We are unclear regarding the value of an Attention Control, which will be a included in one of the cohorts of the feasibility RCT:

Our principal hypotheses would be:

H_1: Tai Chi is superior to Usual Medical Care at 12, 26, and 52 weeks. (Primary time point would be 12 weeks).

H_2: Enhanced Tai Chi (standard + maintenance) is superior to Standard Tai Chi at 26 and 52 weeks. (Primary time point would be 52 weeks).

H_3: Tai Chi is superior to Attention Control at 12, 26, and 52 weeks (assuming we include the AC group). (Primary time point would be 12 weeks).

The primary outcomes would be back-related dysfunction (most critical) and pain.

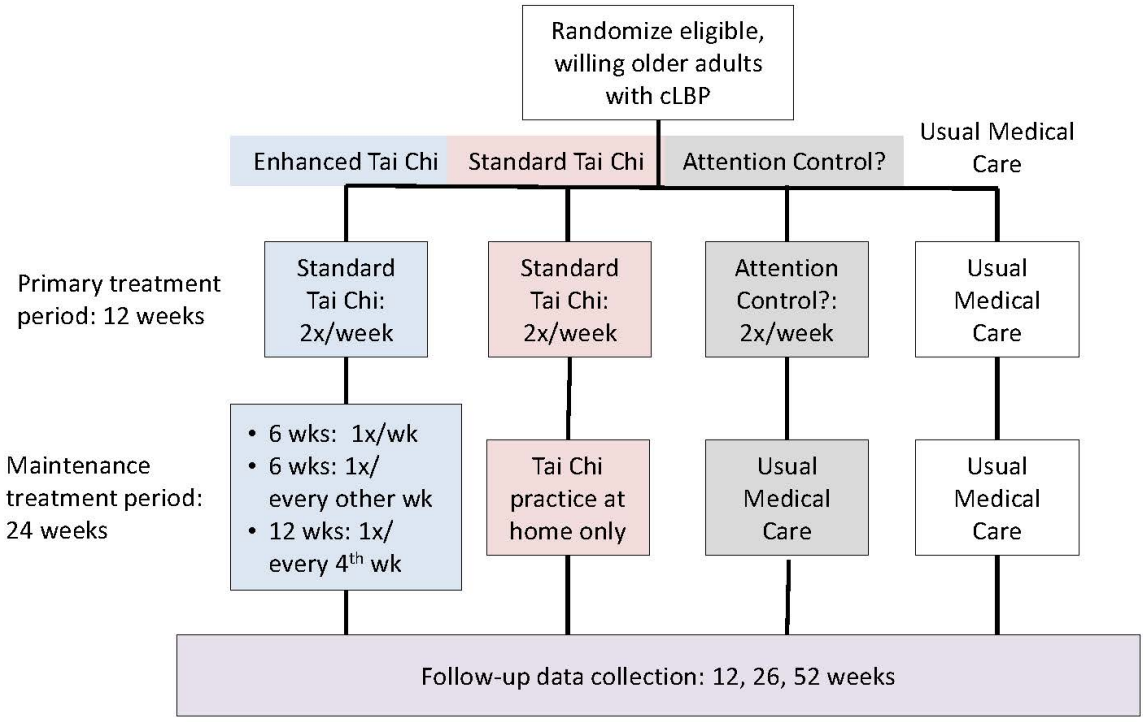

Figure: Anticipated Design of Full-scale Trial

3. STUDY DESIGN

The feasibility study will be a three arm parallel group RCT comparing Enhanced Tai Chi to Comprehensive Health Education (Attention Control) to Usual Medical Care in older adults (65 years and older) with cLBP. We plan to recruit 78 community-dwelling, older adults from Kaiser Permanente Washington, an integrated healthcare system with a large population of Medicare enrollees and from the general population as necessary. We will randomize eligible and willing individuals in a 8:3:5 ratio to Enhanced Tai Chi (n=39), Attention Control (n=15) and Usual Medical Care (n=24) using a computer with a tamperproof program that is not predictable in advance. Participants in the Enhanced Tai Chi will receive 36 weeks of classes (which will be 60 minute classes for 2x/week for 12 weeks; followed by a maintenance schedule of 60 minutes classes 1x/week for 6 weeks, then 60 minute classes every 2 weeks for 6 weeks and then 60 minute classes every 4 weeks for 12 weeks. Participants will be asked to practice at home for 15 minutes on every non-class day. They will be provided with Youtube video access (and, if desired, DVDs), and handouts to assist with this.). All classes will be taught in a Kaiser Permanente Washington classroom. Data on adherence to Tai Chi classes and home practice will be collected during the classes themselves. Because Tai Chi will be taught as a series of progressive classes, participants will be recruited in two cohorts of 32 each; each class of Tai Chi will consist of 16 participants.

Outcome assessments will be collected at baseline, 12, 26, and 52 week during in-person visits. Outcome assessors will be unaware of any participant's study groups,

but participants will be asked to complete their own questionnaires. They will either complete them on paper forms or using a tablet computer designed to minimize errors.

This design will allow us to collect data on recruitment and randomization rates, acceptance and feasibility of the Tai Chi intervention (adherence to the standard and maintenance Tai Chi protocols), and follow-up rates, which are critical to assess feasibility of the full-scale RCT. By including these treatment groups – which represent the extremes in time commitment - in the feasibility RCT, we likely to collect data that is applicable to the other treatment groups (i.e., standard Tai Chi and Attention Control, if the latter is used) included in a full-scale RCT. At the 52 week follow-up, we will also obtain information from debriefing discussions with the study participants about aspects of the study that would require modification prior to the conduct of a larger RCT. We will use the proposed outcome measures and physical measures in their entirety to ensure that these are feasible in terms of participant burden. Because the RCT is underpowered for effectiveness, it is not appropriate to have specific hypotheses regarding effectiveness. Nonetheless, back-related function and pain would be the primary outcomes in the full-scale trial as described above.

4. SELECTION AND ENROLLMENT OF PARTICIPANTS

4.1 Source of Participants

Participants will be recruited from Kaiser Permanente Washington, an integrated health care system serving over 400,000 adult members in their primary care clinics in Washington State. This includes 67,341 members age 65+, of which over 10,000 made medical visits for back pain in 2014. This should provide an ample number of members who have chronic back pain who would be eligible for our study, particularly given our 2001 survey findings[35] that 55% of older adults receiving care from GH reported they would be “very likely” to try “Tai Chi” for their back pain if their provider considered it a reasonable option and it was free. Furthermore, given the growing popularity of mind-body therapies in recent years since our 2001 survey,[41] interest in Tai Chi has probably increased. Recruitment from the GH population will enhance the generalizability of our results to the large fraction of Americans that receive most of their medical care in primary care settings. We will augment the Kaiser Permanente Washington population as necessary by recruiting from the general Seattle area.

4.2 Inclusion Criteria

Participants will need to meet all of the inclusion criteria to participate in the study. Participants must:

- Be men or women at least 65 years of age
- Have low back pain that has persisted for at least three months
- Have had back pain on at least half the days in the last 6 months
- Rate their low back pain at least 4 on a 0 to 10 back pain intensity scale
- Rate their activity limitations due to back pain at least 3 on a 0 to 10 scale
- Be members of Kaiser Permanente Washington integrative health care system or have a regular source of health care and health insurance
- Have normal cognition or only mild cognitive impairment (score of <3 on 6 item Callahan screener)

- Be capable of understanding the study procedures and complying with them for the entire study period.
- Live close enough to the class site for attendance to be practical
- Give informed consent

Because there are a number of back pain diagnoses that might be given to eligible participants, we will cast a wide net using ICD9 or ICD10 codes that could be indicative of back pain without specific cause (i.e., ICD-10 codes: M54.5 Lumbago;M54.9 Backache; unspecified; M45.0 Other symptoms referable to back; S33.6XXA Sprains and strains, sacroiliac; S33.5XXA Sprains and strains, lumbar; S33.8XXA Sprains and strains, sacral; and S33.9XXA Sprains/ strains, unspecified site of back) or due to degenerative disease. Currently, ICD codes do not indicate whether the pain is chronic or not, so that must be determined by telephone interview. These are draft criteria and will be reviewed for completeness during the Administrative year of the grant.

4.3 Exclusion Criteria

Participants who have any of the exclusion criteria during screening or the baseline visit will be excluded study participation. These exclusion criteria include:

- Specific conditions other than degenerative disease or spinal stenosis as cause of LBP (e.g., metastatic cancer, vertebral fracture, spinal infection, ankylosing spondylitis, spondylolisthesis).
- Prior lumbar spine surgery
- sciatica, or scheduled visits to a neurosurgeon or orthopedic surgeon.
- Receiving or seeking compensation for back pain
- Red flags of serious underlying illness (e.g., recent unexplained weight loss of 10 lbs or more, fever, recent increase in pain intensity)
- Have received Tai Chi training in the last 12 months or practiced yoga more than 5 times in that period. Other disabling conditions that might confound treatment effects (e.g., disabling heart or lung disease or diabetic neuropathy)
- Conditions making consent or treatment difficult (e.g., unwilling or unable to attend classes and practice at home, major psychoses, dementia, severe vision or hearing problems, lack of transportation, unable to read or speak English; cannot transfer weight from one leg to another or bend at the hips)
- Conditions making treatment unsafe or inappropriate (e.g., inability to stand independently, absolute contraindications to exercise such as uncontrolled arrhythmia, unstable angina, acute MI or CHF)
- Unwillingness to give informed consent

4.4 Study Enrollment Procedures

Our standard recruitment approach will be to use Kaiser Permanente Washington's electronic administrative and clinical databases to identify potentially eligible GH members who are at least 65 years of age with a visit to a health care provider that resulted in a diagnosis consistent with low back pain. We then mail invitation letters describing key eligibility requirements and describing logistical aspects of the trial to GH members at least 3 months after they have visited a GH provider for back pain. Individuals with interest in the study will be asked to either return a statement of interest or call our toll-free project number with their contact information. A

Research Specialist will then phone interested enrollees to answer questions, obtain oral consent for an initial telephone eligibility screen and determine preliminary eligibility using a computer program to guide the interviewer through a series of screening questions. The screening process will end with documentation in a database of either preliminary eligibility or ineligibility. Individuals whose responses suggest they are provisionally eligible and who interested in the feasibility RCT will then be scheduled to come to a group in-person assessment in a conference room at a large Kaiser Permanente Washington clinic. They will receive information about the details of the conference room location ahead of time. Individuals who were deemed provisionally eligible more than 10 days in advance of the scheduled baseline visit will be re-contacted by phone to make sure that their pain levels were sufficiently high that they remain eligible.

If necessary, we will explore two additional approaches: advertising in newsletters targeted at KP seniors (i.e., members of the KP Senior Caucus and mailings sent to Medicare recipients receiving care at KP) and through mailings to older adults meeting our eligibility criteria (based on data in the EMR) who have not recently visited their physician for back pain. It is likely that a substantial number of these older adults will have impairing cLBP but have given up on seeking medical care because it has not been effective or has had significant side effects.

In addition to inviting Kaiser Permanente Washington enrollees, we will also recruit participants from the general population of seniors in the Seattle-area. For general population recruitment, we will use a variety of recruitment methods such as radio ads, flyers on community bulletin boards, blogs, and direct mail postcards. If we are having trouble reaching seniors with chronic low back pain, we will enlist the help of our patient partners to help identify recruitment sources most relevant for the senior population. For the direct mail postcards, we will use a list service to purchase lists which include the name and addresses of people living within our recruitment area who are within the study age-range. People on the list will be sent a direct mail postcard which gives study information and directions for how to contact study staff if interested in participating. Once an interested person has contacted the study, the process will be the same as detailed above and the phone call will be analogous to returning the study postcard.

Those persons deemed preliminarily eligible will be scheduled to attend one of our in-person group eligibility screening and assessment visits at a Kaiser Permanente Washington Medical Center. While the in-person visits are in a group setting, physical assessments and randomization will take place in a private room adjacent to the group area. This method has worked well in other studies conducted by Drs. Sherman and Rosenberg, but will be modified if suggested by the patient partners. During the group assessment visit, eligibility will be confirmed through completion of a final eligibility screening (e.g. demonstration of sufficient mobility, willing ness to be randomized). If the participant is deemed eligible and is willing to participate, informed consent will be administered by a study Research Specialist. This will include an explanation of interview time commitments and content, intervention commitments (class attendance, home practice, and home practice diary completion), potential risks of participation,

potential benefits of participation, what to do for an adverse event, and options for discontinuation of participation in the study. The Research Specialist will also explain the handling of data and personal health information as dictated by HIPAA. After informed consent is obtained, the baseline questionnaire will be administered using either a study tablet computer or a paper questionnaire, whichever the participant prefers. The Research Specialist will be present and available to answer any questions that might arise while the participant is completing the baseline questionnaire. To ensure that all key outcome measures are collected at the baseline appointment, we will also have participants' complete physical assessments (Short Physical Performance Battery, Four Square Step Test, Gait Speed). Once the baseline questionnaire and physical assessments are complete, the Research Specialist will answer any remaining questions and randomize the participant to one of our study groups. Signed consent forms will be kept at the KPWHRI in a locked filing cabinet only accessible by the appropriate study staff**.**

Study staff will randomize each individual to their treatment group using a computer program, accessible by a laptop, designed to ensure that treatment allocation cannot be changed after randomization and cannot be viewed in advance. Our biostatistician will provide our study programmer with a computer-generated sequence of random numbers that will be then inserted into the computer program. Physical assessments and randomization will be carried out in a private space adjacent to the group visit room. Participants will be randomized in blocks of varying size to ensure balanced but unpredictable assignment of participants to both groups. Participants randomized to Tai Chi will be provided information about the time and location of the first class. This process, modified as necessary for older adults, will be repeated to assemble two consecutive recruitment cohorts of 32 participants. In the first cohort, 19 participants will be randomized to Enhanced Tai Chi protocol and 19 to Usual Medical Care. In the second cohort, 20 participants will be randomized to Enhanced Tai Chi protocol, 15 to the Comprehensive Health Education Classes (AC Group), and 5 to Usual Care. The advice from our patient partners, our team members with experience conducting studies of physical activity in older adults and the experience we gain enrolling participants in our small Tai Chi study this summer, will help ensure that our standard recruitment procedures are modified appropriately for this new study population. We will consider whether we should conduct randomization stratified by age (65-79; 80+) and gender because both are related to baseline measures of back dysfunction and pain.[7]

In our large randomized trial of acupuncture for cLBP, we found no differences in the baseline characteristics of participants recruited through mailings and through advertisements in the health plan's quarterly magazine.[42]

5. STUDY INTERVENTIONS

5.1 Tai Chi

To ensure that our intervention was developed thoughtfully, we adapted the frame work proposed by Sherman[43] for developing yoga interventions, which recommends specification of style of practice, dose and delivery format, components of the

intervention, specific class sequences, use of modifications, selection and training of instructors, home practice facilitation, and intervention fidelity. For this feasibility RCT, treatment protocols were developed for both standard Tai Chi and for a maintenance period wherein the protocol is tapered. The treatment components are outlined below, with further details given in the study protocol along with items to be developed. The intervention includes strategies for ensuring intervention fidelity (i.e., "the extent to which core components of interventions are delivered as intended by the protocols"),[44] because it is essential for accurately interpreting treatment effects. The Treatment Fidelity Workgroup of the NIH Behavior Change Consortium (BCC) developed recommendations for incorporating strategies for monitoring and enhancing treatment fidelity in behavioral interventions.[45] Many are relevant for Tai Chi. Many of these recommendations are covered in Sherman's framework (i.e., provider training, treatment delivery, treatment receipt) but we will ensure the other relevant recommendations are all incorporated into our trial, as described below.

5.1.1 Documentation of the Enhanced Tai Chi Treatment Protocol

The Tai Chi consultants developed a detailed Tai Chi intervention manual. It includes the lesson plans for each class (including a description of the key features and photos and suitable visual imagery).

The latter will be supplemented with a teacher training manual, containing the most effective strategies for ensuring treatment fidelity, the minimum qualifications for Tai Chi instructors, how they will be recruited, trained on the study protocol, tested and monitored for adherence to the protocol, and how their skills will be maintained during the study period. This manual will include all study materials given to participants (e.g., hard copy or DVD descriptions of the movements they are learning), and checklists for evaluating instructor adherence to the treatment protocol.

5.1.2 Standard Tai Chi Protocol for cLBP

Our Standard Tai Chi intervention will include group classes – each 60 minutes – of Yang style Tai Chi twice week for 12 weeks. We chose to use the Yang style because it is the most popular form of Tai Chi worldwide, can be delivered in a simple format that is easily replicated, has been used in numerous RCTs[46] and is known effective for falls prevention.[47] Twelve weeks of twice-weekly classes is the most commonly used dose of Tai Chi in RCTs and has proved practical for older adults in other studies.[46] Therefore, this should be sufficient instruction to understand the fundamentals and practice safely. Consultant Tai Chi instructor Kim. Ivy and Tai Chi researcher Dr. Peter Wayne, who each have over 35 years of Tai Chi training and teaching experience, developed the Tai Chi intervention based on their prior experience with this population. Guided by the literature on beneficial treatments for chronic pain, classes will include the following components: simple classical Tai Chi movements to enhance musculoskeletal strength and flexibility, efficient posture, heightened body awareness, mindful diaphragmatic breathing, and healing imagery and visualization.[16] In addition, by using a class format, psychosocial interaction can be enhanced. All movements were designed to assure safety and emphasize those that are most relevant to persons with cLBP.

In both cohorts, the first class will begin with a short introduction to Tai Chi principles, an overview of the class format and curriculum, and expectations regarding home practice. All subsequent classes will include an initial check-in period to discuss any questions or concerns related to prior classes and/or home practice. Formal Tai Chi instruction will begin with a focus on posture and abdominal breathing followed by basic Tai Chi warm-up exercises to loosen up the physical body, reinforce Tai Chi principles of incorporating mindfulness and imagery into movement, promote overall relaxation, and generating awareness of efficient breathing. The centerpiece of the protocol will include six Tai Chi movement flows over the course of the 12 weeks: 'opening move: step out, raise and lower arms'; 'grasping sparrow's tail on the left side; 'grasping sparrow's tail on the right side'; 'single whip', 'cloud hands'; 'repeat of single whip', 'step back, lower arms'.[48] Classes will end with a closing and centering breathing exercise. These movements will be progressively added to the warm-up and cool down exercises over the 12 week intervention (i.e., movement 1 introduced during week 1; movements 2 and 3 during weeks 2-5; and the remaining movements during weeks 6-10). The class format for each week is shown below.

Table 1. Standard Tai Chi Class Format: Proposed Version

Week	PROPOSED Class Format
1	1. Introduction & Overview of Tai Chi program (5 min) (1st class) and Greetings & Discussion of Home Practice Efforts (5 min) (2nd class) 2. Explanation of Basics: Posture, Breathing, Mental State (5 min) 3. Introduction of Relaxation Sequence, Breathing & Standing Meditation (10 min) 4. Warm-up Exercises: #1 (10 min) 5. Learn Movement #1: Opening Move: Step Out, Raise and Lower Arms (10 Min) 6. Student Practice & Individual Correction/Modification (10 min) 7. Closing, Centering Breath & Visualization of Movement (3 min) 8. Q & A (5 min) 9. Review Homework assignment: Relax & Check Posture; Warm-up #1 & Movement #1 (2 min)
2	1. Greetings & Discussion of Home Practice Efforts (5 min) 2. Review of Basics: Posture, Breathing & Mental State (5 min) 3. Relaxation Sequence, Breathing & Standing Meditation (5 min) 4. Warm-up Exercises #1 & 2 (10 min) 5. Repeat/Practice/ Correct/Modify Movement Flow #1 (5 min) 6. Learn Movement Flow #2, Element #1: Ward Off Left (10 min) 7. Student Practice Movement Flows #1&2 (Element #1), Individual Corrections/Modifications (10 min) 8. Closing, Centering Breath & Visualization of Movement (3 min) 9. Q & A (2 min) 10. Review Homework assignment: Relax & Check Posture; Warm-up #1 & 2 & Movement #1 & 2, element #1 (5 min)

3	1. Greetings & Discussion of Home Practice Efforts (5 min) 2. Relaxation Sequence, Breathing & Standing Meditation (5 min) 3. Warm-up Exercises #1,2,3 (10 minutes) 4. Repeat/Practice/ Correct/Modify previous Movement flows (10 min) 5. Learn Movement Flow #2, Element #2, Grasping Sparrow's Tail: Roll Back, Press & Push (10 min) 6. Student Practice & Individual Correction/Modification (10 min) 7. Closing, Centering Breath & Visualization of Movement (3 min) 8. Q& A (2 min) 9. Review Homework assignment: Relax & Check Posture; Warm-up #1 & 2 & Movement #1 & 2 (entire) (5 min)
4	1. Greetings & Discussion of Home Practice Efforts (5 min) 2. Relaxation Sequence, Breathing & Standing Meditation (5 min) 3. Warm-up Exercises #2,3,4 (10 min) 4. Repeat/Practice/ Correct/Modify Previous Movement Flows (10 min) 5. Learn Movement Flow #3, Transition & Grasping Sparrow's Tail, right side; (10 min) 6. Student Practice & Individual Correction/Modification (10 min) 7. Closing, Centering Breath & Visualization of Movement (3 min) 8. Q& A (2 min) 9. Review Homework assignment: Relax & Check Posture; Warm-up #2,3,4; Movement #1,2 & 3 (5 min)
5	(Repeat Week #4) 1. Greetings & Discussion of Home Practice Efforts (5 min) 2. Relaxation Sequence, Breathing & Standing Meditation (5 min) 3. Warm-up Exercises #2,3,4 (10 minutes) 4. Repeat/Practice/ Correct/Modify Previous Movement Flows (10 min) 5. Review Movement Flow #3, Transition & Grasping Sparrow's Tail, right side; (10 min) 6. Student Practice & Individual Correction/Modification (10 min) 7. Closing, Centering Breath & Visualization of Movement (3 min) 8. Q& A (2 min) 9. Review Homework assignment: Relax & Check Posture; Warm-up #2,3,4; Movement #1,2 & 3 (5 min)
6	1. Greetings & Discussion of Home Practice Efforts (5 min) 2. Relaxation Sequence, Breathing & Standing Meditation (5 min) 3. Warm-up Exercises #2,3,4 & 5 (10 minutes) 4. Repeat/Practice/Correct/Modify Previous Movement Flows (10 min) 5. Learn Movement Flow #4, Single Whip (10 min)

	6. Student Practice & Individual Correction/Modification (10 min) 7. Closing, Centering Breath & Visualization of Movement (3 min) 8. Q& A (2 min) 9. Review Homework assignment: Relax & Check Posture; Warm-up #2,3,4; Movement #1,2,3 & 4 (5 min)
7	(Repeat Week #6) 1. Greetings & Discussion of Home Practice Efforts (5 min) 2. Relaxation Sequence, Breathing & Standing Meditation (5 min) 3. Warm-up Exercises #2,3,4 & 5 (10 min) 4. Repeat/Practice/Correct/Modify Previous Movement Flows (10 min) 5. Review Movement Flow #4, Single Whip (10 min) 6. Student Practice & Individual Correction/Modification (10 min) 7. Closing, Centering Breath & Visualization of Movement (3 min) 8. Q& A (2 min) 9. Review Homework assignment: Relax & Check Posture; Warm-up #2,3,4,5; Movement #1,2,3 & 4 (5 min)
8	1. Greetings & Discussion of Home Practice Efforts (5 min) 2. Relaxation Sequence, Breathing & Standing Meditation (5 min) 3. Warm-up Exercises #2,3,4 & 5 (10 minutes) 4. Repeat/Practice/Correct/Modify Previous Movement Flows (10 min) 5. Learn Movement Flow #5, Cloud Hands & Repeat Single Whip (10 min) 6. Student Practice & Individual Correction/Modification (10 min) 7. Closing, Centering Breath & Visualization of Movement (3 min) 8. Q& A (2 min) 9. Review Homework assignment: Relax & Check Posture; Warm-up #2,3,4, 5; Movement #1,2,3,4, 5& 4 (5 min)
9	(Repeat Week #8) 1. Greetings & Discussion of Home Practice Efforts (5 min) 2. Relaxation Sequence, Breathing & Standing Meditation (5 min) 3. Warm-up Exercises #2,3,4 & 5 (10 minutes) 4. Repeat/Practice/Correct/Modify Previous Movement Flows (10 min) 5. Learn Movement Flow #5, Cloud Hands & Repeat Single Whip (10 min) 6. Student Practice & Individual Correction/Modification (10 min) 7. Closing, Centering Breath & Visualization of Movement (3 min) 8. Q& A (2 min) 9. Review Homework assignment: Relax & Check Posture; Warm-up #2,3,4, 5; Movement #1,2,3,4, 5, & 4 (5 min)

10	1. Greetings & Discussion of Home Practice Efforts (5 min) 2. Relaxation Sequence, Breathing & Standing Meditation (5 min) 3. Warm-up Exercises, Choose from: #1-6 (10 min) 4. Repeat/Practice/Correct/Modify Previous Movement Flows (10 min) 5. Learn Movement Flow #6, Cross Hands, Close (10 min) 6. Student Practice & Individual Correction/Modification (10 min) 7. Closing, Centering Breath & Visualization of Movement (3 min) 8. Q& A (2 min) 9. Review Homework assignment: Relax & Check Posture; Warm-up #2,3,4, 5; Movement #1,2,3,4,5, 4 &6 (5 min)
11	1. Greetings & Discussion of Home Practice Efforts (5 min) 2. Relaxation Sequence, Breathing & Standing Meditation (5 min) 3. Warm-up Exercises, Choose from: #1-6 (10 min) 4. Review entire sequence (15 min) 5. Student Practice & Individual Correction/Modification (15 min) 6. Closing, Centering Breath & Visualization of Movement (3 min) 7. Q& A (2 min) 8. Review Homework assignment: Relax & Check Posture; Warm-ups 1-6, Entire Flow Sequence (5 min)
12	(Repeat Week #11) 1. Greetings & Discussion of Home Practice Efforts (5 min) 2. Relaxation Sequence, Breathing & Standing Meditation (5 min) 3. Warm-up Exercises, Choose from: #1-6 (10 min) 4. Review entire sequence (15 min) 5. Student Practice & Individual Correction/Modification (15 min) 6. Closing, Centering Breath & Visualization of Movement (3 min) 7. Q& A (2 min) 8. Review Homework assignment: Relax & Check Posture; Warm-ups 1-6, Entire Flow Sequence (5 min)

In each class, modifications will be employed as necessary for participants who have physical limitations. The most common modifications are reducing slightly the depth of the postural stance due to knee pain and lowering the height of the arms due to shoulder issues. However, we will take note of all physical issues and see whether the protocol should be modified or additional modifications should be recorded as part of the protocol finalization for the full-scale trial.

The Tai Chi classes will be offered in large, quiet classrooms at Kaiser Permanente Washington facilities that are centrally located and that provide easy access for persons with physical limitations. We have successfully used such classrooms in previous studies.

Study participants who are randomized to the Tai Chi intervention will be asked to practice at home on all non-class days for 15 minutes. The home practice assignments are shown in Table 2. We will prepare home practice aides to assist with this (e.g., videos with the sequences available on Youtube or a DVD).

Table 2. Home Practice Assignments

Week(s)	Home Practice Assignment
1	Relax & Check Posture; Warm-up #1 & Movement #1
2	Relax & Check Posture; Warm-up #1 & 2 & Movement #1 & 2, element #1
3	Relax & Check Posture; Warm-up #1 & 2 & Movement #1 & 2 (entire)
4, 5	Relax & Check Posture; Warm-up #2,3,4; Movement #1,2 & 3
6 & 7	Relax & Check Posture; Warm-up #2,3,4, 5; Movement #1,2,3 & 4
8 & 9	Relax & Check Posture; Warm-up #2,3,4,5; Movement #1,2,3,4, 5 & 4
10	Relax & Check Posture; Warm-up #2,3,4, 5, 6; Movement #1,2,3,4,5, 4 & 6
11&12	Relax & Check Posture; Warm-ups 1-6, Entire Flow Sequence

5.1.3 Maintenance Tai Chi Protocol for cLBP

A key feature of receiving benefits from mind-body interventions like Tai Chi is the probable need to continue regular practice in order to continue receiving their benefits. Consequently, investigation of strategies for maintenance of long term practice is important. We will therefore investigate a suite of strategies for achieving this goal. We have adopted ideas from the health promotion literature as well as from the chronic pain literature. We plan to investigate the value of adding additional classes at the end of the primary intervention period. By tapering class frequency over the course of an additional 24 weeks, we can investigate whether such a strategy is practical, leading to better maintenance of a Tai Chi practice over the longer term and therefore improving back function, pain, balance, mood and overall quality of life. During this maintenance period, we propose 6 weeks of weekly classes, 6 weeks of classes every other week (i.e., 3 classes) and 12 weeks of monthly classes (i.e., 3 classes) to offer a high enough dose to encourage long term maintenance.[49] Classes will be 60 minutes as in the Standard Tai Chi protocol and will include the movement flows and as well as the other components that were part of the Standard Tai Chi classes. Participants will be asked to practice at home for 15-minutes on all non-class days.

The Tai Chi classes will be offered in large, quiet classrooms at Kaiser Permanente Washington facilities that are centrally located and that provide easy access for persons with physical limitations. We have successfully used such classrooms in previous studies.

5.1.4 Selection and training of instructors

Tai Chi consultant Kim Ivy will teach the classes for our two Tai Chi cohorts. She is exceptionally experienced with over 35 years of practicing Tai Chi and has run a successful Tai Chi school in Seattle for over 20 years. In a future trial, we will require all instructors to have a minimum of 10 years of practice of Yang style Tai Chi, have taught for at least seven years with five years of experience teaching seniors, have current CPR certification and be willing to adhere to our study protocol. In addition, we will require an in-person demonstration to ensure that they have relevant mastery of Yang style Tai Chi, general teaching competence, comfort giving verbal instruction, flexibility in teaching style and excellent interpersonal dynamics. The demonstration will include evaluation of their own Yang style form as well as their ability to instruct others in warm-ups and selected tai chi flows that are relevant to this protocol. In addition, they will attend our in-person teacher training, which will include an introduction to the study design and participant inclusion and exclusion criteria, an in depth discussion of the protocol, with practice teaching for consistency among instructors and special issues that may arise in this population. Because Ms. Ivy is very well connected with the Seattle tai chi community, she will be able to easily recruit instructors who are likely to be successful as instructors in this study. If additional instructors are necessary for this feasibility study, Ms. Ivy will train them.

5.1.5 Home practice facilitation

We will supplement classes with 15-minutes of home practice on several non-study days and practice incorporating Tai Chi principles into life. We will use Youtube videos and if requested, DVDs to guide the participant through the movement flows. Home practice logs will be used to track home practice, a strategy we have used with some success in prior studies. Results from our pilot study of using an iPad app designed to enhance adherence to exercise found that it was not easy for study participants to use.

5.1.6 Intervention fidelity:

i. Class protocol

For this feasibility study, Research Specialists who staff the classes will complete intervention fidelity checklists at all classes. Dr. Sherman, who has developed familiarity with the Tai Chi protocol during the development of the intervention manual, will attend two randomly selected classes in each of the class series to ensure the instructor is adhering to the protocol. She will note all observed protocol violations, both errors of omission and commission on the checklists developed for this purpose. Dr. Sherman will also be in weekly contact with Kim Ivy during each class series to ensure any questions or concerns are quickly identified and resolved (Consultant Wayne will be brought in if necessary). We will focus on the suitability of these procedures for a larger study and to making any necessary modifications.

ii. Optimizing treatment dose

Tai Chi requires some focused attention to learn the fundamentals undergirding this mind-body therapy and requires continued practice in order to maintain benefits.. Participants will receive a reminder call before the first class and whenever they miss any classes.. During each class, participants will be reminded of the importance of attending classes and of practicing at home. A portion of each class will be devoted to answering questions that arise during home practice and, if necessary, to exploring any perceived barriers to adherence. Research Specialists will take attendance at each class.

iii Develop strategies to assess participants' understanding of intervention and ability to engage in Tai Chi

We will evaluate several methods to assess the extent to which participants feel comfortable and understand the techniques they are being taught and their confidence in performing them in class and practicing them at home. This will include having a Research Specialist observe each class and note any observed difficulties (as well as corrections given by Instructor Ivy), asking about these issues on our follow-up questionnaires, and possibly having another Tai Chi instructor observe and rate each participant's movements during classes (e.g., unable to perform movements, low/moderate/high skill in performing the movements).

iv. Documentation of intervention fidelity

In addition to identifying any general problems with our implementation procedures or with specific aspects of the treatment protocols, we will determine the level of adherence to class attendance and home practice in the standard and maintenance time periods. Class attendance will be documented by a Research Specialist who will attend all of the classes to manage study-related processes and allow the Tai Chi instructor to pay full attention to her students. We will also collect data from students on home practice. At the first class, we will give participants weekly logs to record their home practice throughout the 36-week intervention period (We will ask that they bring their logs to class once a week and to give them to the Research Specialist). We have used this process in our recent yoga RCT[55] with moderate success. In addition, we will ask participants during the 12, 26 and 52-week follow-up interviews about the number of days they practiced during the prior week and the average number of minutes they practiced on those days. This method of collecting data on home practice has worked well in our previous RCTs. Finally, we will assess treatment fidelity by reviewing the information we collected evaluating the ability of the Tai Chi instructor to adhere to the treatment protocols and the extent to which participants were able to grasp what they were taught and translate it into skillful Tai Chi movements.

5.1.7 Allowed Interventions

For ethical and legal reasons, all participants will be permitted whatever care they would receive as part of their medical coverage provided by Medicare and any other supplemental insurance they have.

5.2 Usual Medical Care

This group will receive whatever care they would normally receive during the study period. Usual medical care for chronic back pain typically includes continued use of

medications (mostly non-steroidal anti-inflammatory medications) and visits to primary care physicians, physical therapists, and complementary medicine providers. In order to adequately describe the care that has been provided, we will collect information from the GH electronic medical record describing any imaging and other tests ordered, medications (prescribed or recommended use of over the counter), written advice given, notes on activity level, exercise, referrals to physical therapy, complementary therapies, medical specialists, any surgeries performed) as recommended by Somerville et al.[57]

We think this is the best control group for this study because it is the only one that can answer the practical question of whether Tai Chi, when added to usual medical care, is beneficial for relieving cLBP and associated dysfunction. Guidelines for optimal care of older adults with cLBP do not exist and we therefore cannot use guideline-driven case. No clear package of standard care exists and thus, careful documentation of usual medical care, including the need for specialist care and for surgeries will be clearly documented.

A substantial fraction of persons with chronic back pain rely on self-care, only occasionally seeking professional help. In order to minimize disappointment at not being randomized to Tai Chi, participants in the Usual Medical Care group will receive a gift from the study, which will be a stainless steel water bottle with the Kaiser Permanente logo. Compensation has helped maintain high response rates (i.e., close to 90%) from control group participants in our previous trials, but we suspect that a gift will be more appreciated than cash in this population. However, we will follow the guidance from our patient partners.

5.3 Attention Control

Our attention control is designed to match on attention and time in the standard tai chi intervention (i.e., 2x/week of 12 week 60 minutes) and credibility (health education topics of value to seniors that they think could impact their back pain). Each of the 60 minute sessions will include interesting didactic material along with questions and a brief discussion. The sessions will be presented by students in the University of Washington nurse practitioner training program, pharmacy interns and the Study Investigators, geriatric fellows and other expert colleagues when available. We will have a Research Assistant attend the classes to provide continuity and they will be selected for their interest and ability to work with this age group. The didactic material has been selected from a variety of medical (e.g., UptoDate; various Kaiser Permanente Washington guidelines), scientific (e.g., PubMed, National Institutes of Health, CDC), and community sources (e.g., National Caregiver Association).

Table 3: Health Education Classes

Week	1st Class	Topic	2nd Class	Topic
1	1	Healthy Living	2	Back Pain
2	3	Nutrition	4	More Nutrition
3	5	Using Meds Safely	6	Flu/Pneumonia Prevention
4	7	Osteoporosis	8	Fall Prevention

5	9	Brain Health	10	Heart Health and Stroke
6	11	Safe Driving	12	Diabetes
7	13	Communicating with your physician	14	Skin Health
8	15	Caregiving	16	Osteoarthritis
9	17	Housing Options	18	Depression
10	19	Bladder Problems	20	Sleep
11	21	Social Support	22	Stress Reduction
12	23	Footwear	24	Wrap Up

To minimize the likelihood that the seniors will achieve improvement in pain and functional status, we placed those topics we thought most relevant to chronic pain for many older adults(e.g., depression, osteoarthritis, sleep, stress reduction) toward the end of the intervention. We will also inquire about any changes they made in their life as a result of the classes.

6. DESCRIPTION OF STUDY VISITS AND OUTCOME MEASURES

Table 4 presents the schedule of evaluations, while Table 3 further displays the physical and questionnaire assessments.

TABLE 4. Schedule of Evaluations

ASSESSMENT	Screening/ Baseline	Tai Chi Classes/ Attention Control	12/26-Wk	52-Wk
Informed Consent	x/			
Demographics [baseline]	/x			
Medical History [some screening, some baseline]	x/x			
Inclusion/exclusion criteria [screening]	x/		x	x
Physical Assessments	x		x	x
Questionnaire with Outcome Measures [see Table 3]	x		x	x
Enrollment/Randomization	/x			
Class Attendance		x		
Home Practice Logs		x		
Adherence to Tai Chi Protocol/Attention Control Protocol		x		
Adverse events		x	x	x
Qualitative discussion [subset of participants]		x	x	x

6.1 Screening Evaluation

The screening evaluation will be performed by telephone with KPW members who have returned a statement of interest or called our toll-free project number with their contact information or with members of the public who have responded to various forms of outreach. A Research Specialist will phone those members to answer

questions, obtain oral consent for an initial telephone eligibility screen and determine preliminary eligibility using a computer program to guide the interviewer through a series of screening questions based on the final inclusion and exclusion criteria. The screening process will ends with documentation in a database of either preliminary eligibility or ineligibility. Individuals whose responses suggest they are provisionally eligible and who interested in the feasibility RCT will then be scheduled to come to a group in-person assessment in a conference room at a large Kaiser Permanente Washington clinic. They will receive information about the details of the conference room location ahead of time. Individuals who were deemed provisionally eligible more than 10 days in advance of the scheduled baseline visit will be recontacted by phone to make sure that their pain levels were sufficiently high that they remain eligible.

6.2 Enrollment, Baseline and Randomization

Study participants will be enrolled in the study when they have completed their written informed consent, their baseline physical assessments, baseline questionnaire, and been randomized (see Section 4.4 for further details). Documentation of randomization will take place by computer. All participants will be enrolled within two weeks of the first class of each cohort. We will use the recommendations made by the NIH Task Force on Research Standards for Chronic Low Back Pain for studies of chronic low back pain. and for specific baseline information, including a core set of baseline outcome domains, and appropriate PROMIS measures for these domains[58] Baseline information will include sociodemographic characteristics (gender, age, race, ethnicity, education level, employment status, and marital status), back pain history (e.g., years since first episode of back pain, duration of current episode) and other factors that are prognostic of resolution of back pain (e.g., number of pain sites and patient expectations of treatment outcome). The core set of recommended outcomes includes physical function, low back pain intensity, pain interference, depression, sleep disturbance, and catastrophizing. The Baseline Schedule of assessments in shown in Table 3 and the specific outcome assessments are described further in Section 6.2.4.

6.3 Blinding

Research Specialists who collect data on physical measures will be masked to treatment group at all time points. Participants, the instructor and the many study staff will necessarily be aware of group assignment.

6.4 Follow-up Visits

To maximize response rates, reminder letters will be sent before each follow-up visit. The contents of the in-person follow-up visits (12, 26 and 52 week) is shown in Table 2. While participants are provided an opportunity to complete their assessments in a group format (with instructions not to discuss their group assignment), physical assessments (Short Physical Performance Battery, Four Square Step Test, Gait Speed) will take place in a private room adjacent to the group area. The follow-up questionnaire will be administered using either a study tablet computer or a paper questionnaire, whichever the participant prefers. Questions about experiences with specific aspects of the Tai Chi intervention that might cause participants to think differently about their outcomes will be asked at the end of an interview, after all other outcomes are

assessed. We will attempt to obtain outcome data from all participants in the trial. The Research Specialist, masked to study group, will be present and available to answer any questions that might arise while the participant is completing the follow-up questionnaire. Our patient partners will be asked about the value of the group format at follow-up and the likelihood we can maintain our masking with multiple participants in a room. If this is believed unfeasible, we will schedule visits in the same location (GH clinic classroom) for one individual at a time.

The NIH Task Force on Research Standards for Chronic Low Back Pain made recommendations for a core set of baseline outcomes.[58] These measures include many of the key outcome domains recommended for us used in trials of chronic low back pain.[59-61] We will therefore include all of these in our questionnaire along with a few others. Table 3 summarizes the measures, with the NIH Task Force recommendations being shaded in blue. Relevant additional secondary measures of interest for virtually all older adults include scales assessing fear of falling and measures of balance.[62,63]

We will modify our outcome measures in consultation with our patient partners in the Administrative Year prior to the RCT. Because older adults have a variety of symptoms, we might, for example, include the MYMOP measure,[64] which allows patients to assess progress on their own desired outcomes from health care. Careful attention will be paid to ensure that the questionnaire is not too burdensome for older adults. We would aim for approximately 20 minutes for the follow-up questionnaires.

TABLE 5:Content of Baseline and Follow-up Assessments
SOURCES OF DATA FOR BACK TAI CHI TRIAL

MEASURES	Baseline	12-Wk	26-Wk	52-Wk
BASELINE INFORMATION				
Patient characteristics (age, gender, ethnicity, race, employment status, education, height, weight, smoking status, excessive use of drugs or alcohol) (NIH Task Force Research Standards); education	x			
Back pain history (pain duration, leg pain, other pain sites, low back operation, use of selected treatments, work loss due to back pain, disability status, catastrophizing, fear avoidance)	x			
Expectations and knowledge of Tai Chi/Health Education	x			
CORE SET OF OUTCOMES FOR BACK PAIN STUDIES				
* Back dysfunction (24-item Roland Morris Disability Questionnaire-RMDQ)	x	x	x	x
* Low back pain intensity (0-10 numerical rating scale)	x	x	x	x
Pain interference (4-items PROMIS)	x	x	x	x
Pain Interference and enjoyment of life (2-items PEG)	x	x	x	x
Physical Function (4-items PROMIS)	x	x	x	x

Depression (4-items PROMIS)	x	x	x	x
Anxiety Screener (GAD-2)	x	x	x	x
Sleep disturbance (4-items PROMIS)	x	x	x	x
Patient Global Impression of Change (7 item scale)		x	x	x
Participant Disposition (see Section 6.4.iv)		x	x	x
TREATMENT-RELATED INFORMATION				
Adverse events		x	x	x
Perceptions of Tai Chi & HE classes, including instructors		x	x	
Adherence to assigned treatment, including home practice		x	x	x
Willingness to participate in a RCT of Tai Chi with an Attention Control (Cohort 1)	x			
POTENTIAL CONFOUNDERS				
Use of co-interventions (medications, other treatments, etc.)	x	x	x	x
Daily exercise and job-related activity	x	x	x	x
MEASURES FOR FALLS AND BALANCE				
Short Physical Performance Battery (balance, gait speed, chair stand)†	x	x	x	x
Four Step Square Test†	x	x	x	x
Fear of Falling	x	x	x	x

**Co-Primary Outcome Measures*
† Physical Assessment

i. Co-Primary Outcome Measures

Back-related dysfunction will be measured with the Roland Disability Questionnaire ("Roland scale")[65] which asks whether 24 specific activities were limited due to back pain during the past week (yes or no). This measure has been found to be reliable, valid and sensitive to clinical changes, and is appropriate for telephone administration and patients with moderate disability. This legacy questionnaire will be included as our primary outcome because we have used in all of our previous trials. We will also include the PROMIS physical function to see how they perform relative to each other.

Pain will be measured by asking participants how they would rate their back pain on average using a 1 to 10 numerical rating scale.[58] This is likely to be very comparable to our previously used 0 to 10 scales to measure either the pain intensity or bothersomeness of back pain during the previous week on a 0 to 10 scale (0 = "not at all bothersome" and 10 = "extremely bothersome"). The validity of numerical rating scales of pain has been well documented, and such scales have demonstrated sensitivity to detecting change in pain after treatment.

ii. Other Core Recommended Outcomes:

Physical function will be assessed using the 4-item PROMIS measure.[58]

Depression will be assessed with the 4-item PROMIS measure, for which there is a published "crosswalk" to the Patient Health Questionnaire-8 (PHQ-9) which measures both depression severity and current DSM-IV depression diagnostic status and which we have used in prior studies.[66]

Anxiety will be measured by means of the 2-item Generalized Anxiety Disorder scale (GAD-2), which has demonstrated high sensitivity and specificity in detecting generalized anxiety disorder in primary care populations [61, 62].

Pain Interference with normal daily activities will be measured with 4 PROMIS measure.[58]

Sleep disturbance will be measured with the 4-item PROMIS measure.[58]

Patient Global Impression of Improvement [of cLBP related dysfunction] will be asked on a seven point scale ranging from "very much improved" to "very much worse". This standard rating has worked well in our prior studies.

iii. Selected Other Outcomes

Use of back-related medications and exercise in past week will be measured on the 12, 26 and 52-week questionnaires to provide an indication of how these behaviors were affected by the interventions. They also provide an indication of "co-interventions" that occurred during the follow-up period.

Qualitative outcomes: Inclusion of open-ended questions in our previous trials has yielded valuable insights into participants' feelings about the value of specific components of the interventions and the impact of the interventions on their lives. We will, therefore, include open-ended questions asking about these issues at the end of the 12, 26 and 52-week follow-up interviews.

Fall outcomes: The Short Physical Performance Battery is a group of physical performance tests that combines the results of gait speed, chair stand and balance test into one measures that predicts disability in diverse populations.[62,63] The Four Square test is another reliable and valid measure of balance.[67] Fear of falling will be measured with the well validated, 7-item short form version of the Falls Efficacy Scale – International.[68]

iv. Maximizing Follow-up Rates and Documentation of Follow-up

We will attempt to obtain outcome data from all RCT participants, including those who have moved out of state. We will collect information on the outcomes at every stage of our recruitment, randomization, and treatment process so that we can report patient flow according to the CONSORT guidelines,[69] which is necessary for assessing the feasibility of the study. We will attempt to ensure high response rates by paying participants $25 for each completed interview. We will calculate follow-up rates for our 12, 26 and 52-week interviews separately for the Tai Chi, Attention Control and Usual

Medical Care groups. In our other trials we have consistently achieved short-term follow-up rates over 90% and one-year follow-up rates of close to 90% in our previous RCTs evaluating CIM treatments for cLBP[70-73] by keeping interviews reasonably short, and compensating participants for completing the interviews.

v. Assessment of Feasibility:

We will collect data on the key components of the feasibility trial from four sources: 1) feedback from members of the research team, 2) information from the Tai Chi instructor and consultant Wayne, 3) data collected during the feasibility trial (e.g., recruitment rates, class attendance, home practice, follow-up rates, adverse events), and 4) data from debriefing group discussions with 30 RCT participants (16 from Tai Chi, 6 from Attention Control and 8 from Usual Medical Care). At the 52-week follow-up, 30 participants (16 from Tai Chi, 6 from Attention Control and 8 from Usual Medical Care) will be invited to attend an intervention-specific group discussion (just after their final outcome assessment) to provide feedback on their experiences with all aspects of the study (e.g., recruitment process, Tai Chi or Attention Control protocols, outcome measures, adverse effects, home practice support procedures and materials).

7. ASSESSMENT OF SAFETY

In a systematic review of adverse events in RCTs of Tai Chi, Wayne and colleagues[19] reported no serious adverse events. Other adverse events were primarily minor musculoskeletal pain (back and knee) and occasionally falls were reported.

7.1 Methods and Timing for Assessing, Recording, and Analyzing Safety Parameters

We will collect data on adverse events from several sources and incorporate them into a database. These sources are: 1) reports from the Tai Chi instructor(s) of any extraordinary occurrences of concern to them, 2) the questionnaires completed by participants at 12, 26 and 52-weeks will inquire about: any harm they felt from the Tai Chi classes or home practice, and any serious health problems, and 3) participants themselves because the consent form directs participants with injuries they believe may be related to the mind-body programs to call the Principal Investigator, Co-Investigators or the Human Subjects Representative, whose names and phone numbers are listed on the copy of the consent form retained by the participant.

7.2 Adverse Events and Serious Adverse Events

We will define an **Adverse Event (AE)** as any unfavorable and unintended diagnosis, symptom, sign (including an abnormal laboratory finding), syndrome or disease which either occurs during the study, having been absent at baseline, or if present at baseline, appears to worsen. Adverse events will to be recording regardless of their relationship to the study intervention.

For this study, **Serious Adverse Events (SAE)** are defined as any research-related event (occurring at any dose or level of intervention) that results in any of the following outcomes:

- Death;

- Life-threatening event;
- Inpatient hospitalization or prolongation of existing hospitalization;
- A persistent or significant disability/incapacity; OR
- Any event that when based upon appropriate medical judgment may jeopardize the health or well-being of the subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

7.3 Reporting Procedures

Adverse event data from the questionnaires will be provided to the Project Manager within a week (and will be transferred to the AE database). These will be reviewed, as will AE reports from all sources, by Dr. Sherman, with the assistance of Co-Investigator Rosenberg (a psychologist) and James Ralston (a GHRI physician; Co-Investigator Phalen will be available for geriatric specific issues)) on a weekly basis. Any SAEs identified will be reported promptly to the Kaiser Permanente Washington Human Subject Review Committee (the GH IRB) and the Independent Monitoring Committee (IMC). If an AE is reported by phone, the study staff member will complete an Adverse Events form, which will be entered into the database and will alert Project Manager Hawkes and PI Sherman of the new AE report. If a SAE is identified by phone, it will be reported as outlined below. Adverse events that are not serious will be recorded and included in regular DSM Body reports, but will not be reported early to the IMC. Appendix A details adverse event reporting as required by the Kaiser Permanente Washington IRB.

Serious Adverse Events that are fatal will be reported to the IMC chair within 7 days of discovery, regardless of attribution. The table below details the adverse event reporting schedule and actions:

Table 4. Adverse Event Reporting Procedures

Adverse Event	Action taking by study team
Serious	
Fatal	
Tai Chi Related[a]	Record on AE and SAE forms Report to DSM Body Chair within 3 days of discovery
Not Tai Chi Related[b]	Record on AE form Report to IMC within 7 days of discovery
Not Fatal	
Tai Chi Related[a]	Report on AE and SAE forms Report to IMC within 7 days of discovery
Not Tai Chi Related[b]	Record on AE form Report to IMC as part of regular reports
Not Serious	Record on AE form

[a] possibly, probably or definitely
[b] definitely not

7.4 Follow up for Adverse Events

For non-serious adverse events, participants will be contacted to see how they are doing. They will be followed until any adverse events, at least possibly related to the study are resolved. The GH IRB will offer guidance about follow-up required for other conditions unrelated to the study.

7.5 Safety Monitoring

This is an unmasked Phase trial comparing Enhanced Tai Chi and Usual Medical Care for chronic back pain. Given the favorable safety profile from previous studies of Tai Chi including Dr. Wayne's coupled with the small numbers of adverse events reported in the literature, we propose that this trial will be monitored for safety by an Independent Monitoring Committee. The IMC was established with NCCIH's approval, and consists of a primary care physician, a biostatistician and a Tai Chi instructor.

The IMCs job will be to evaluate the adverse-experience data we will provide them on a regular basis to protect the safety of the study participants. Based on the observed adverse effects of the treatment under study, the IMC will make recommendations on a regular basis to the PI and the Office of Clinical and Regulatory Affairs at the National Center for Complementary and Integrative Health (NCCIH) regarding continuation, termination, or other modifications of the trial.

8. INTERVENTION DISCONTINUATION

There are a variety of conceivable reasons participants may prematurely discontinue the class series and study staff will use the following groupings to categorize them:

- Practice of Tai Chi associated with unacceptable or serious adverse events from perspective of participant
- Continued participation considered inadvisable by investigator, class instructor or participant's physician due to concerns that continued participation poses an unacceptable risk to the patient.
- Participants do not care for the class environment
- Tai Chi perceived as ineffective by participant
- Events in participant's life unrelated to trial (e.g., illness or death in family)
- The study is stopped by the GH IRB, the NCCIH or the OHRP

A study withdrawal form will be completed for individual who discontinues the intervention. In all cases, participants who discontinue treatments will be encouraged to complete the remaining follow-up assessments using the regular follow-up schedule (i.e., 12, 26, and 52 weeks).

9. STATISTICAL CONSIDERATIONS

9.1 General Design Issues

In this feasibility study, we chose a parallel group design using three arms (Enhanced Tai Chi, Comprehensive Health Education Control and Usual Medical Care)

that would be part of a 3 or 4-arm full-scale RCT if an assessment indicates that the larger study is feasible.

By assembling information from interviews with study participants, the Tai Chi instructor, members of the research team, and from study records, we will be able to perform a thorough evaluation of our study procedures and protocols. This evaluation will be guided by the criteria for assessing the adequacy of specific study components clearly specified in the Administrative Year. This information will allow evaluation of the overall feasibility of conducting a large RCT, the size of the pool of potential participants required (and therefore the number of study sites), the feasibility of including the maintenance Tai Chi intervention, and the adequacy of recruitment and follow-up procedures. Finally, this trial will provide estimates of the baseline means and standard deviations of the primary outcome measures, albeit with small sample sizes. If this evaluation concludes that conducting a full-scale RCT of Tai Chi for older adults with cLBP is feasible, this study will provide the information necessary for preparing a grant proposal for successfully conducting such a RCT.

9.2 Sample Size and Randomization

Because this is a feasibility study, the sample size is not designed to detect clinically important effects of the primary effectiveness outcomes, back-related dysfunction and pain intensity.[74] Rather, for this type of study, the sample size needs to be large enough to provide a high likelihood of surfacing any important problems that may exist in the study execution.[74] Our sample size of 78 was chosen based on practical considerations to provide ample opportunity to identify problems with the study procedures, intervention protocols (including adherence), outcome measures, and follow-up rates. Therefore, a trial of this size is insufficiently powered to detect clinically important effects in our outcomes; for example the power would be only 48% assuming a 10% loss to follow-up, α=0.05 and an effect size of 0.5 (similar to a clinically important difference on the RMDQ in younger adults). However, we believe that our proposed sample size is sufficient to determine whether the trial is feasible.

If we conclude that a full-scale RCT of Tai Chi for cLBP in older adults is feasible, we would calculate our sample size requirements using estimates of the standard deviations from large previous RCTs of other CIM interventions of older adults,[75] accepted criteria for the minimum clinically important difference for the RMDQ (our primary outcome measure, which would be measured as a continuous variable),[76] standard levels of type I (α=0.05) and type II (β between 0.1 and 0.2, for power between 80% ad 90%) errors, and dropout rates and missing data rates estimated from this study's follow-up rates. If appropriate, the contemporary "best practice" method of imputation for missing data (e.g., multiple imputation) would be used.

Participants would be randomized to each of the three study arms (Enhanced Tai Chi, Comprehensive Health Education and Usual Medical Care). Our study biostatistician would prepare a computer-generated sequence of random numbers that will be inserted into a special computer program for randomization. The program will contain blocks of varying sizes to ensure balanced but unpredictable assignment of participants to both groups. We will consider whether we should conduct randomization

stratified by age (65-79; 80+) and gender because both are related to baseline measures of back dysfunction and pain.[7] If we decide to do this, we would incorporate a stratified randomization scheme into the computer program. We are experienced with both methods of randomizing participants. Further details related to randomization were provided in section 4.4.

9.3 Definition of Populations

In a full-scale trial, we would perform an intention to treat analysis. Therefore we would include all participants who were randomized into the trial, regardless of whether they participated in the assigned treatments. By using this approach, we would minimize biases that often occur when participants who do not receive the assigned treatments are excluded from analysis. In the full-scale trial, we would also perform a per protocol analysis that included only individuals who adhered to the Tai Chi class protocol, using a threshold that we will determine in our Administrative Year.

9.4 Interim Analyses and Stopping Rules

We are not planning any interim analyses for this feasibility study.

The trial will be stopped only if the Safety Monitoring Body (SMB), the KPW IRB, the NCCIH or the OHRP believes there is an unacceptable risk of serious adverse events in the Tai Chi treatment arm. In this case, the SMB could decide to terminate the entire trial. Based on our previous research and on the small number of reports of adverse events from these treatments reported in the literature, we believe the risk of Serious Adverse Events related to our Tai Chi intervention is quite small, having never been documented in the literature. We are not planning to stop the study for slow accrual or high losses to follow-up because in this feasibility study, we would make changes in recruitment and follow-up procedures to try to maximize the feasibility of the study. We would therefore consider difficulties in these areas as signals that changes in our proposed methods are necessary.

9.5 Outcomes

Our feasibility outcomes will include the information we would to report participant flow in the feasibility RCT according to the CONSORT guidelines,[69] This will include collect information on the outcomes at every stage of our recruitment, randomization, and treatment process and follow-up time periods. Many of these outcomes will be collected directed by computer, while others will first be collected with paper forms and then transferred to our database.

At the baseline and 12, 26, and 52-week follow-up study visits, outcome measures and physical assessments will be collected as described in Table 3 (section 6.2.4). The primary outcome measures in the full-scale trial would be back-related function (Roland Morris Disability Questionnaire) and back pain intensity. Further details on these measures are provided in Section 6.2.4.

9.6 Data Analyses

i. Feasibility of a full-scale RCT

We will use descriptive analyses to examine many aspects of feasibility, including recruitment, randomization, Tai Chi adherence, adverse events and follow-up rates. To assess recruitment feasibility, we will collect information at every stage of our recruitment and randomization process. We will compute the rates of screening and enrollment per month. This will let us know how many invitation letters we would need to send to potentially eligible persons to meet recruitment goals in a large RCT. Our primary method of recruitment will be through mailed invitations to persons meeting our initial inclusion and exclusion criteria according to the information in the EMR (see sections 4.2 and 4.3). This recruitment method will allow us to calculate the percentage of these potentially eligible persons who end up agreeing to participate in the trial. Because ICD codes do not distinguish between chronic and acute pain and do not always distinguish between pain in the lumbar spine (low back) from pain in mid-back or neck, most potentially-eligible persons will be found during screening interviews to not have cLBP. This information will help determine the number of recruitment sites that would be necessary to conduct an adequately-powered RCT. If our primary recruitment method proves inadequate for efficiently meeting our goals, we will evaluate the ability of alternative methods determined in the Administrative Year (e.g., advertising in the health plan's quarterly magazine) to accrue significant numbers of additional participants.

To assess RCT retention rates, we will compute the treatment specific retention rates, which are typically large in our trials. For Tai Chi treatment adherence, we will compute the number of classes attended and the amount of home practice per week. Benchmarks for Tai Chi adherence will be derived (in the Administrative Year) by a thorough literature review of adherence in RCTS evaluating exercise for cLBP, Tai Chi for chronic pain and Tai Chi in the elderly. Additional information, such as ratings of how well participants perform key aspects of the Tai Chi protocol, will be obtained.

To assess safety, we will compute the proportion of persons reporting adverse events as well as the type and seriousness of the event. In our prior studies, 15 to 29% of participants reported mild transient increases in pain when stretching or doing yoga. We think adverse events for Tai Chi may be similarly mild , but slightly less common because of the nature of the movement.

To assess follow-up rates, we will compute treatment specific and overall follow-up rates at each time point. While our prior trials have consistently had post-treatment follow-up rates over 90% in the short term and close to that at one-year follow-ups, we will consider follow-up rates of 80% or better to indicate feasibility.

As described in Section 6.2.4iii, we will obtain qualitative feedback on all aspects of the study from 30 participants. Our prior experience suggests this number is sufficient to elicit a broad range of experience and to begin to see themes and experiences repeated across respondents (i.e., achieve "response saturation")[77,78] Dr. Rosenberg, an experienced qualitative researcher, will conduct these discussion groups, which will be audio recorded and transcribed. We will also invite suggestions for improvement in the study procedures and protocols. Because these debriefing interviews will inquire

about specific experiences and suggestions for improving our procedures and protocols, our analyses will be largely descriptive and not require resource-intensive ethnographic analysis techniques.

ii. Information required for full-scale RCT

If we conclude that a full-scale RCT of Tai Chi for cLBP in older adults is feasible, we will calculate our sample size requirements using estimates of the standard deviations from large previous RCTs of other CIM interventions of older adults,[75] accepted criteria for the minimum clinically important difference for the RMDQ (our primary outcome measure),[76] standard levels of type I and type II errors, and dropout rates estimated from this study's follow-up rates.

We plan to analyze the data in the full-scale RCT using the recommendations from the RTF.[58] Because most of the outcome measures they propose are relatively new, it is important for us to compute summary statistics for these measures (e.g., means, percentages) so that we can compare our population to others reported in the literature and so that we can identify issues with missing data, etc. Using data from this feasibility RCT, we plan to conduct preliminary analyses using the recommendations from the RTF (i.e., examine continuous outcomes, perform responder analyses [the proportion of study participants who achieve specific thresholds], and look at the cumulative distribution function for improvement by treatment group to see what challenges, if any, we encounter. Finally, we will also stratify patients in this study by the personal impact of cLBP on them. We will use the recommended Impact Stratification approach to see what the distribution would be in this population and whether sub-group analyses are likely feasible in the full-scale RCT.

iii. Preliminary Outcome Analyses

Preliminary analyses will <u>not</u> be properly powered, but will alert us to potential analytic challenges in the full-scale trial. We will employ the analytic techniques we would propose in a full-scale trial. In our comparisons of treatments on the outcome measures, we will analyze outcomes from all follow-up time points in a single model, adjusting for possible correlation within individuals and treatment group cohorts using generalized estimating equations (GEE).[79] Because we cannot reasonably make an assumption of constant or linear group differences over time, we will include an interaction term between treatment group and time point. We plan to adjust for baseline outcome value, gender, and age of analyses The general form of the regression model will be: $g(Y(t)) = \beta_0 + \beta_1 Baseline + \alpha_1 Trt + + \alpha_2 Trt \times Time + \alpha_3 z + \varepsilon$, where $Y(t)$ is the response at follow-up time t, *Baseline* is the pre-randomization value of the outcome measure, *Trt* include a dummy variables for the Tai Chi group or the Comprehensive Health Education Control group, *Time* is a series of dummy variables indicating the follow-up times, and z is a vector of covariates representing other variables being adjusted for. (Note that α_1, α_2, and α_3 are vectors.) The referent group in this model is the Usual Medical Care group. For binary and continuous outcomes, we will use appropriate link functions (i.e., logit for binary).

10. <u>DATA COLLECTION, QUALITY CONTROL AND CONFIDENTIALITY</u>

10.1 Data Collection Forms

Eligibility information will be collected directly in a computer assisted telephone interviewing database. Baseline and follow-up questionnaires will be self-report on paper forms or, if necessary, via telephone interview. Masked assessors (trained Research Specialists) will collect data on the physical assessments using paper forms.

Individual records will be identified by a unique study identification number. Records linking study ID with participant names or other identifying information that may be needed for follow-up interviews, class attendance, etc. will be kept separate from the study data and will be accessed only by study team members on a need-to-know basis. All study files will be kept in a locked filing cabinet. Computer files will be secure and password protected.

10.2 Data Management

We will employ our time- tested procedures for interview data collection and quality control, scanning self-administered forms or using double key entry verification of paper forms or to minimize data collection errors during baseline and follow-up interviews. If possible, self-report interview data will be collected in –person and inspected for completeness before the participant leaves to minimize errors. We will employ our standard quality control procedures to ensure that data collection is proceeding smoothly, electronic data are password protected and paper forms are stored in locked filing cabinets to ensure confidentiality of information.

We will implement procedures to ensure that all data collection processes are proceeding smoothly. These procedures will ensure that randomization is proceeding as planned, recruitment is on schedule, data collection forms are accurately entered into databases, the database is storing data correctly and that data can be accurately transferred and retrieved as needed. We will develop a relational database to track information on every stage of recruitment, randomization, class attendance, and outcomes assessment so we can report patient flow automatically and in an integrated fashion using standard, automated reports. All data system processes will be thoroughly tested prior to the start of recruitment.

All questionnaire databases will contain range and logic checks. Participant attendance information collected during the classes will be double key entered into a computer database that also contains logic checks. Prior to recruitment, all data systems will be tested with imaginary participants. Data will be examined for completeness using computer programs developed specifically for that purpose. In addition, we will test all analytic programs to ensure that the analyses are accurate. Computer files with participant names will be password protected with access restricted to staff using this information to recruit participants, contact class participants or obtain follow-up data, and interact with any patients reporting adverse events. Any paper data forms, such as homework logs, identifiable only by unique study ID numbers, will be kept in locked filing cabinets. Finally, all analysis data files will be password protected. Full data backup procedures are performed nightly, with partial data back-up throughout the day.

10.3 Quality Assurance

10.3.1 Training

All study staff will have had prior experience with RCTs, will have been trained in Good Clinical Practice Guidelines, and will be trained specifically on the procedures for this trial. A study Manual of Operations will be created that details the procedure for each element of the study implementation. Prior to the start of recruitment, the study team will participate in training sessions with mock participants to ensure an understanding of all study procedures and consistency in application.

10.3.2 Protocol Deviations

Protocol deviations will be captured through weekly review of study recruitment and follow-up reports and through routine bi-weekly data checks of study data being collected, entered, and stored in our study databases. The weekly review of study recruitment and follow-up reports will be conducted by PI, Sherman and Project Manager Hawkes. The bi-weekly data check of the study databases will be performed by the programmer and reviewed by PI Sherman and Project Manager Hawkes. In addition, study staff responsible for conducting these activities will meet with Project Manager Hawkes on a weekly basis to discuss study progress and any potential violations that may have occurred. Protocol violations will be reported to the Kaiser Permanente Washington IRB as a part of the annual continuing review report. In addition, protocol violations will be reported to the Independent Monitoring Committee as a part of the reports completed every six months during active recruitment, intervention, and follow-up periods.

10.3.3 Monitoring

Project Manager Hawkes will meet with study staff responsible for conducting RCT activities on a weekly basis to discuss and review recruitment, intervention and follow-up activities. A study data quality assurance (QA) tracking file will be created in EXCEL and will be used to track adherence to the study protocol. Examples of elements including on the QA tracking file are: confirmation of signed consent form, confirmation of home practice logs (for those randomized to Tai Chi), and attendance information. The study QA tracking file will be completed by our study research specialists and will be reviewed by Project Manager Hawkes. Any protocol deviations will be shared with PI Sherman and will be reported to the Kaiser Permanente Washington IRB and our study DSMBody at the next regularly scheduled reporting period. In addition, our study programmer will run data QA checks to ensure that study data being collected is complete and accurate. Any abnormalities in data will be immediately reported to PI Sherman and Project Manager Hawkes so that a solution can be created.

11. ETHICAL PRINCIPLES

11.1 Institutional Review Board

The investigators are responsible for obtaining initial and continuing review (at intervals of not less than yearly) of the study by their IRB. Written approval from the IRB will be on file prior to commencement of study activities. All study personnel have Human Subjects Research Training certification on file with the IRB, including Good Clinical Practice training

11.2 Informed Consent:

Kaiser Permanente Washington members who are have received an invitation letter to the study and are interested in participating will sign and return a statement indicating their willingness to be contacted by study staff. A toll-free study line will also be included for potential participants who prefer to contact study staff via telephone. A Research Specialist will then phone interested enrollees to answer questions, obtain oral consent for an initial telephone eligibility screen and determine preliminary eligibility using a computer program to guide the interviewer through a series of screening questions. The screening process ends with documentation in a database of either preliminary eligibility or ineligibility. Once a potential participant has been deemed preliminarily eligible, they will be scheduled to attend one of our in-person group eligibility screening and assessment visits at a Kaiser Permanente Washington Medical Center. While the in-person visits are in a group setting, physical assessments, informed consent, and randomization will take place in a private room adjacent to the group area. During the group assessment visit, eligibility will be confirmed through completion of a final eligibility screening (e.g. demonstration of sufficient mobility, willing ness to be randomized). If the participant is deemed eligible and is willing to participate, informed consent will be administered by a study Research Specialist. This will include an explanation of interview time commitments and content, intervention commitments (class attendance, home practice, and home practice diary completion), potential risks of participation, potential benefits of participation, what to do for an adverse event, and options for discontinuation of participation in the study. The Research Specialist will also explain the handling of data and personal health information as dictated by HIPAA. Signed consent forms will be kept at the Kaiser Permanente Washington Research Institute in a locked filing cabinet only accessible by the appropriate study staff**.**

11.3 Health Insurance Portability and Accountability Act (HIPAA)

Kaiser Permanente Washington has instituted a protocol that ensures research is conducted in compliance with the federal law entitled, “Health Insurance Portability and Accountability Act (HIPAA)”. Permission to use, create, and release personal health information for research will be obtained before potential participants can be enrolled in this study. One of the study Research Specialists will explain HIPPA as it relates to this research study to potential participants to ensure that they understand it and have the opportunity to ask any questions pertaining to their personal health information as it relates to this study. This process will explain what is meant by health information, how health information is obtained, how the researchers may use health information, and detail the steps a participant must take if s/he decides to revoke this permission.

11.4 Confidentiality of Participant Records

The investigators and their study teams will maintain strict confidentiality of the participant records. Individual records will be identified by a unique study identification number. Records linking study ID with participant names or other identifying information that may be needed for follow-up interviews, class attendance, etc. will be kept separate from the study data and will be accessed only by study team members on a need-to-know basis. All study files will be kept in a locked filing cabinet. Computer files will be

secure and password protected. Any information about any participant will not be released without the written permission of the participant, except as necessary for monitoring by the KPW IRB, the NCCIH and the OHRP.

11.5 Study Discontinuation

The study may be discontinued at any time by the KPW IRB, the NCCIH or the OHRP as part of their duties to ensure that research participants are protected.

12. ORGANIZATION AND ADMINISTRATION

12.1 Funding and Organizational Oversight

The Back Tai Chi study would be a two year single-site clinical trial funded as an R34 by the National Center for Complementary and Integrative Health (NCCIH). The NCCIH Project Officer assigned to this project would provide NCCIH oversight on the project. A specially-created Safety Monitoring Body will ensure the safety and welfare of patients enrolled in this trial. Budgetary oversight will be provided by NCCIH staff. The study would be reviewed and approved by NCCIH's Office of Clinical and Regulatory Affairs.

12.2 Organizational Structure

Administrative Leadership is based at the Kaiser Permanente Washington Research Institute in Seattle. Overall scientific and administrative responsibility for the project resides with Dr. Karen Sherman, the Principal Investigator. Ms. Rene Hawkes, Project Manager, is responsible for day-to-day project administration, human resources issues, correspondence with the IRB, supervision of study staff, and coordinating liaison with the Tai Chi class instructor(s). Dr. Sherman and the Programmer will have responsibility for ensuring data integrity. The Safety Monitoring Body will have responsible for ensuring the safety of study participants.

Biostatistician Wellman will ensure that the project team is aware of relevant statistical issues that could affect study design, will create the randomization scheme, analyze the data and anticipate the needs of a large RCT. Project Manager Hawkes will have responsibility for preparation of materials for the IRB, for hiring and supervising project staff, and for maintaining the budget. There will be monthly meetings of all team members, and weekly meetings of those team members actively involved in the specific activities underway at the time.

13 PUBLICATION POLICIES AND PROCEDURES

The Principal Investigator has responsibility for developing and maintaining a list of proposed publications including topic, names of the primary authors and date proposed. It is the first author's responsibility to determine who will be listed as co-authors and in what order. We will follow the International Committee of Medical Journal Editors' guidelines on authorship on all manuscripts deriving from this study. "Publications" will be a standing item on the agenda for team meetings to ensure open and frequent discussion of this issue. The P.I. will be first author on the primary manuscript, but first authorship on all other manuscripts will be shared.

14 STUDY TIMELINE: MILESTONES

The proposed study timeline is shown below for the feasibility study. The Administrative Year, during which the protocol will be finalized, all other study documents created, and approvals obtained from the GH IRB, the NCCIH Office of Clinical and Regulatory Affairs, and the Independent Monitoring Committee is not shown. However, all approvals will be obtained before the study is started.

TASK	COHORT 1	COHORT 2
Recruit, randomize, collect baseline data	Month 1-4	Month 5-8
Conduct Standard Tai Chi classes	Month 5-8	Month 9-11
Conduct Maintenance Tai Chi Classes	Month 8-13	Month 12-17
Collect 12 week follow-up data	Month 8-9	Month 12-13
Collect 26 week follow-up data	Month 11-12	Month 15-6
Collect 52 week follow-up data	Month 17-18	Month 21-22
Conduct debriefing discussion groups	Month 17-18	Month 21-22
Analyze data	Month 20-23	
Prepare report, manuscripts, grant proposal	Month 22-24	

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Appendix A: Kaiser Permanente Washington IRB (Human Subjects Review Committee – HSRC) Reporting Requirements related to Adverse Events

Principal Investigator Reports to HSRC:	Report Within 1 Business Day	Report within 15 Days of Rect or before next HSRC Meeting Deadline (whichever is first)	Report at PI Discretion	Summarize at Continuing Review
Adverse Events (AE)				
Unexpected death of research participant that is at least possibly related to the study	✓			✓
Unexpected death of research participant that is not related to the study				✓
Adverse Events which are unexpected, serious, and at least possibly related to the study—(these AE's also represent Unanticipated Problems)		✓		✓
Unexpected and serious, but definitely not related to the study, and not an Unanticipated Problem				✓
Serious Adverse Events that are expected (see definition) in some subjects, but are determined or suspected to be occurring at a significantly higher frequency or severity than expected.		✓		✓
Expected (see definition) adverse events, serious or not serious, at least possibly related, not occurring at a higher frequency or severity than expected				✓
Any event leading to the PI's concern regarding health, safety, or rights of research participants		✓		✓
Other Unexpected Adverse Events, regardless of severity, that may alter the HSRC's analysis of the risk versus potential benefit of the research because they suggest that the research places subjects or others at greater risk of physical or psychological harm than was previously known or recognized and, as a result, may warrant consideration of substantive changes in the research protocol or informed consent process / document.		✓		✓
Summarize **ALL** Adverse Events (whether previously reported to HSRC or not) at				✓

time of yearly continuation review)				
If DSM Body determines that an Adverse Event that was not previously reported to the HSRC, is now determined to also represent an Unanticipated Problem (for example due to increased frequency), then the Investigator must report it promptly to the HSRC. Include the monitoring entity's report with any actions taken with the submission to the HSRC. In addition, summarize the event(s) at time of Continuing Review.