Feasibility of Remote-Delivery Interventions: Tai Chi and Wellness for PTSD and Pain in Veterans

Funding Agency: National Center for Complementary and Integrative Health (NCCIH)

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Abstract

Posttraumatic stress disorder (PTSD) affects almost one quarter of military Veterans seeking care from Veterans Administration healthcare facilities. PTSD is associated with many health-related issues, especially chronic musculoskeletal pain, and is increasingly considered a systemic disorder, affecting both mind and body. Accessible treatments that address PTSD and chronic pain are urgently needed. Tai Chi is an ancient Chinese exercise that uses an integrated mind-body approach to enhance quality of life. Tai Chi delivered in groups has been shown to improve both mental health and physical health in patients with a variety of chronic conditions. However, no studies to date have examined Tai Chi for PTSD and pain in Veterans. Since the onset of COVID-19, interventions that can be delivered without the need for face-to-face contact are greatly needed. Remote mind-body interventions delivered via videoconferencing platforms can reduce barriers to treatment for Veterans isolated by PTSD-related avoidance, travel related challenges, or public health social distancing restrictions. The proposed study will evaluate the feasibility of remotely delivered Tai Chi for PTSD and pain in Veterans. This trial represents first steps toward a long-term goal of establishing this mind-body treatment to address these maladies for Veterans via a remote videoconferencing platform. In Phase One, the research team will adapt and do a 'dry run' of two existing 12-week, twice per week interventions (Tai Chi and a Wellness control) for delivery via videoconferencing for the study population. In Phase One, the team will recruit 12 participants (6 in each group) and utilize quantitative and qualitative feedback to refine and standardize the interventions. In Phase Two, 36 participants will be randomly assigned over 3 cohorts (n = 12 for each cohort, n = 6 for each group) to either a Tai Chi or a Wellness group for 12 weeks with a post-treatment and three-month follow up assessment. The feasibility and acceptability of a remotely delivered randomized trial of these two interventions and the assessment protocols will be determined. Feasibility will be quantified using rates of participant eligibility, recruitment, attrition, and adherence to the treatment and assessment protocols. Feasibility will be indicated (1) by the ability to meet recruitment goals, including women and minority participation, and (2) by having at least 75% of participants regularly attend sessions and engage in home practice and 70% complete post-intervention and follow-up assessments. Acceptability will be assessed via participants' ratings on a standardized measure of treatment satisfaction, supplemented by qualitative exit interviews. Acceptability will be indicated by 70% of the participants reporting treatment satisfaction and credibility. Information from this trial will be utilized to design a large, randomized control study evaluating the efficacy of Tai Chi for improving outcomes for Veterans with PTSD and chronic musculoskeletal pain. The proposed study will be pivotal to establish procedures to fully evaluate a novel, accessible, nonpharmacologic approach for symptom management of PTSD and chronic pain in a future large-scale trial of Tai Chi.

List of Abbreviations

VA	Veterans Affairs
VHA	Veterans Health Administration
BMC/BUMC	Boston Medical Center/Boston University Medical Campus
IRB	Institutional Review Board
SMART Goals	Specific, Measurable, Attainable, Realistic, Timely
HIPAA	Health Insurance Portability and Accountability Act
VA ORD	Veterans Affairs Office of Research and Development
CPT	Cognitive Processing Therapy
PTSD	Posttraumatic Stress Disorder
PE	Prolonged Exposure
IOM	Institute of Medicine
R&D	Research & Development
IRGT	Individually Randomized Group Treatment Trial
ICF	Informed Consent Form
CSQ	Client Satisfaction Questionnaire
CEQ	Credibility/Expectancy Questionnaire
SAE	Serious Adverse Event
BSD	Behavioral Science Division
CAPS*	Clinician-Administered PTSD Scale
PAR-Q*	Physical Activity Readiness Questionnaire
BPI*	Brief Pain Inventory
SF-36*	Short Form Survey (36 questions)
30-s STS*	30-Second Sit to Stand Test
PCL-5*	PTSD Checklist
PHI*	Personal Health Inventory

*only included in tables

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1.0 Study Personnel

This study will be conducted at VA Boston Healthcare System. It is funded by the National Center for Complementary and Integrative Health through Boston University Chobanian & Avedisian School of Medicine. Below is the list of personnel working on this study.

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2.0 Introduction

Posttraumatic stress disorder (PTSD) is a debilitating psychological disorder that affects 6% of U.S. adults in their lifetimes[1]. In military Veterans seeking care in Veterans Health Administration (VHA) facilities, the prevalence of PTSD rises to 23%[2]. PTSD is associated with a host of psychosocial and health ailments[3,4], including increased mortality[5], that severely impact society at large. If symptoms remain untreated, the negative impact of PTSD on the functioning and medical status of Veterans may worsen over time. Current treatments for PTSD have been primarily concentrated on trauma-focused psychotherapies that direct the client to recall and process traumatic events in a controlled fashion. Two trauma-focused treatments, cognitive processing therapy (CPT)[6] and prolonged exposure (PE)[7] have been recommended as first-line PTSD treatments in clinical practice guidelines[8]. However, a large proportion of individuals with PTSD drop out of trauma-focused treatment[9, 10]. Accumulating evidence indicates that persistent symptoms of PTSD can improve with the evidence-based treatments described above but, for many, they do not remit. A recent review of clinical trials of CPT and PE in Veteran and military populations indicated that although mean scores on relevant outcome measures drop both significantly and substantially[11], at least one third of individuals do not achieve a therapeutic response to treatment. Moreover, roughly two-thirds of patients involved in these clinical trials retained their PTSD diagnoses posttreatment.

While PTSD historically has been considered a psychological disorder, ongoing research highlights its deleterious effects on physical health, and it has been increasingly considered a *systemic disorder*, affecting not only the brain and an individual's psychological functioning, but also the entire body[12, 13]. Individuals with PTSD have been shown to be at greater risk for a wide range of medical problems, such as chronic pain[3], cardiovascular disease[14], stroke[15, 16], metabolic syndrome[17], certain types of cancer[18], and mortality[5]. Recent research into the biological correlates of PTSD indicates that a pathological, accelerated aging process may also occur[19, 20]. Chronic pain is a common ailment in Veterans using VA services, with prevalence estimates around 50%[21]. PTSD and chronic pain have striking co-morbidity with one-another, especially in VA populations: 60 to 80% of Veterans with PTSD report chronic pain symptoms[3, 22] and up to 50% of patients seeking relief of chronic pain report symptoms consistent with PTSD[23-26]. The presence of both disorders is associated with higher levels of symptomatology and disability[25, 26]. Asmundson and colleagues [27, 28] mutual maintenance and shared vulnerability model suggests that heightened physiologic arousal and sensitivity to anxiety may both predispose individuals to develop and fuel perpetuation of comorbid PTSD and chronic pain. Reductions in symptoms of one disorder may help break a cycle of mutual maintenance and then reduce symptoms of the other. Mind-body treatments that address both disorders can have an important synergistic effect to improve symptoms and functioning. Treatments that focus on general health promotion may be more appealing to Veterans with PTSD and have the potential to improve both physical and mental health functioning. Complementary and integrative treatments, such as mindfulness meditation, yoga, and Tai Chi, have received increasing attention in clinical settings as alternative or adjunctive treatments for PTSD. Almost all VHA specialized PTSD programs offer some integrative therapies[29] and over 30% of individuals diagnosed with PTSD utilize one or more of these treatments for mental health issues[30]. The Institute of Medicine (IOM) called for more research on complementary and integrative approaches on the treatment of PTSD[31] and randomized controlled trials have accumulated in recent years to support the use of integrative therapies such as mindfulness, yoga, and relaxation[10]. Yet, despite the increasing interest in and use of these practices, <u>there have been no randomized clinical trials to date examining Tai Chi as a treatment for PTSD</u>.

3.0 Objectives

<u>HYPOTHESIS:</u> Remotely delivered Tai Chi and Wellness interventions will be feasible and acceptable integrative treatments for PTSD and chronic musculoskeletal pain in Veterans.

The proposed two-phase feasibility trial represents first steps toward our long-term goal of establishing Tai Chi as an effective remotely delivered mind-body treatment for Veterans with PTSD and chronic musculoskeletal pain. In *Phase One*, we will adapt two existing 12-week, twice per week interventions (Tai Chi and Wellness control) for delivery via a videoconferencing platform for the study population. We will recruit 6 participants for Tai Chi and 6 participants for Wellness to conduct a 'dry run' of each condition. We will utilize quantitative and

qualitative data to refine and standardize the interventions. In *Phase Two*, 36 participants will be randomly assigned over 3 cohorts (n = 12 per cohort, n = 6 per group) to either the Tai Chi or Wellness condition for 12 weeks with a 3-month post-treatment follow up assessment.

We will accomplish the following Specific Aims:

> **AIM 1.** During *Phase One*, we will refine and standardize two treatment protocols for Veterans diagnosed with PTSD and chronic musculoskeletal pain. Tai Chi and a Wellness control condition intervention will be adapted for delivery via a videoconferencing platform for the population.
> **AIM 2.** During *Phase Two*, we will determine the feasibility and acceptability of a remotely delivered randomized trial of these two interventions and the assessment protocols.
> **AIM 3.** We will use information from this trial to plan and design a large, randomized control study evaluating the efficacy of Tai Chi for improving outcomes for Veterans with PTSD and chronic musculoskeletal pain.

4.0 Resources and Personnel

The proposed research will be primarily housed at the Behavioral Science Division (BSD) of the National Center for PTSD located at the VA Boston Healthcare System/Jamaica Plain Campus in Boston, MA. All project staff working on the proposed project will either have their own office space, or access to office space if it is needed. All office spaces have computers, office furniture including locked filing cabinets and locked desks, and phones with designated phone numbers.

For video-teleconferencing for study interventions, investigators and group intervention leaders have access to updated versions of a VA approved videoconferencing platform (e.g., Cisco Webex or Microsoft Teams). Assessment data will be collected through Qualtrics. All computers are equipped with external cameras (e.g. Logitech cameras). Tai Chi instructors will have access to large screen monitors where they will be able to see high quality images of all participants in their class at once.

Barbara L. Niles, Ph.D., Principal Investigator, (Effort: .6 calendar months)

Dr. Niles is a staff research psychologist at the Behavioral Sciences Division of the National Center for PTSD at VABHS and an Associate Professor of Psychiatry at the Boston University Chobanian and Avedesian School of Medicine. In the proposed study, Dr. Niles will use her expertise in post-deployment distress, mind body interventions, and present centered therapy to serve as PI and direct the project. She has past working relationships with all key personnel and has assembled a team of talented co-investigators with particular expertise in Tai Chi, behavioral medicine, PTSD, and statistical analyses. She will work with Tai Chi instructors, who they have contracted with, to develop the Tai Chi protocol and to run the Tai Chi groups. She will work closely to coordinate with all personnel to ensure that the study runs smoothly, manage the budget and ensure that all necessary IRB approvals (VABHS and BMC/BUMC) are obtained. Dr. Niles will oversee study recruitment, supervise the implementation of the interventions, and monitor data management and analyses. Dr. Niles will manage all aspects of data collection, data analyses and interpretation, as well as manuscript and report preparation.

DeAnna L. Mori, Ph.D., Co-Principal Investigator, (Effort: 4 calendar months)

Dr. Mori is a Clinical Psychologist with expertise in Behavioral Medicine and an Assistant Professor of Psychiatry at the Boston University Chobanian and Avedesian School of Medicine. Dr. Mori will use her expertise in health behavior and promoting behavior change to assist in the development, implementation and running of the proposed study. She will oversee the development and implementation of the Wellness group control intervention and will supervise and/or deliver the intervention. Along with Dr. Niles, she will work with

the contracted Tai Chi instructors to develop and implement Tai Chi group for Veterans with PTSD. She will assist with recruitment efforts. In addition, she will provide supervision to the research assistant and project coordinator, and assist with data management, analysis, and interpretation, as well as preparation of presentations and manuscripts.

Anica Pless Kaiser, Ph.D., Co-Investigator, (Effort: .24 calendar months in years 1 and 3)

Dr. Pless Kaiser is a Staff Psychologist at the Behavioral Science Division of the National Center for PTSD at VABHS and a Research Assistant Professor of Psychiatry at Boston University Chobanian and Avedesian School of Medicine. Dr. Pless Kaiser will use her expertise with all aspects of qualitative data collection, management, and analysis to contribute to the current project. She will work with Dr. Niles and Mori to design and implement individual feedback interviews. She will assist in participant recruitment and will also contribute time to aid with data analysis and interpretation--qualitative analysis in particular--as well as with presentation and manuscript preparation.

Terence M. Keane, Ph.D., Co-Investigator, (Effort: .12 calendar months for years 1 and 2, .24 calendar months for year 3)

Dr. Terence Keane is the Associate Chief of Staff for Research and Development at VA Boston Healthcare System and Director of the National Center for Posttraumatic Stress Disorder's Behavioral Science Division. Dr. Keane is an internationally renowned expert in the field of PTSD, and he has devoted his career to providing the foundation for understanding PTSD.

As a faculty member and Assistant Dean for VA Research at Boston University Chobanian and Avedesian School of Medicine, Dr. Keane will bring expertise in the assessment, phenomenology, and treatment of PTSD in many diverse populations to help in subject recruitment, data analyses and interpretation of findings, and manuscript preparation.

Research Assistant (Effort: 12 calendar months for year 1 and 2)

The research assistant (RA) will provide informed consent at baseline and conduct the assessments for the study at baseline, post-treatment, and follow-up periods. Throughout the recruitment phase of the study, the RA will also assist investigators with recruitment efforts including making phone calls, screening participants over the phone, scheduling and conducting assessments, data entry, transcribing scripts, organizing participant data and data files. They will also assist the PIs in maintaining approvals on the study protocol for IRB and R&D committees and for maintaining communication with the committees (e.g., unanticipated events, etc.).

Brian Muccio and Ben Warner, Tai Chi Instructors.

Both Mr. Muccio and Mr. Warner are Tai Chi instructors who have extensive experience working with our research team conducting Tai Chi mind-body research programs. In preparation for Phase I, Mr. Muccio and Mr. Warner will work closely with Drs. Niles and Mori to adapt an existing Tai Chi protocol to meet the needs of Veterans with PTSD and pain and to be deliverable using a videoconferencing system. They will work with the team to further refine the protocol based on feedback and data that is obtained during Phase I. In addition, they will develop a video recording for the Tai Chi intervention that participants can follow for home practice. Mr. Muccio and Mr. Warner have current approved WOC appointments and are credentialed to conduct research at VA Boston.

All team members above have access to protected health information, and therefore will receive the required human subjects and confidentiality training, which includes information about maintaining data integrity and security. For further information, please see section 7.0 (Privacy and Confidentiality).

4.0 Study Procedures

4.1 Study Design

In the proposed trial, we plan to refine interventions that will later be used to conduct a small, randomized trial to provide critical information to inform a future large-scale randomized efficacy trial of Tai Chi for PTSD and chronic pain. Building on our combined experience the proposed study will:

(1) Adapt, refine, and standardize two 12-week treatment protocols (Tai Chi and a Wellness control condition) for Veterans diagnosed with PTSD and chronic musculoskeletal pain during *Phase One*. Tai Chi and Wellness interventions will be adapted for delivery via a videoconferencing platform for the population and piloted in a 'dry run'.

(2) Determine the feasibility and acceptability of a remotely delivered randomized trial of these two interventions and the assessment protocols during *Phase Two*.

(3) Utilize information from this trial to plan and design a large, randomized control study evaluating the efficacy of Tai Chi compared to Wellness for improving outcomes for Veterans with PTSD and chronic musculoskeletal pain.

Study Interventions:

Tai Chi Intervention and Instructors

Tai Chi will be practiced using a standardized Tai Chi protocol developed for Veterans with PTSD that will be based on protocols that have been well-tested in our previous trials[32-34], and adapted with information obtained while conducting the Introduction to Tai Chi for PTSD study[35], and the currently running Gulf War Illness study. Tai Chi Instructors Brian Muccio and Ben Warner have had extensive experience conducting Tai Chi programs at VA Boston and are credentialed through the VABHS Research Service to provide Tai Chi instruction to Veterans in research studies. They will utilize their knowledge of Veterans with chronic disorders and will work with Dr. Wang and VA study staff to develop a suitable and replicable Tai Chi program specifically for Veterans with PTSD and chronic pain. They will adapt the protocol to minimize movement across the floor (e.g., removing sequential stepping and instead include Tai Chi movements that involve single steps so participants will not encounter obstacles in their homes or move out of range of their camera and to maximize instructor demonstration ability on screen (e.g., providing front and side views, and close ups) to help participants see and learn the movements. Due to the time limited nature of the group intervention, the 108 postures of Classical Yang style Tai Chi will be condensed to 10 forms that are easily comprehensible and can be learned within 12 weeks. Sessions will not be videorecorded to protect participant privacy. For missed sessions, participants will be encouraged to practice using the video recordings that will be available on the study website.

*Wellness Control Intervention and Facilitators***.** We will utilize a Wellness program for the comparison group because this approach has been successfully used in other studies conducted by our team, including a pilot feasibility study conducted with Veterans with PTSD[36-38]. The Wellness intervention will be based on the VA Whole Health Program which helps individuals identify and achieve their personal health goals. The Whole Health Program include modules that address physical activity, personal development, healthy eating and drinking, stress management, relationships, personal surroundings, and spirituality. The Wellness intervention has been adapted with updated information from the VA Whole Health website and other resources to make it suitable for a population with PTSD and chronic pain. Using the SMART goals model, participants will set health and wellness goals each week, and discussions about ways to address potential barriers will be included in this condition. This group will be facilitated by doctoral level psychology staff, and/or psychology trainees and research staff who will be supervised by licensed and credentialed study staff.

For both interventions, study staff will hold "tech sessions" with participants prior to the initial session to ensure that audio and video connections are adequate, and participants know how to navigate the VA-approved videoconferencing platform used (e.g., Cisco Webex or Microsoft Teams). In addition, participants randomized to the Tai Chi group will have the opportunity to provide updates on any physical issues or limitations they would like to make the instructor aware of. Study staff will be available by telephone to help with connectivity

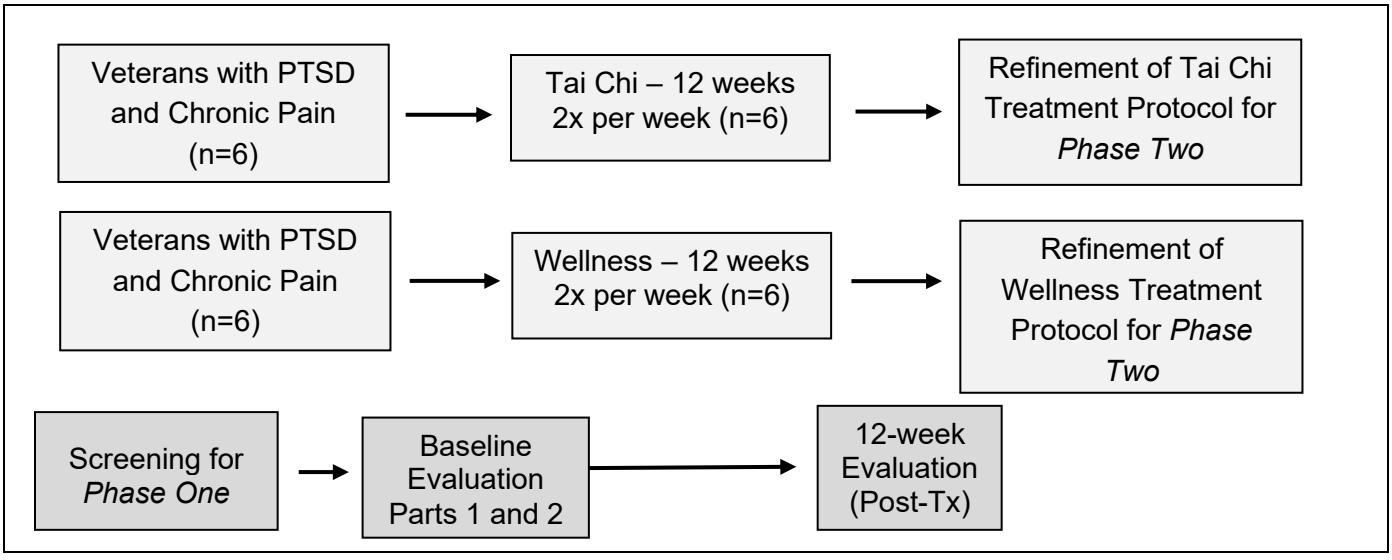
and technical issues at the beginning of each session and will call participants who have not logged in to offer assistance.

Participants may be given a water bottle after attending Tai Chi or Wellness class. The water bottles have a logo that says "VA Boston Health & Wellness Research" and display the circular VA emblem. These water bottles may be mailed to participants with a thank you note from the study team.

Participants in both conditions will receive assessments at baseline and at 12 weeks (post-intervention). Participants in Phase Two (described below) will also receive a 3-month follow-up assessment. Weekly measures will be administered electronically using Qualtrics and entered into a secure database. (Please see section 5.5 below for more information about assessments). In addition, participants will receive phone calls each week where they will report on their home practice in the Tai Chi Group, and report on their SMART goals in the Wellness group. During these calls, participants will have the opportunity to provide feedback that may be used to improve their group experience. This could include topics such as: best ways to maximize telehealth visibility and at-home Tai Chi setup; any feedback to relay to the instructor including updates on physical issues or limitations; preferences for the amount of sitting vs. standing for the class; preferences for the amount of group discussion vs. didactic instruction, etc. This information will be recorded in an Excel spreadsheet that will use subject ID identifiers only and will be saved to a previously approved folder in the Drive: "\\r04bhsnas61\resgroups$\PTSD\DATA\RESEARCH\TeleHealth - Niles\Tai Chi Studies\1.NCCIH_R34". Information will be discussed at weekly lab meetings to help the study team improve the TeleHealth experience for group participants.

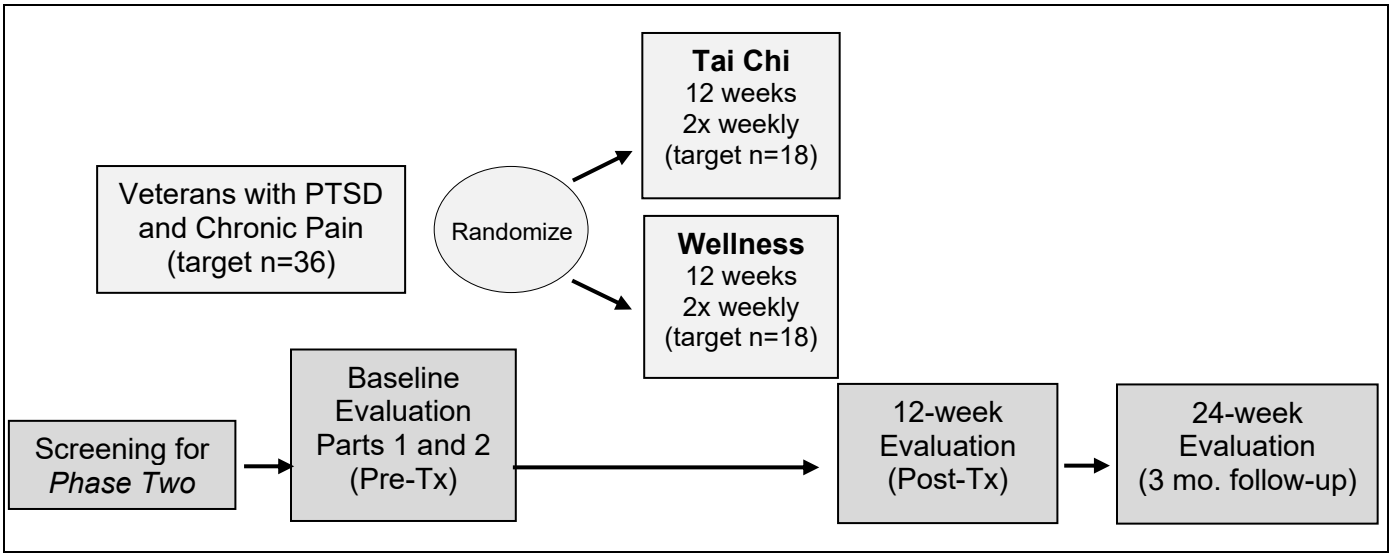
In *Phase One*, we will conduct a 'dry run' of each treatment with 6 participants for Tai Chi and 6 participants for the Wellness control (recruited separately for expediency). After participants complete the group treatment, staff will schedule participants for a post-treatment assessment. In addition, participants will be interviewed about their group experience. These interviews will be conducted using a VA-approved videoconferencing platform (e.g., Microsoft Teams or Cisco Webex) *without* video, and participants will be called at a telephone number that they provide. With participant permission to audio record, these interviews will be recorded and transcribed using the transcription feature available with the platform. The feedback obtained will be used to make modifications to our methods to optimize the delivery of the remotely delivered interventions. We will examine issues regarding instructor style, session content, and written materials for both interventions using participant feedback interviews and will modify the participant manuals, videos, and protocols as appropriate. The revised participant manuals will be used for *Phase Two*. (See Figure 1 below).

Figure 1: ***Phase One*** **Schema**



In *Phase Two*, we will use an individually randomized group treatment trial (IRGT) design. A target goal of 36 participants will be recruited and randomly assigned over 3 cohorts (n = 12 for each cohort, n = 6 for each group) to either a Tai Chi or a Wellness group for 12 weeks. Evaluations will occur at baseline, post-treatment (12-weeks) and 3-month follow-up (24-weeks). (See Figure 2 below.) Both groups will be delivered using a videoconferencing platform.

Figure 2: ***Phase Two*** **Schema**



To ensure that our development efforts benefit from the perspectives and ideas of the Veterans with symptoms of PTSD and chronic pain, study staff will also interview each participant individually during the post-treatment (12-week) evaluation and 3-month follow-up (24-week) evaluation about their experience. Staff will utilize an interview guide and will elicit suggestions from the participants for optimizing the effectiveness of the videoconferencing platform and appeal of the program, recruitment procedure, class logistics, adherence, and outcome measures. These individual interviews will be conducted virtually using a VA-approved video conferencing platform (e.g., Microsoft Teams or Cisco Webex), and with participant permission, will be video-recorded. Participants will be informed that the recording will be transcribed using the transcription feature in the platform used. Participants who decline being video recorded will be asked permission for study staff to take notes on their comments.

The video recording and transcript data will be saved in the restricted-access study folder.

We will instruct participants to maintain their regular medications and routine visits to their doctors throughout the study. The investigators will record any changes in medication therapy but will not be involved in any changes of therapy. The changes in treatment will be determined through the Electronic Medical Records and patient report.

We will conduct this trial through the National Center for PTSD at the Veterans Affairs Boston Healthcare System (VABHS). Information from this trial will be used to plan and design a larger study evaluating the efficacy of Tai Chi in improving health outcomes in Veteran populations with PTSD and chronic pain.

Participant Enrollment

For both phases of the study, after determining preliminary eligibility via telephone screening and examination of electronic health record, a study staff member will schedule and conduct a remote session with each

participant via a secure videoconferencing platform approved by VA Boston for patient use (e.g. Cisco Webex, Microsoft Teams). Study details and alternatives to participating in the study will be reviewed. If participants report that they understand the study procedures and are willing to participate in the study, staff will ask participants to sign the ICF and HIPAA forms either electronically using DocuSign program or on a hard copy with a wet signature if unable to do so electronically. (See below for Informed Consent Process).

Dropout/Unenrollment

Participants will not be unenrolled in the study if they do not attend sessions. We will use an intention-to-treat approach and attempt to capture all potential data at all assessments unless participants request that we do not contact them. (Examples: If a participant does not attend the post-treatment assessment, we will nonetheless contact them to ask them to complete the 3-month follow-up. If a participant gets a new job and cannot attend group sessions, we will nonetheless contact them for the post-treatment and follow-up assessments. If a participant tells us that they would like to drop out of the study and do not want to be contacted for additional assessments, we will not contact them again.) A dropout will be defined as someone who requests that we do not contact them again for study assessments.

Use of Email

Study staff may use e-mail with participants to send: 1) instructions on how to access the remotely delivered intervention groups, 2) date, time and link to assessments that will be conducted remotely, and/or 3) previously approved participant manuals or measures to participants as needed (e.g. if postal mail is delayed or participants ask for copies), **3) a standardized email with instructions for the baseline assessment.** Standard VA-approved language indicating that Veterans should not reply to these e-mails will be included in each e-mail.

Risks to Human Subjects

While the risks of both the Tai Chi and Wellness group protocols are minimal, there are some potential risks. There is potential for minor injury from the Tai Chi exercises, including muscle tears, strain, sprains, and joint pain. In the Wellness Group Condition, some individuals may feel discomfort discussing goals with other participants and staff. In addition, participants may feel some stress, frustration, or boredom while completing the questionnaires. There will be a mental health professional available throughout the study for participants to talk with if needed. The social risks of participating in this protocol are minimal. There may be some embarrassment as participants learn to do Tai Chi or share in a group with other participants, but the instructors will be trained to be very sensitive to the individual needs of each participant and create an environment that feels safe and nonjudgmental. There is no economic risk associated with participating in this study.

Some discomfort may occur when discussing traumatic experiences during the assessment interviews. Drs. Niles, Mori, and Pless Kaiser are all licensed psychologists with extensive experience in handling emotional discomfort and risk management of patients with psychological disorders. They will directly supervise the study staff who will be conducting diagnostic interviews and one of them will always be on call when interviews are taking place to handle emergencies, such as safety concerns.

Protection Against Risk

- Given that this study will take place fully remotely, it will be important to ensure that participants have a safe and private location where they will be able to participate in the study. In order to protect the confidentiality of everyone in their group, participants will need to be in place where others are not able to see their video screen or hear the audio.

- Study staff will monitor participants on screen (grid view) during the classes, direct them to stay in front of their cameras, and take appropriate actions (e.g. calling out to them, calling by phone) if participants are not visible on screen.
- Participants will also need to provide the address where they will be participating in the study, and contact information of someone who can be called in the event of an emergency. The local police number will also be obtained for emergency purposes
- Participants will be informed in the ICF that "*to comply with laws and regulations, we may need to share safety-related information such as that relating to child abuse or neglect; elder or disabled person abuse; specific reportable diseases; harm to yourself or others".* Although there will be no questions asked in the assessments regarding suicidal or homicidal thoughts or intentions, if suicidal or homicidal intentions are disclosed, confidentiality may be broken in order for protective measures to be taken. Although there will be no questions asked in the assessments regarding care of children or geriatric persons, if a participant were to disclose child or elder abuse, appropriate agencies would be contacted, and participants will be so informed in the consent form.
- All personnel involved in this proposed project will have completed the required ethics, human subjects, and confidentiality training, which include information about maintaining data integrity and security. Careful monitoring of participants during all phases of study participation will be conducted by the project staff. Participants will be instructed to contact study personnel at any time (including during the follow-up interval) in the event of worsening of symptoms. Participants who begin treatment and experience adverse outcomes sufficient to require removal from the study will receive appropriate clinical care.
- Drs. Niles, Mori, and Pless Kaiser are all licensed psychologists with extensive experience in handling emotional discomfort and risk management of patients with psychological disorders. They will directly supervise the study staff who will be conducting screening interviews, assessments, and intervention sessions. One of the psychologist investigators will always be on call during interactions with study participants to handle emergencies, such as safety concerns, and to make appropriate referrals for mental health services. Participants who are screened out due to recent suicide attempts or active suicidality will be referred for appropriate VA mental health services.
- As in any type of treatment or clinical research program, participants' confidentiality must be carefully guarded and respected. All data with identifying information will be stored in locked files or password-protected computer files. Data being analyzed will be identified by subject codes and identifying information will be removed. The identity of participants will not be revealed in the presentation or publication of any results from the project. All project staff working on the project will be educated about the importance of strictly respecting participants' rights to confidentiality and will have completed several training courses including proper practice in accordance with HIPAA regulations, protection of human subjects, and computer security.
- The VABHS will provide care to participants during their enrollment in this study for any study-related adverse events or injuries. Participants will not be required to pay for any services they receive as a subject in an approved VA research study. However, some Veterans are required to pay co-payments for medical care and services provided by the VA. These co-payment requirements will continue to apply to medical care and services (including, but not limited to, dental services, supplies, medicines, orthopedic and prosthetic appliances, and domiciliary or nursing home care) provided by the VA that are not part of this research study. In the event that emergency care is needed during the intervention classes, study staff will call either the Veteran's identified emergency point of contact, the local police number, or the enhanced-911 number (267-908-6605) to alert emergency services in the geographic area where the patient is located.

Potential Benefits of the Proposed Research to Research Participants and Others

While there are some minimal risks associated with the proposed risks, they are offset by some potential benefits. Specifically, the current research shows that Tai Chi has both physical and mental health benefits and appears to be safe and effective in promoting balance control, muscle strength, flexibility, and cardiovascular fitness. For the Wellness condition, health behaviors with known physical health benefits (e.g., healthy eating, improving sleep habits, engaging in physical activity) and mental health benefits (e.g., stress management, relationship skills) will be promoted.

4.2 Recruitment Methods

Participants will be recruited in the following ways:

1. IRB approved flyer and link to the study website may be posted on VA Facebook pages (e.g., Health Promotion Disease Prevention Facebook Page). Information contained in the approved flyer and posted on the approved website [https://www.research.va.gov/for_veterans/ptsd-pain-holistic.cfm] may be used by researchers, clinicians, or other interested parties outside VA Boston to inform populations of Veterans about this study (e.g., researchers of studies taking place at other VA sites, researchers at non-VA institutions, personnel from local or national Veterans organizations).
2. IRB approved flyer and webpage developed on a VA ORD website may be distributed at public events for Veterans and/or at public research affiliated events (e.g., Museum of Science Annual Brain Health Fair).
3. IRB approved language approved for the flyer and website may be used to promote the study in newsletters distributed by the VA.
4. IRB approved flyer may be posted throughout VABHS and Vet Centers.
5. Investigators will inform medical center staff about the study and encourage them to inform Veterans with symptoms of PTSD of the study or provide them with IRB-approved pamphlets.
6. We may utilize the National Center for PTSD's electronic referral database which consists of over 500 potential research participants. Participants are entered into the repository on a voluntary basis, and written permission for future contact has already been established. The IRB of the VABHS has approved this recruitment mechanism (IRB#1293: "Multiproject Subject Recruitment by the National Center For PTSD").
7. IRB approved flyer and link to the study website may be posted to Veteran social media platforms such as Veterans Facebook groups and pages. Our research team will contact the administrator of each page we wish to post to and inquire if they are willing to post the study flyers, brochures, and link. If yes, the approved recruitment materials will be shared.
8. Study staff may post directly to social media about research study. In addition to asking administrators of social media groups to post to pages and groups, study staff may announce the study on various Veteran social media platforms such as New England Friends of Veterans, Boston Veterans Collaborative and Veterans Facebook groups, directly. Our research team will post the IRB approved study flyer and link to our website. The study will continue to track the source of recruitment for each participant in order to evaluate and maximize recruitment strategies throughout the study. The ability to post directly will allow us to reach a wider audience as often the administrators miss the study team's requests to post.

If additional recruitment materials are developed in the future, we will submit those for IRB approval before employing them.

Study staff will contact potentially eligible Veterans by telephone and describe logistical aspects of the study. Interviewers will answer any questions and obtain oral consent for screening to inquire about inclusion and exclusion criteria. Participants who are not screened out will be scheduled for a remote informed consent and baseline assessment during which the remaining inclusion/exclusion criteria will be evaluated. At no time will study staff engage in "cold-calling" to contact potential participants.

To ensure success in meeting the target recruitment goal of averaging 6 participants per group (12 participants for Phase One and 36 participants for Phase Two), we will recruit up to 10 participants per group for a total of 20 participants for Phase One and 60 participants for Phase Two.

4.3 Informed Consent Procedures

One of the Investigators or a trained, research-credentialed member of the study staff will go through the informed consent process prior to the baseline evaluations for each patient who elects to participate. In order to ensure consistent and thorough administration of the ICF process for this study, study research staff will be trained by the study investigators on the ICF process and will conduct mock ICF sessions with investigators prior to performing the ICF process with participants. The ICF process will take place on a private remote videoconference (e.g., Cisco Webex, Microsoft Teams).

At the scheduled ICF and initial baseline assessment, a study staff member will confirm inclusion and exclusion criteria reported at the initial phone screening call and verbally review each section of the ICF and HIPAA forms with the Veteran. They will explain alternatives to participating in the study, such as treatment available at VA Boston Healthcare System. The study staff member will answer any questions about the study the participant might have. Participants will be given as long as they like to consider participation. If they report that they understand the study procedures and are willing to participate in the study, staff will ask participants to sign the ICF and HIPAA forms electronically using the DocuSign program. This method of informed consent and documentation has been approved for other studies by the VA Boston IRB. If DocuSign is unavailable or the participant does not want to sign the form electronically, study staff will send two hard copies of the ICF to the participant in advance of this meeting. Participants will sign the hard copies and will then be asked to hold the signed signature pages of the ICF and HIPAA forms up to the screen so study staff can capture screen shots of the signed forms to save in secure files. Given the variability in screen-shot quality, study staff will also instruct the veterans to send signed copies of the ICF and HIPAA back to Dr. Niles for VA Boston study records and to keep a signed copy of the forms for their own records.

After the informed consent document is signed, additional screening procedures covered in the informed consent document will be conducted prior to randomization. The investigators consider this consent process to be an ongoing process maintained throughout the study to provide participants with a continued understanding of the protocol, their participation, and their rights as human research subjects.

All discussions concerning consent will emphasize that participation is voluntary and that the participant's medical care/benefits will be unaffected by his or her decision regarding participation. Participants will be informed that they will be compensated for time and inconvenience at a rate of $25 for each of the two baseline assessment sessions and $65 for the post-treatment assessments. Those participants who are recruited for Phase Two will be compensated $80 for the 3-month follow-up assessment. Participants will also receive $5 for completing the weekly measures, $5 for the weekly phone calls with study staff who track home practice/goals, and $5 for each intervention group session they attend for a grand total of up to $355 for those in Phase One and $435 for those in Phase Two. In the event that a participant completes the baseline assessment twice (see paragraph below for scenario where this could occur), the potential total compensation for Phase Two could be $485. This remuneration for time, inconvenience, and ongoing commitment is not so high as to coerce an individual to participate who would otherwise not participate. Compensation will be provided in one of three ways: 1) gift cards to a national chain store (e.g., Target or Walmart) which would be mailed to them, 2) electronic funds transfers to the participants' bank accounts (bank account information including bank routing number, account number, bank name, account type will need to be confirmed), or by 3) debit card payments using Direct Express (participants will need to request a debit card or provide account information if they already have one) and payments will be made directly to the debit card. If gift cards are sent to participants, a templated thank you letter with a breakdown of the gift card payments will be mailed with the gift cards to ensure participants can keep track of (for their own records) the payments they have received throughout the study and what they were for.

Some participants may complete the consenting process but not complete the entire baseline assessment in a timely manner due to illness or other unforeseen reasons. If a participant completed or partially completed a baseline assessment, but is not able to participate in the upcoming cohort, they may be considered for a later cohort. In this case, the participant will be reconsented, baseline measures will be readministered, the participant will be compensated for the additional baseline assessment, and the original baseline measures will not be included for analysis.

[Note: If there is a delay before the second baseline session and the only measure the participant is asked to re-take is the sit to stand task (see below under Study Evaluation for explanation of that), no additional compensation will be provided. This measure takes approximately 5 minutes to administer.]

There will be no circumstances under which a legal authorized representative will provide consent for a participant enrolled in the study. Participants will also be informed that if suicidal intentions, or child or elder abuse are disclosed, confidentiality may be broken for protective measures to be taken.

4.4 Inclusion/Exclusion Criteria

The primary inclusion criteria for this study will be Veterans with PTSD and chronic musculoskeletal pain who agree to abstain from initiating other formal treatments for PTSD during the study period. A more complete description of both the inclusion and exclusion criteria is located in the table below.

An initial screening will take place over the telephone (or in person if the potential participant stops by the research office) to determine if the veteran meets initial inclusion criteria. (Please see Telephone Screening Form.) Telephone screening forms for veterans, including those who do not meet all inclusion criteria, will be completed digitally and kept in a secure data folder on our shared drive (specified below). In the event that we seek and gain IRB approval to amend our inclusion criteria at a future date (e.g. loosen the criteria to include more veterans), we will submit a HIPAA waiver for IRB approval to allow us to access the forms for those who did not originally meet eligibility criteria and to re-contact those individuals who may now be eligible to participate. Additionally, participants who are deemed ineligible after screening will be asked if they would like to be added to the Subject Recruitment Database, in which case they will be mailed the relevant form at a later date.

Final eligibility for the study will be determined after the baseline assessment is completed. The informed consent process will occur prior to initiating the baseline assessment. The CAPS-5 interview to determine the PTSD case definition will take place during part two of the baseline assessment after the informed consent process in part one of the baseline assessment. If veterans do not meet the diagnostic criteria on the CAPS-5, they will be determined ineligible at this point. In addition, if information comes to light during the baseline assessment that indicates ineligibility (e.g., veteran mentions they recently began a new treatment or had a psychiatric hospitalization), they will not be added to the list of participants to be randomized. We anticipate that a small number of veterans may be screened out after the informed consent process and prior to randomization. These veterans will be compensated for participation in the baseline assessment but will be deemed ineligible for the remainder of the study and will not be randomized.

Inclusion criteria	**Exclusion criteria**
- Veteran status as indicated by self-report - **PTSD Case Definition**. Veterans who meet DSM-5 diagnostic criteria *according to DSM-5 diagnostic algorithm* for current PTSD as assessed on the Clinician-Administered PTSD Scale for DSM-5 (CAPS-5) will be eligible for the study. A diagnosis of current PTSD requires: a traumatic stressor (Criterion A) and the requisite number of symptoms at a severity level of 2 or higher in each symptom cluster. Each symptom is rated on a severity scale of 0 (no symptoms) to 4 (extreme), with 2 representing clinically significant and clearly present symptomatology. An individual must endorse at least one reexperiencing (Criterion B) symptom, at least one	- Lacks the capacity to provide consent. - Diagnosed major medical disorder (e.g., neurological disorder, cancer, chronic infectious disease or liver disease) or has a moderate or severe traumatic brain injury, which could otherwise explain the health symptoms or interfere with their ability to safely engage in Tai Chi exercises. - Change in psychotropic or pain medication during the past month. This will minimize amount of symptom change due to medication alterations. (Once enrolled, medication changes are nonetheless expected and will be monitored.) - Regular current Tai Chi, formal mindfulness meditation program, or yoga practice, defined as at least three hours per week for more than three months. (Veterans with

avoidance (Criterion C) symptom, at least two symptoms of negative alterations in cognition and mood (Criterion D), and at least two hyperarousal (Criterion E) symptoms. In addition, these symptoms must have been present for at least one month (Criterion F) and cause either clinically significant distress or functional impairment (Criterion G). - Chronic pain as indicated by complaints of musculoskeletal pain in one or more body regions for six months or more. - Willing to abstain from initiating evidence-based and mindfulness-based psychotherapy for PTSD, pain and related disorders until completion of the study (i.e., prolonged exposure, cognitive processing therapy, cognitive-behavioral treatment for insomnia or pain, acceptance and commitment therapy, dialectical behavior therapy, mindfulness-based stress reduction). Once enrolled, however, if other providers prescribe treatment or if participants require additional intervention (such as to manage a safety or substance abuse condition), treatment will be allowed, and appropriate referrals will be made. Individuals who are currently engaging in short-term (e.g., 12-week protocol) evidence-based treatment will not be eligible until treatment has ended. - Access to internet and home computer or tablet device that will allow telehealth delivery of intervention. - Available to attend either intervention group at the times they are scheduled. - Enrolled and eligible to receive care in Veterans Health Administration (VHA). We will facilitate enrollment for Veterans not currently enrolled but wish to take part in the study.	prior experience who do not currently engage in regular practice at this level *will* be eligible.) - High risk from a mental health perspective e.g., recent psychiatric hospitalization, high risk flag or a note in their VA electronic health record indicating current high-risk factors, entered into a drug or alcohol detoxification or rehabilitation program, or attempted suicide within the previous year as indicated in their VA electronic health record. - Pregnant or breastfeeding or plans to become pregnant within the year, assessed via self-report. Enrollment of pregnant or breastfeeding participants could potentially complicate outcomes, as new symptoms are likely to arise during the course of the intervention that are attributable to the pregnancy or breastfeeding and not the intervention or symptoms related to PTSD. - Reports difficulty standing on feet for the majority of a Tai Chi class (approximately 60 minutes). - Reports that they have been told by a doctor that they should not engage in physical activity unless recommended by a medical team. - Reports other reason they cannot safely participate in physical activity. - Concurrent participation in another clinical trial - Participants who engage in behavior that is disrespectful or disrupts the group may be terminated from the study. - Participants who demonstrate evidence of falsifying data may be terminated from the study

4.5 Study Evaluations

Our primary evaluation measures for this feasibility trial will be measures of feasibility, acceptability, and adherence. Our secondary measures will be administered to pilot the administration of psychometric measures for future trials. Evaluations will be conducted during two baseline sessions (prior to randomization), at post-treatment (12-week evaluation), and (for Phase Two only) at 3-month follow-up (24-week evaluation). A VA approved videoconferencing platform (e.g., Cisco Webex, Microsoft Teams) will be used to administer the measures that need to be conducted by staff (see below). Study staff will also instruct participants regarding how to complete the questionnaires collected electronically using the Qualtrics program and will be available to answer participants' questions in order to facilitate completion. Post-treatment and 3-month follow-up assessments will be completed in one or two sessions.

In order for the baseline data to be valid, the baseline assessment should be completed within approximately one month prior to group assignment. The sit to stand task (planned to be administered at the first baseline session) may be readministered closer to the group start date if delays have taken place. Also, if participants were unable to complete the sit to stand task at the first baseline assessment (e.g. if they do not have an appropriate chair available), it may be completed later.

A. Primary Measures: Feasibility and Acceptability, Measures of Participant Satisfaction and Adherence	
Measure	**Description, Citation, and Metric for Current Study**
The Client Satisfaction Questionnaire (CSQ)	The CSQ assesses participants satisfaction with patient care[39]. Administered at post-treatment, and 3-month follow-up (for *Phase Two* only) via Qualtrics. There are 8 original items that focus on client satisfaction and 3 supplementary items that measure global life satisfaction, general health status and global effectiveness of services received. **Metric**: At least 70% of participants will have a mean item-score of 3 or greater on the 1-4 scale of the 8 original items at post-treatment.
Participant Adherence Attendance/Compliance	Study staff will monitor number of missed sessions, reasons given for missing sessions, and completion of assessments. **Metric:** 75% of participants will attend at least 70% of the treatment sessions. 70% of participants will complete all assessments (baseline through follow-up).
Credibility/Expectancy Questionnaire (CEQ).	Assesses participants' perceptions of treatment credibility and outcome expectancy in clinical outcome trials.[41] Administered at weeks 1,2,4, and 9 via Qualtrics **Metric:** At least 70% of participants will report a mean item-score of 6 or greater on the 1-9 scale by week 4 for both credibility and expectancy
Weekly Log Sheets	Participants will keep logs of homework/practice that will be reported via telephone to the project coordinator weekly during the 12-week intervention period. In the Tai Chi condition, they will record the number of minutes per day spent on home practice. In the Wellness condition, they will record weekly goals. **Metric:** At least 75% of participants will complete at least 70% of weekly log sheets.
B. Secondary Measures Outcome Measures to Be Administered to Ascertain Burden and Calculate Intra-Class Correlation Coefficients Administered at baseline, post-treatment (12-weeks), and 3-month follow-up (24-weeks), for *Phase Two* only) (Note that CAPS-5 will only be administered at baseline and post-treatment for *Phase Two*)	
Construct and Measure	**Description and Citation**
PTSD severity: Clinician Administered PTSD Scale – 5th Edition (CAPS-5)	The CAPS-5 is a structured diagnostic interview for PTSD administered by study staff.[42] The interviews will take place using a VA approved platform (e.g., Cisco Webex or Microsoft Teams). During Phase Two, this diagnostic interview will be video-recorded, with participant permission and administered at baseline and post-treatment. The recordings will be used to ensure reliability of assessor ratings.
Pain: The Brief Pain Inventory – Short Form (BPI)	The BPI is a self-report measure that examines pain intensity and interference with functioning in various life domains.[43,44] Administered via Qualtrics. [43, 44]
Medical Outcomes Study Self-Reported Measure of Health Status: 36-Item Short Form Survey (SF-36)	The SF-36 is a 36 item self-report questionnaire that assesses self-perception of health status in the following domains: physical functioning, role limitations due to physical and emotional factors, social functioning, bodily pain, general health, vitality, and mental health.[45] Administered via Qualtrics.

Physical Functioning: 30 second Sit to Stand Test (30-s STS)	The 30-s STS is an objective measure of lower body strength.[46] Administered by study staff over videoconference platform.

C. Weekly Outcome Measures to Be Administered to Ascertain Burden
Administered weekly using Qualtrics throughout intervention period (both *Phase One* and *Phase Two*)

Construct and Measure	Description and Citation
PTSD: The PTSD Checklist for DSM-5 (PCL-5)	The PCL-5 is a 20-item self-report measure that examines symptoms of DSM-5 posttraumatic stress disorder criteria over the past week.[47,48] Administered via Qualtrics.
Pain: The Brief Pain Inventory – Short Form (BPI)	In addition to being administered at the primary assessment points (baseline, post-treatment, 3-month follow-up) as noted above, the BPI will be administered weekly during the intervention period using Qualtrics. [43, 44 43,44]

D. Other Descriptive Measures

Demographics	This information will be used to provide a comprehensive description of the sample of Veterans and variables may be used as covariates in sensitivity analyses. Administered at baseline. Administered via Qualtrics.
Life Events Checklist Extended Self Report	The LEC-5 will be used to establish Criterion A for the CAPS-5 interview with study staff. Administered at baseline. Administered via Qualtrics.
Psychoactive and Pain Medication Usage	A list of current, prescribed psychoactive and pain medications will be obtained through VA electronic medical record and verified through participant self-report at baseline and updated at subsequent assessments. For each prescribed medication, staff will ask whether participants have been taking medications as prescribed during the previous period and will document lapses and changes.

E. Other Measures

Telephone Screening Form	Potential participants will be screened over the telephone by study staff to determine if they meet inclusion criteria. Individuals who meet this initial criteria will be scheduled for the baseline assessment where the Informed Consent will be reviewed and signed.
Feedback Interview Form	Semi-structured interview developed to obtain feedback from each participant about their participation in the study. This feedback will be obtained through interviews that will take place at post-treatment (12-weeks) and, in Phase Two, at 3-month follow-up (24-week evaluation). Interviews will take place using a VA approved platform (e.g., Cisco Webex or Microsoft Teams), and with participant permission, will be video recorded and transcribed.
Additional Feedback Questions	Some additional satisfaction items will be administered via Qualtrics to address participants' response to the specific interventions used in this study.

Personal Health Inventory (PHI)	The PHI is a 12-item self-report measure that assesses participants' relationship with 8 areas of health and well-being from the VA Whole Health Circle (model that is used in the Wellness Intervention) including relationships, sleep, exercise, food and drink, personal development, spirituality, surroundings, and power of the mind.[49] This scale will be administered using Qualtrics to participants who are in the Wellness Intervention to measure potential growth across these 8 areas of self-care over the course of the study. It will be administered during the intervention at week 2 and week 12 in *Phase 1*, and also at the 3-month follow-up (24-weeks) in *Phase 2.*

4.6 Group Assignment and Randomization

For Phase 1, participants will be assigned to groups based on when they are enrolled. Once we have a group of 6-10 veterans, we will begin one of the groups (either Tai Chi or Wellness based on instructor availability). We then will gather another 6-10 participants for the next group.

For Phase 2, randomization will occur after baseline assessments for all members of the cohort are completed. A study staff member will make a list of available cohort participants in order of completion of initial telephone screening. The cohort list is password-protected and unavailable to the rest of the staff. Another staff member will then use the list randomizer from Random.org (https://www.random.org/lists/) to create a randomly ordered list of the group assignments equally distributed between Tai Chi and Wellness and equal to the size of the cohort, rounding up to an even number. The list of group assignments is then matched with the numbered list of participants. Study staff then call participants to inform them of their condition assignment and the days and times of the group intervention to which they have been assigned.

4.7 Data Analysis

Sample Size Calculation

In this pilot study we are primarily concerned with feasibility and data gathering with a target goal of 48 participants (12 in *Phase One* and 36 in *Phase Two*). Based on our prior experience, we feel confident we can reasonably recruit 48 participants during the study period over 4 waves of recruitment for these intensive (twice per week for 12 weeks) interventions. From our previous experience with remote Tai Chi groups, we found 6 to be an optimal group size as it permitted the instructor to see each participant well on the video screen to provide individualized attention and facilitated a feeling of camaraderie among the participants. For this study's primary outcomes of satisfaction (measured by the CSQ) and credibility of the interventions (measured by the CEQ), we anticipate that more than 70% of the participants will meet the metrics identified. If 26 of 36 participants enrolled in *Phase Two* meet the metric the estimated completion percent would be 72% (95% CI: 55% to 86%). For the primary outcomes of compliance/attendance (measured by sessions and assessments attended), and completion of weekly log sheets, we anticipate that more than 75% of the participants will meet the metrics identified. If 28 of 36 participants enrolled in Phase Two meet the metric the estimated completion percent would be 77% (95% CI: 60% to 89%).

Phase Two of this trial will use an individually randomized group treatment trial (IRGT) design, where individual participants are randomized to one of the interventions and the interventions are delivered in small groups. In *Phase Two*, after a cohort of approximately 12 eligible participants are identified, research staff will contact eligible participants by phone to confirm that they still wish to participate in the study and are able to attend sessions at the days and time of the interventions. Once confirmed, half will be randomly assigned to each of the two conditions (Tai Chi and Wellness). If we are unable to recruit 12 Veterans over a one-month recruitment push, we may randomize a smaller cohort of Veterans so that Veterans who have agreed to participate will not be kept waiting too long to begin the interventions.

If we are successful in recruiting more than 12 Veterans over the recruitment push, we may randomize up to 20 Veterans to help ensure that we will end up with an average of 12 Veterans who are able to participate in the groups. Random assignments to condition will be managed by study staff who will generate the randomization scheme. Participants will be randomized in order of completion of initial telephone screening.

Study staff will then call participants to inform them of their condition assignment and the days and times of the group intervention to which they have been assigned.

AIM 1. During *Phase One*, we will refine and standardize two treatment protocols for Veterans diagnosed with PTSD and chronic musculoskeletal pain. Tai Chi and Wellness interventions will be adapted for delivery via a videoconferencing platform for the population.
Using information gathered from group and individual feedback sessions, we will edit and refine the participant manuals to optimize remote delivery issues such as sound quality, ability to see and follow instructors, instructor ability to view Veterans, and connectivity difficulties. We will also inquire about frequency, duration, and time of day of sessions, class size, ease of use of printed materials and log sheets. We will use adherence and satisfaction data and qualitative feedback to modify the interventions and improve the protocol before moving to *Phase Two*.

AIM 2. During *Phase Two*, we will determine the feasibility and acceptability of a remotely delivered randomized trial of the two interventions and the assessment protocols.
Feasibility and acceptability will be quantified by evaluating rates of eligibility, enrollment, satisfaction, adherence, retention, and credibility expectancy, and compliance with home practice. Specifically:

- Successful eligibility and enrollment will be indicated by our ability to meet overall recruitment goals (in addition to successfully recruiting a representative sample of women and minorities as projected in the Enrollment Table).
- Treatment satisfaction will be indicated if at least 70% of participants have a score of 3 or greater (corresponding to mostly or very satisfied) on the 1-4 scale of the CSQ.
- Adherence and retention will be determined by meeting the metric of at least 75% of participants attending at least 70% of the treatment sessions and 70% of participants completing all baseline and follow-up assessments.
- Credibility will be measured by the CEQ with at least 70% of participants reporting a credibility rating of 6 or greater on the 9-point scale.
- Compliance with home practice will be measured by 75% of participants completing 70% of weekly log sheets.

Measures to be examined for participant burden for the larger trial will assess PTSD symptom severity, pain levels, global health, and physical functioning at baseline, post-treatment and (for *Phase Two* only) 3-month follow-up. In the qualitative feedback interviews, we will further assess these issues to determine if changes are needed regarding recruitment, retention, adherence, and participant burden. If we do not meet the feasibility goals, we will reevaluate to make refinements before developing protocols for a future large trial.

AIM 3. We will utilize information from this trial to plan and design a large, randomized control study evaluating the efficacy of Tai Chi compared to Wellness for improving outcomes for Veterans with PTSD and chronic musculoskeletal pain.
The Tai Chi and Wellness control protocols developed, revised, and finalized as part of the proposed project will be used in a future larger study designed to evaluate Tai Chi for PTSD and chronic pain. The current study will provide preliminary data on feasibility, acceptability, adherence, and participant burden. In addition, the preliminary trial will allow us to work out technology issues to optimize our use of remote videoconferencing and to develop methods to maximize efficiency for research staff that will help guide the design of this large-scale trial. If we fall short of recruitment and/or retention goals, we will use the information gathered during the qualitative interviews and study staff experience to make further refinements to our remote protocol (e.g. providing additional resources for assistance with technology issues for participants, providing videocams or tablets to all participants, assistance with home setup, etc.).

Qualitative data will be analyzed using an iterative coding process. Individual Interviews will be transcribed and then analyzed by a committee of study staff using a general inductive approach. Raters will independently code several transcripts to identify themes, starting with specific categories such as positive experiences, negative experiences, areas for improvement, and other. Next, the committee will meet to review identified themes, to discuss discrepancies, and to refine the suggested coding rubric. Raters will code the remaining

transcripts and continue to meet until consensus is reached on the identified themes and on the distribution of participant quotes under appropriate themes. The committee will then choose participant quotes that best represent the identified themes. This information will be used to inform refinement of the Tai Chi and Wellness protocols to be used in future studies.

5.0 Reporting

Monitoring of safety and data quality in the proposed study will be the responsibility of all personnel on the project, under the guidance and supervision of the Principal Investigators, and with the oversight of an Independent Safety Monitor, John Otis, Ph.D. Dr. John Otis is an expert in the field of pain management and behavioral medicine from VA Boston Healthcare System and Boston University Chobanian and Avedesian School of Medicine. He has a strong track record of conducting research on non-pharmacological pain management interventions and has worked with and developed interventions for Veterans with co-morbid pain and PTSD. Given his experience in working with the specific population we will be recruiting for this study, and his expertise in non-pharmacological interventions for pain and PTSD, he will be an ideal Independent Safety Monitor for this study. Dr. Otis will review our participant safety processes upon initiation of the study and will assess the progress of this study at least once a year. This will include evaluating the processes that are delineated below.

The VA Boston and Boston Medical Center/Boston University Medical Campus (BMC/BUMC) Institutional Review Boards will approve the Statement of Informed Consent for the study and provide institutional oversight of data and safety issues. The study protocol will be approved prior to recruiting or consenting any participants. Moreover, the study will be reviewed on an annual basis by the VABHS IRB committee. Each participant will sign the Informed Consent Form prior to participating in the study. To ensure participant safety, once participants are enrolled in the study, study staff will immediately report all adverse and serious adverse events to one of the PIs. The PI will, per standardized procedures, report them to the VA and BMC/BUMC IRBs for their review. With regard to monitoring of data quality and protected health information, all required personnel proposed for this project will have the required human subjects and confidentiality training, which includes information about maintaining data integrity and security. Confidentiality will be guarded using established procedures such as storing data in locked cabinets within locked offices or locked data rooms, coding by study identification numbers rather than any personally identifying information to avoid revealing the identity of subjects, and aggregating data across participants. The key linking names and study identification numbers will be kept separately from the data sets with limited access by study personnel. Only study personnel will have access to the data sets on protected servers. Data will not be removed from the VA protected environment at any time, except by methods approved through a Data Use Agreement. The investigators may seek a Data Use Agreement at a later date to transfer deidentified data for analysis. Data will be securely transmitted using VA approved methods. Oversight of all aspects of data management will occur with the PIs.

Questionnaire data will be collected using the Qualtrics survey tool for online data collection or will be collected by study staff through participant interviews and record reviews. On study forms, participants will only be identified using the participant's ID number (no names or identifying information will be on the forms). Data collected by study staff will be entered in the computer independently by trained data entry staff, and data entry discrepancies will be corrected by the project coordinator, based on source documents. The quality of the data will be monitored on an ongoing basis. Data quality will be monitored by inspection of the completed forms by a research assistant and any problems detected will be discussed with the PIs. Electronic data will be stored in password-protected database files on a password-protected network system. Only the study staff will have access to the data. Telephone screening forms for Veterans who are ineligible or are eligible but decide not to participate will be kept in a secure electronic file separate from data collected on enrolled participants and will not be accessed by study staff after being placed there.

Records will be destroyed in accordance with the VA Record retention schedule. Records will be destroyed, when applicable, in the following manner: All research data for this study that is maintained on electronic storage and memory devices (e.g., computers, laptops, CDs, recordings, etc.) will be destroyed in a manner in which it cannot be retrieved. All paper records will be destroyed by shredding. Research records and the

information within them will not be used for any purpose other than that which is described in the study as approved by the VA IRB.

In the proposed study we will use the FDA definition of adverse events (AE) and serious adverse events (SAE). Any SAE, whether related to study intervention or not, will be reported within the required 5-day reporting period to the VA IRB and will be followed by an additional letter detailing the nature of the SAE. In the event that a participant either withdraws from the study or the PIs decide to discontinue a participant due to a SAE, the participant will be monitored by the investigators until (a) a resolution is reached (e.g., the problem has resolved or stabilized with no further change expected), (b) the SAE is determined to be clearly unrelated to the study intervention, or (c) the SAE results in death. Outcomes of SAEs will be regularly reported to the VA IRB. A summary of all AEs and SAEs that occurred during the previous year will be included in the annual VA IRB renewal.

Unanticipated Problems will be submitted to the BMC/BUMC IRB within 7 days; AEs/SAEs will be submitted to the BMC/BUMC IRB every three years during the required status check-in for minimal risk research.

We will specifically outline in the Informed Consent Forms the availability of emergency services to participants who may seek them during and after normal working hours. In the Informed Consent Form, we will provide specific information about emergency contacts. Participants are instructed to contact Dr. Niles or Dr. Mori during working hours.

6.0 Privacy and Confidentiality

In order to protect participant privacy, all personnel proposed for this project will have the required human subjects and confidentiality training, which includes information about maintaining data integrity and security. Confidentiality will be guarded using established procedures such as storing electronic data in password-protected database files on a password-protected network system, and hard copy data will be stored in locked cabinets within locked offices or locked data rooms. Data will be coded by study identification numbers rather than any personally identifying information to avoid revealing the identity of subjects, and data will be aggregated across participants. As noted above, the codes that link names and their ID numbers will be kept confidential by the PI in a password protected file on a password-protected network system. Only study personnel will have access to the data, and the datasets will be kept on protected servers. Oversight of all aspects of data management will occur with the PI and Co-Is.

Research records and the information within them will not be used for any purpose other than that which is described in the study as approved by the IRB.

In order to ensure that participants are adequately informed about the protocol and any anticipated risks, research staff will carefully review the IRB approved Informed Consent with the participants. A summary of the potential risks to participants will be provided, and study staff will provide participants with an opportunity to ask questions to insure an adequate understanding.

This study is funded by the NCCIH, one of the institutes of the National Institute of Health (NIH). Certificates of Confidentiality (CoCs) are automatically deemed to be issued for any NIH-funded clinical trials. The NIH does not issue a physical CoC for NIH-funded research projects.

7.0 Communication Plan

The PIs will provide oversight of the entire research project, including the development and implementation of the study. Drs. Niles and Mori have been working collaboratively for over a dozen years and have successfully and jointly conducted two small pilot studies relevant to the proposed project, along with a currently running larger randomized controlled trial where the efficacy of Tai Chi and Wellness interventions

are being investigated with a population of Veterans with Gulf War Illnesses. They are a strong team that provides seamless and comprehensive coverage for the studies they manage. As both PIs have competing responsibilities, sharing interchangeable roles has enhanced their ability to be fully responsive to any administrative or safety issues that arise with their projects. When a question or issue comes up, they can respond quickly and provide immediate resolution. Consequently, they are viewed as a highly responsible research team that takes minimal risks and is capable of conducting complex research protocols with Veteran populations, while always adhering to Good Clinical Practice standards. Drs. Niles and Mori will be in regular communication with each other and with the Co-Investigators regarding project decisions. Conflicts will be resolved through group consensus with the team.

Approval through the VA Boston and Boston Medical Center/Boston University Medical Campus Institutional Review Boards will be obtained prior to recruiting or consenting any participants.

To ensure participant safety, once participants are enrolled in the study, study staff will immediately report all adverse and serious adverse events to one of the PIs. The PI will, per standardized procedures, report them to the IRB for their review.

Any SAE, whether related to study intervention or not, will be reported within the required 5-day reporting period to the IRB and will be followed by an additional letter detailing the nature of the SAE. In the event that a participant either withdraws from the study or the PIs decide to discontinue a participant due to a SAE, the participant will be monitored by the investigators until (a) a resolution is reached (e.g., the problem has resolved or stabilized with no further change expected), (b) the SAE is determined to be clearly unrelated to the study intervention, or (c) the SAE results in death. Outcomes of SAEs will be regularly reported to the IRB.

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