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Study Protocol for a Revised Randomized Trial: Remotely Delivered Tai Chi and Wellness for Gulf War Illness

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Abstract

Background—Many of the 700,000 American military personnel deployed to the Persian Gulf region in 1990 and 1991 have since reported health symptoms of unknown etiology. This cluster of symptoms has been labeled Gulf War Illness and include chronic musculoskeletal pain, fatigue, headaches, memory and attention difficulties, gastrointestinal complaints, skin abnormalities, breathing problems, and mood and sleep problems[1, 2]. There have been few high-quality intervention trials and no strong evidence to support available treatments[3]. Tai Chi is an ancient Chinese martial art with benefits that include enhancing physical and mental health and improving quality of life for those with chronic conditions.

Proposed Methods—In this randomized controlled trial, GW Veterans are randomly assigned to either Tai Chi or a Wellness control condition, with both remotely delivered intervention groups meeting twice a week for 12 weeks. The primary aim is to examine if Tai Chi is associated with greater improvements in GWI symptoms in Veterans with GWI compared to a Wellness intervention. Participants will receive assessments at baseline, 12 weeks (post-intervention), and follow-up assessments 3- and 9-months post-intervention. The primary outcome measure is the Brief Pain Inventory that examines pain intensity and pain interference.

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Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Conclusion—This trial will produce valuable results that can have a meaningful impact on healthcare practices for GWI. If proven as a helpful treatment for individuals with GWI, it would support the implementation of remotely delivered Tai Chi classes that Veterans can access from their own homes.

Keywords

Gulf War Illness; Tai Chi; Wellness; Veteran; Complementary; Integrative

1. Introduction

1.1. Gulf War Illness

Approximately 700,000 American military personnel were deployed to the Persian Gulf region in 1990 and 1991 as part of the multinational coalition that responded to Iraq's invasion of Kuwait. Following deployment, many service members and Veterans reported a cluster of health symptoms of unknown etiology that were subsequently labeled Gulf War Illness (GWI). These disparate and seemingly unrelated symptoms include widespread chronic musculoskeletal pain, fatigue, headaches, memory and attention difficulties, gastrointestinal complaints, skin abnormalities, breathing problems, and mood and sleep problems[1, 2]. This symptom complex has persisted for decades for many Veterans, and it is estimated that up to a third of those Veterans deployed to the Gulf War (GW) may have GWI[4, 5]. GWI has been characterized as a chronic multisymptom illness and includes 1) musculoskeletal pain, 2) fatigue, and 3) mood-cognition symptomology[6]. To be diagnosed with GWI, a Veteran must have served in the GW and experience at least one symptom in two of these symptom domains for at least six months[6].

Since the 1990s when service personnel returning from the GW first evidenced higher rates of health problems, substantial research has focused on identifying possible etiologies with limited success. For example, a recent longitudinal study demonstrated an association between different neurotoxicant exposures (i.e., propane fuel emissions from tent heaters, anti-nerve gas pyridostigmine bromide pills, and proximity to a munitions demolition of the chemical warfare agents sarin/cyclosarin) and increased odds of reported cognitive/mood, fatigue, and neurological symptoms[7]. Despite these efforts, a summary of the 2016 Institute of Medicine (IOM) report[8] concluded that "it is unlikely that a single definitive causal agent will be identified this many years after the war" (p.1508).

Importantly, GWI symptoms have not diminished over time but instead have remained stable or increased[7]. In fact, deployment to the GW is associated with higher rates of chronic health conditions common in the normative aging process: hypertension, diabetes, arthritis, and chronic bronchitis[9] along with other significant health conditions, such as amyotrophic lateral sclerosis[10]. GW Veterans appear to age more quickly, exhibiting rates of medical conditions similar to non-deployed individuals a decade or more older[9]. Evidence of worsening of GWI symptoms and general accelerated aging intensifies the need for effective, safe, and tolerable treatments for these Veterans.

1.2 Tai Chi

Tai Chi, an ancient Chinese martial art and form of neuromotor exercise, may hold promise for Veterans experiencing GWI. Tai Chi is often described as “meditation in motion,” using an integrated mind-body approach that combines several therapeutic components in a synergistic way. The varied components of Tai Chi are generally considered to be: physical activity in the form of slow, graceful, low-impact movements; range of motion exercises and balance training; mental focus, visualization of body position and choreographed sequential forms; and deep diaphragmatic breathing and mindful relaxation[11–13]. The benefits of Tai Chi are wide-ranging, and it has been shown to be safe and to enhance physical and mental health and improve quality of life in patients with chronic conditions including, heart failure, cancer, osteoarthritis, fibromyalgia, rheumatologic disease, and pulmonary disease[14–21].

An umbrella review conducted by members of this investigative team examined studies of in-person Tai Chi. Five distinct symptom categories of GWI that Tai Chi has been demonstrated to benefit were enumerated: fatigue and sleep problems, psychological health, cognitive function, chronic pain, and respiratory function[22]. The review concluded that Tai Chi may have the potential to improve functioning in GW Veterans though “a diverse, interrelated, reciprocal and potentially synergistic set of mechanistic pathways” (p. 170) including deep breathing and relaxation, group participation, physical activity, learning and memorization of movement patterns, and mindful awareness, attention, and meditation.

Other indications that Tai Chi may prove useful in the treatment of GWI is the empirical support for the treatment of another multicomponent disorder, fibromyalgia[23], which has important parallels to GWI. Compared to healthy GW Veterans, GW Veterans with chronic musculoskeletal pain report exercise as more painful, and they experience increased pain sensitivity following acute exercise at similar rates as individuals with fibromyalgia[24, 25]. Abnormal central nervous system processing of sensory and painful stimuli has been identified in subgroups of Veterans with GWI[24, 25], similar to what has been found in those with fibromyalgia. Tai Chi has also been shown to have a positive effect on other symptoms associated with GWI, including both mood[23] and fatigue[26]. These findings, taken together, suggest that Tai Chi may benefit Veterans with GWI.

The practicality of delivering Tai Chi in military populations has been demonstrated in several small-scale feasibility or pilot studies[27–30]. For example, research conducted by the current authors showed that recruitment of Veterans for Tai Chi is feasible with reported high satisfaction[29]. Qualitative findings indicated that Tai Chi may be a particularly good fit for military populations as it is derived from the martial arts and defense training, resonating in a positive way with their military training and ‘warrior spirit.’ Thus, investigation of Tai Chi to address symptoms of GWI is merited at this time.

1.3 Remote delivery of mind body interventions

Pre-pandemic research demonstrated the feasibility and acceptability of synchronous videoconferencing therapies in the treatment of Veterans. When compared with in-person care to address PTSD in Veterans, for example, videoconferencing dropout rates were similar, outcomes were non-inferior, and both satisfaction and therapeutic alliance were

comparable[31]. Since the onset of the COVID-19 pandemic, both the need for behavioral health treatment and the use of videoconferencing have increased dramatically[32, 33] Online mind-body interventions, such as Tai Chi, yoga, and mindfulness, have been highly utilized for general stress reduction[34], though most are asynchronous . It is important to determine if interactive and synchronous remote delivery of these interventions can lead to a reduction in key symptoms associated with Gulf War Illness, such as pain.

1.4 The current investigation

In March 2020, our randomized trial for GWI symptoms comparing Tai Chi to Wellness (an attention control group) was halted mid-way due to the onset of COVID-19. In the latter part of 2020, the investigators received permission from the funding source and Investigational Review Board (IRB) to shift from conducting an in-person intervention study to develop and examine Tai Chi and Wellness delivered via synchronous video teleconferencing. Important changes included: Tai Chi movement sequences that requiring stepping across the floor were replaced with components that could be done standing in one place; physical activity and neuropsychological outcome measures were replaced with psychometric measures that could be completed remotely; since the virtual platform affords fewer opportunities for spontaneous interaction among group members and instructors, group leaders were more directive in facilitating interactions and providing feedback. Given the distinct differences between the in-person and virtual protocols, we elected to consider them as two separate studies. The protocol for the ongoing fully remote trial is presented here.

In light of the opioid crisis, there is a need for research that focuses on identifying effective nonpharmacologic treatments for chronic pain. The primary aim of the current study is to examine if a synchronously delivered remote 12-week Tai Chi intervention is associated with greater improvements in pain and other GWI symptoms compared to the 12-week synchronously delivered remote Wellness intervention. The second aim is to examine if Tai Chi is associated with greater improvements in other physical and psychological measures compared to the Wellness intervention. The third aim is to examine the feasibility and acceptability of both the Tai Chi and Wellness interventions. This trial will produce valuable results that can have a direct and immediate impact on healthcare practices for GWI. If proven as helpful, these non-pharmaceutical, remotely accessible interventions could be implemented across VA nationwide with Veterans able to participate from their own homes.

2. Materials and Methods

2.1 Participants

Participants are up to 72 Veterans who were deployed to the Persian Gulf region in 1990–1991 in Operation Desert Shield and/or Operation Desert Storm and report symptoms consistent with GWI[1, 6]. Please refer to Table 1 for the list of inclusion and exclusion criteria and rationale.

2.2 Study design

In this single-blind randomized controlled trial, GW Veterans are randomly assigned to either the Tai Chi or the Wellness conditions, with both groups meeting remotely twice a

week for 12 weeks. Participants in both conditions receive assessments at baseline, 12 weeks (post-intervention), 24 weeks (approximately 3 months post-intervention) and 48 weeks (approximately 9 months post-intervention). Six cohorts of 12 Veterans each are planned. See Figure 1 for the participant flow.

2.2.1 Adaptations to study design and procedures for telehealth format—In order to adapt the protocol from an in-person to a fully remote format, a number of changes and adaptations were made to the consent process, the assessments and procedures, and the synchronously delivered telehealth interventions. Please see Figure 2 for a summary.

2.2.2 Ethical oversight—The study protocol is approved by the IRB at the VA Boston Healthcare System. Clinical trial registration was completed at ClinicalTrials.gov (NCT02661997).

2.3 Study procedures

2.3.1 Recruitment—Participants are recruited using a variety of strategies. Please see Table 2 for a description of the methods used. As all aspects of the study are conducted remotely, Gulf War Veterans from anywhere in the United States are eligible to participate.

2.3.2 Screening—In the initial telephone screening, Veterans are provided with an overview of the study. If they express interest, study staff briefly assess for all inclusion/exclusion criteria (see Table 1). Veterans are recruited in cohorts of 8 to 16 during one-month intensive recruitment periods. Once a cohort of Veterans is assembled, baseline assessments are scheduled.

2.4 Randomization

Randomization occurs after baseline assessments for all members of the cohort are completed. Within the week prior to randomization, study staff confirm that each participant is still interested and able to attend at the time that both interventions are scheduled. A study staff member then makes a list of available cohort participants in order of completion of initial telephone screening. The cohort list is password-protected and unavailable to the principal investigator (PI). The PI then uses 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 PI's 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.

2.5 Assessment Instruments and Procedures

Assessments consist of staff-administered interviews and self-report assessment questionnaires. Assessments last approximately 90 to 120 minutes and the staff-administered components are completed via WebEx. Treatment condition is assigned after the baseline, so all study staff are blind to condition throughout the baseline assessment. Please see Table 3 for full list of measures and time of administration. Instruments that align with

the GWI domains and Common Data Elements (CDEs) recommended by GWI research community stakeholders[35] are also indicated. Two measures included in the post-treatment and follow-up assessments (Qualitative feedback interview and Seven-day physical activity recall) lead participants to discuss treatment condition, so they are administered by an unblinded staff member who does not lead the group to which the participants are assigned. Weekly phone calls are made during the interventions to assess pain, group cohesion, and home practice, also conducted by an unblinded staff member not leading the group. The remaining post-treatment and follow-up measures are administered remotely (via postal mail).

2.6 Treatment Conditions

2.6.1 Tai Chi Treatment.—The standardized protocol was modeled after a Tai Chi program tested in previous randomized controlled trials[19, 20, 23, 55]. The program is derived from the classical Yang Tai Chi 108 postures[56], which has been shown to be a moderate-intensity exercise[13]. The movements and postures were selected by the instructors (BM and BW) because they: (1) are easily comprehensible and can be taught via remote instruction; (2) represent progressive degrees of stress to postural stability, with weight-bearing moving from bilateral to unilateral supports; (3) emphasize increasing magnitude of trunk and arm rotation with diminishing base of support and, as such, will potentially improve physical function without excessively stressing the joints; and (4) include meditative qualities. The Qigong movements included are: Expanding the qi field, Arching the chest to cleanse the body, Pour qi down the bai hui, Push the mountains side to side, Press forward and settle the wrists, Bear swims in water, Eagle gathers the prey, and Crane spreads wings. The Tai Chi forms included are: Begin Tai Chi, Repulse the monkey, Brush knee, and Cloud hands. Classes are tailored as needed for participant flexibility and endurance.

Each Tai Chi session lasts approximately 60 minutes and occurs twice per week for 12 weeks. Participants are also provided with a printed Participant Manual which includes Tai Chi principles, practicing techniques, and safety precautions. Throughout the group sessions, the instructors provide education about the guiding principles of Tai Chi that can help both the mind and body. Every session includes the following components: (1) warm up and a review of Tai Chi principles; (2) meditation with Tai Chi movement; (3) breathing techniques; and (4) relaxation. A research assistant attends each session and completes a fidelity checklist to record instructor adherence to the above components. Participants are encouraged to practice at home using home practice exercises described in the Participant Manual and video recordings accessible to participants on a website. During weekly phone calls with study staff, participants provide information on how many minutes of Tai Chi home practice they engage in each day of the week.

2.6.2 Wellness Comparison.—Previous randomized trials by our investigative group have used a Wellness Education control intervention as an attention control comparison for Tai Chi and found that Tai Chi had a significantly greater impact on symptoms[23, 55]. Given the successful use of Wellness Education control as a comparator to Tai Chi, it was determined that a Wellness intervention is a suitable attention control group for this randomized controlled trial. Participants in the Wellness condition also attend two 60-minute

sessions per week for 12 weeks. A standardized protocol was developed to correspond to the VA Whole Health Program[57] and to emphasize wellness across various domains that impact physical and emotional health. Topics covered during the 12-week group include physical activity, personal development, healthy eating and substance use, relationships, spirituality, mind-body connection, and personal environment and surroundings. Participants are encouraged to set SMART (**S**pecific, **M**easurable, **A**ttainable, **R**ealistic and **T**imely) goals each week to increase the likelihood of meeting their objectives[58]. Every session includes: (1) review of the written materials for that session; (2) a brief video clip related to the topic being discussed; (3) a brief mindfulness meditation exercise led by an instructor; and (4) review of SMART goals. One of the group leaders completes fidelity checklists after each group to record coverage of the topics and treatment components.

2.6.3. Expertise and program adherence of Tai Chi instructors—Two instructors trained in Yang-style Tai Chi (BM and BW), each with over 20 years of experience teaching Tai Chi are hired for the project. Each instructor will teach 3 cohorts of 24 classes, with occasional substitutions for each other in cases of illness or travel.

2.6.4 Expertise and program adherence of Wellness group leaders—The Wellness group is co-facilitated by two study staff consisting of at least one clinical psychologist or trainee with a doctorate in clinical psychology. All groups are facilitated or supervised by one of the Principal Investigators who are licensed clinical psychologists.

2.7 Safety Protocol

To optimize safety, we exclude individuals with major medical, psychiatric, or neurological disorders or moderate to severe traumatic brain injury and any medical conditions that carry a risk to safe participation. Each Tai Chi session begins with warm-up and stretching exercises to prevent injury and participants are provided with opportunities to report any negative effects they may have experienced. At least one research staff member is present at all intervention classes.

All study personnel complete required trainings in ethics, human subjects, data integrity, and information security. All data with identifying information is stored in locked files or password-protected computer files on secure servers. Data for analysis are identified by participant codes, and identifying information is removed. The identity of participants will not be revealed in the presentation or publication of any results from the project.

2.8. Strategies to minimize nonadherence and attrition

To minimize the likelihood that participants will drop out due to schedule conflicts, study staff call participants prior to randomization to verify availability on the days and times of sessions. During the treatment phase, study staff call participants who cancel or do not show for sessions. Participants who have not been in contact for more than a week or who cancel several consecutive sessions are called by study staff and every effort is made to reengage them. During weekly phone calls to administer measures and record home practice, participants are given opportunities to provide feedback. Study classes are scheduled mid-day (between 11am and 2pm Eastern) to maximize ability for employed

participants to attend during lunch breaks and to include participants in other time zones. To minimize cancellation and rescheduling of sessions, back-up instructors are available for both treatment conditions. Tai Chi instructors and the Wellness Group leader and/or supervisor attend weekly team meetings to problem-solve issues that arise (i.e. unable to access videos for home practice, limitations related to previous injuries, ongoing physical or mental health issues) that may interfere with class participation. In response to feedback obtained in a feasibility study of Tai Chi[29], one of the study investigators attends each Tai Chi class to address issues that may arise to allow the Tai Chi instructor to focus on session content.

2.9 Data analytic strategy

2.9.1 Participant Attrition and Missing Data.—Rigorous attempts are made to keep participants engaged in the study and to gather complete data regardless of treatment completion. We anticipate incomplete data due to factors such as attrition, participant unwillingness, and time constraints. We plan to conduct intention-to-treat analyses with all randomized participants to protect against potential bias and will use recommended imputation procedures for missing data[59].

2.9.2 Aims 1 and 2: Differential treatment effects—For Aim 1, we will utilize two approaches to determine whether participants in the Tai Chi Condition show more advantageous change on the BPI than those in the Wellness Condition. First, using the 4 assessment points (baseline, post-intervention, 3-month follow-up, and 9-month follow-up), we will fit longitudinal mixed models and will include a treatment condition by time interaction term to evaluate whether there are differential changes in the treatment groups over time. Log-transformed scores for the outcomes will be used in the analysis as needed. Results will be presented as between-group differences with 95% confidence intervals based on estimates from the longitudinal models. All model assumptions will be checked with standard regression diagnostic evaluations. These analyses will be based on all available data.

Second, we will utilize data from the weekly administrations of the BPI to model the trajectories of each group over the intervention period and present them graphically. We will fit longitudinal mixed models and will include a treatment condition by time interaction term to evaluate whether there are differential changes in the treatment groups over the intervention period.

For Aim 2, we will use a similar approach to Aim 1 to determine whether participants in the Tai Chi Condition show more advantageous change than those in the Wellness Condition across the 4 assessment points on the other physical and psychological measures. (There are no weekly administrations of the secondary measures.)

2.9.3 Aim 3: Feasibility and acceptability—For Aim 3, to examine the feasibility and acceptability of the two treatments, descriptive and summary statistics will be utilized to examine participant adherence (number of sessions attended) and satisfaction as reported on the client satisfaction questionnaire. Qualitative analysis of interviews will be conducted using an iterative coding process. Qualitative data will be transcribed and then analyzed

by the research team using a general inductive approach[60]. Two or more raters will independently code several transcripts to identify themes. The team will review identified themes, discuss discrepancies, and refine the coding rubric. Raters will code the remaining transcripts and meet until consensus is reached on the identified themes and on the distribution of participant quotes under appropriate themes. The team will then choose and report participant quotes that best represent the identified themes.

2.9.4 Power analyses and sample size for Aims 1 and 2—With the anticipated 72 participants enrolled (36 in each condition), assuming that 15% do not complete the post-treatment assessment, we will have sufficient (.80) power to show a medium-large between group effect (0.72) as has been found in previous similar trials[23, 61].

3. Discussion

This manuscript describes the first fully remote clinical trial to address symptoms of GWI using Tai Chi. We were spurred by pandemic restrictions to switch from in-person to remote delivery for this trial. However, even prior to 2020, examination of remotely delivered interventions for Veterans was important for behavioral treatments in general and for GWI populations in particular. Videoconferencing telehealth therapies gained prominence over the past decades due to their convenience and potential to save costs for both providers and patients. Remote interventions that allow synchronous interactions simulate in-person treatment delivery and allow real time feedback from instructors as well as live interactions among group members.

To adapt to the remote format in the current study, practical and substantive changes were made to the interventions and assessment instruments. Differences in remote group dynamics and virtual interactions among participants and instructors may affect outcomes. For example, muting participants during Tai Chi class is needed to ensure clear delivery of instruction and directed taking of turns in Wellness discussions avoids talking over other group members. The virtual platform and these necessary adaptations may inhibit socialization, constrain development of group cohesion, and limit the sense of camaraderie among participants. Nonetheless, for GW Veterans who appreciate connection with other Veterans of their era, videoconferencing may have a particular advantage in improving access to care. The relatively small numbers of GW Veterans in most geographic areas make in-person group treatments targeting GWI largely impractical. Thus, focus on the remote delivery of these two interventions will provide the opportunity to advance our understanding of the effectiveness of mind body treatments when delivered via synchronous telehealth.

After three decades of research on GWI, high quality clinical trials to identify feasible, acceptable, and efficacious treatments for GWI symptoms have been scant. The 2016 IOM report[5] recommended a shift in focus—from attempts to establish etiology to the development and evaluation of therapeutic interventions for managing the symptoms of GWI. Investigation of mind-body treatments that focus on “the interconnectedness of the brain and body” (p. 249)[5] were specifically recommended. Indeed, recent studies have suggested that complementary and integrative mind-body therapeutic approaches such as

yoga[61], acupuncture[62], and mindfulness[63] may be fruitful approaches to explore to reduce GWI symptoms and improve functioning. However, current VA/DoD Clinical Practice Guidelines for the Management of Chronic Multisymptom Illness indicates that evidence to support these interventions remains weak[3]. The current study will add to this growing body of literature on integrative, nonpharmacologic approaches by providing evidence on the viability of telehealth delivery. If shown to be effective and engaging, the remotely delivered Tai Chi interventions offered in this study can be used to promote health while also providing social connection for Veterans suffering from GWI. Offering home-based synchronous teleconferencing interventions that address mind and body to Veterans who served in the Gulf over 30 years ago will represent a notable step in health promotion for this important group of Veterans.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

GW	Gulf War
GWI	Gulf War Illness
BPI	Brief Pain Inventory
IOM	Institute of Medicine
SMART	Specific, Measurable, Attainable, Realistic and Timely

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Highlights:

- There is a need for high-quality intervention trials for Gulf War Illness
- Tai Chi shows promise to address pain and improve functioning in Gulf War Illness
- Using telehealth therapies for Gulf War Veterans can improve access to care

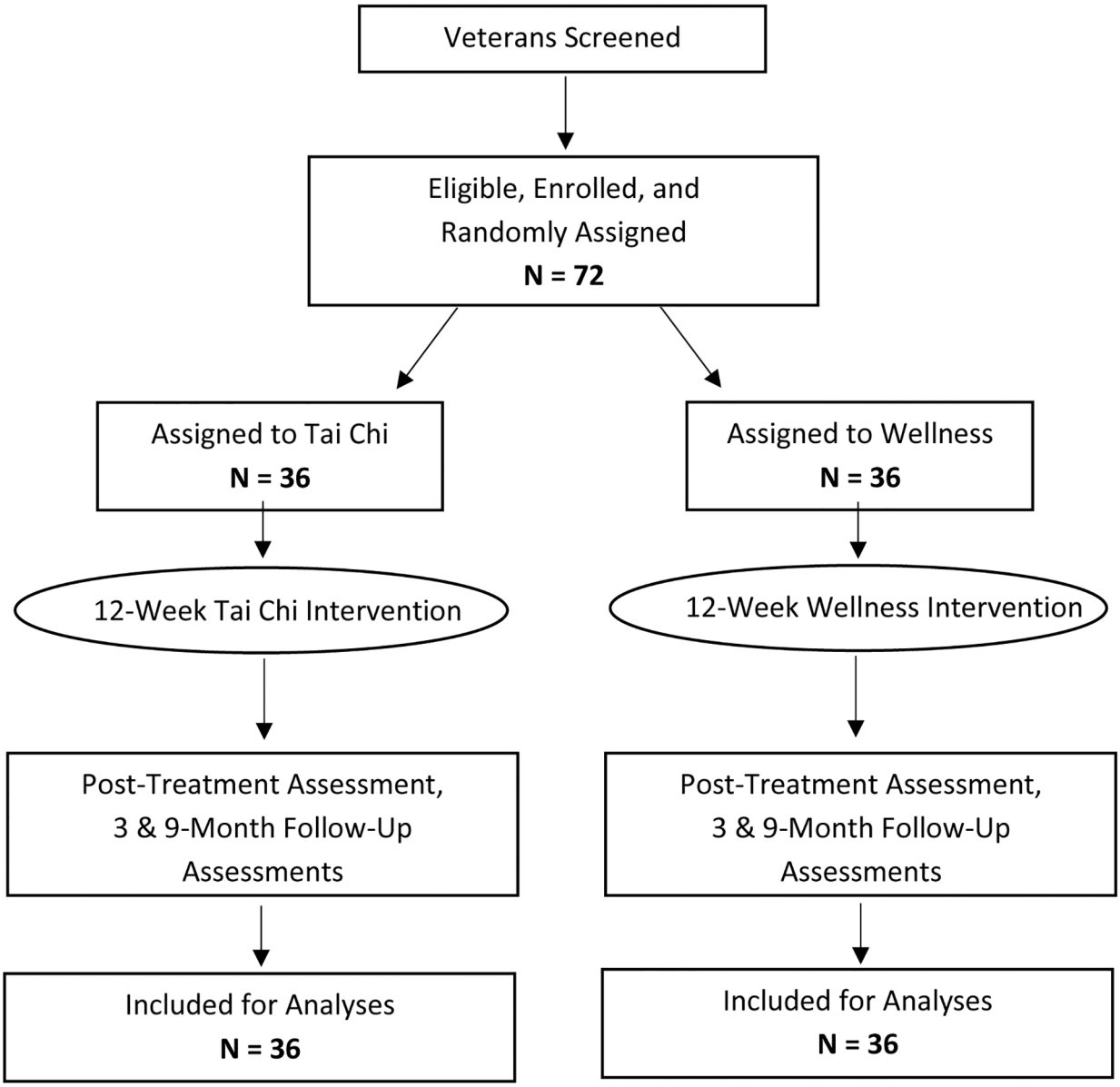

Figure 1.
Planned Participant Flow

Design Adaptations and Procedures	
Consent, Assessments, and Procedures	Hard copy informed consent and HIPPA forms and assessment questionnaires are sent to the Veterans' homes prior to the baseline assessment. Links to WebEx meetings are sent to participants' email addresses.
	At the outset of the baseline assessment, participants voluntarily sign the informed consent form and HIPAA during the WebEx sessions before any study-related procedures are initiated. Screenshots of the signature pages are captured.
	Objective measures of physical health (body mass index, blood pressure, measures of fitness and balance) and cognitive functioning instruments that are not possible to administer in the remote format are not included.
	Satisfaction with the telehealth aspect of the intervention is assessed at the post-treatment and follow-up assessments.
	Staff instruct participants to complete the paper and pencil self-report measures (see Section 2.5). (Although remote administration of study assessment measures would have been preferred, platforms such as REDCap and Qualtrics were not approved by the IRB at the time of study initiation.)
	For post-treatment and follow-up assessments, staff administer the standardized clinical interviews over the telephone and audio recordings are captured with no identifying information.
	Participants are asked to return consent forms (at baseline) and paper and pencil assessment materials in a stamped addressed envelope provided for each assessment.
	Consistent with VA clinical safety protocol for remote visits, study staff obtain contact information for an emergency contact person and confirm the participant's location at each visit to ensure that staff can respond rapidly in the event of an emergency.
	A research assistant is available during each intervention session to provide technical assistance as needed.
Tai Chi Group	A checklist is sent before groups begin to instruct participants regarding optimal ways to set up their environment for Tai Chi (e.g., keep a chair nearby, place electronic device high enough for a full body view). "Tech sessions" are set up prior to the first class to review technical set-ups and troubleshoot any problems with connection and visibility.
	Tai Chi movements and postures are selected with consideration of what participants can do with limited floor space and static camera views. Specifically, Tai Chi components that are done in one place and do not require movement across the floor are used.
	Instructors enhance the participants' ability to follow instructions and movements by: (1) modeling the movements from various views (e.g., front view, side view, back view), (2) providing clear verbal instruction to help participants follow along, (3) using props to emphasize points (e.g., using a stick to show directionality of movement), (4) wearing clothing or colors that enhance contrast so that the movements can be clearly seen.
	Technology is optimized to enhance the virtual experience: (1) instructors use large screens so that they could easily view all group participants at once, (2) instructors use clip-on microphones to improve audio quality (particularly important when facing away from the microphone attached to the computer, and (3) participants without cameras or poor-quality cameras are provided with portable webcams to ensure a good view for the instructor.
	To avoid distracting interference from participant audio feeds, participants are muted once the instruction begins. Participants are encouraged to raise
	a hand or make a comment in the chat box if they have a question during the session, and they are encouraged to unmute at the beginning and end of class for comments and discussion.
Wellness Group	"Tech sessions" are available prior to the first class to review technical set-ups and troubleshoot any problems with connection and visibility.
	Weekly telephone calls are initiated by staff to record SMART goals and ratings of progress towards goals,
	Group facilitators are directive in inviting participation to facilitate discussion of topics and "going around the [virtual] room" to ensure that all group members are able to participate.

Figure 2:
Study Design Adaptations and Procedures for Telehealth Format

Table 1.

Inclusion and Exclusion Criteria and Rationale

Inclusion criteria	**Rationale**
Veteran who served in the 1990–91 Gulf War Theatre	Population under study
Meet GWI criteria using criteria of having at least 1 chronic symptom in 2 symptom domains (i.e., 1) musculoskeletal pain 2) fatigue, and 3) mood-cognition symptomology)[6]	Population under study
Musculoskeletal or joint pain or stiffness for at least 6 months must be one of the GWI symptoms	Population under study
English speaking	Practical consideration
Ability to attend group sessions at scheduled times	Practical consideration
Access to a computer or tablet device for sessions	Practical consideration
Exclusion criteria	**Rationale**
Lacks capacity to consent	Human subjects concern
Major medical, psychiatric, or neurological disorder or brain injury that could interfere with ability to safely engage in study activities	Human subjects concern and safety consideration
Change in psychotropic or pain medication in past month	Treatment confound
Current Tai Chi, mindfulness, or yoga practice for at least 3 hours per week for more than 3 months	Treatment confound
Difficulty standing for 60 minutes	Safety consideration
Disruptive, disrespectful, or threatening to staff or Veterans and non-responsive to limit setting	Safety consideration
Current involvement in a treatment study for GWI or pain	Treatment confound

Table 2.

Recruitment Methods

Description of Recruitment Methods
Medical center staff are informed and provided with IRB-approved pamphlets describing the study. If Veterans sign IRB-approved “permission to contact” forms, study staff contact them for telephone screening.
Utilization of an electronic referral data repository maintained by the National Center for PTSD into which Veterans were previously entered on a voluntary basis and written permission for future contact was established.
Mailing IRB-approved letters to Veterans in the VA Boston Healthcare System identified as serving on active duty in 1990 and/or 1991. A pre-addressed, postage paid postcard is enclosed to provide the ability to opt out of being contacted. Veterans who do not opt out within two weeks of letters being mailed are eligible to be contacted by study staff.
Recontacting Veterans who were screened for a previous trial who may be eligible to participate (as allowed by IRB approval of a HIPAA waiver).
IRB approved flyers, brochures and link to the study website posted to Veteran social media platforms such as GW Veterans Facebook groups and pages.

Table 3.

Schedule and Description of Measures

Measure	Pre	Post	3-Mo	9-Mo	Weekly During Tx
Gulf War Illness Outcome Measures					
Primary Outcome Measure					
Brief pain inventory – short form. A 9-item self-report measure that examines pain intensity and interference with functioning in various life domains[36, 37]. [Aligns with CDE Domain: Pain[35]]	X	X	X	X	X
Secondary Outcome Measures					
Multi-dimensional fatigue inventory. A 20-item self-report measure that examines symptoms of fatigue. The questions pertain to general, physical, and mental fatigue in addition to reduced motivation and activity[38]. [Aligns with CDE Domain: Fatigue[35]]	X	X	X	X	
Depression anxiety stress scales. A 21-item self-report measure that examines emotional states of depression, anxiety and stress[39].[Aligns with CDE Domain: Neuropsychological[35]]	X	X	X	X	
Physical and Psychological Outcome Measures					
Pain Catastrophizing Scale. A 13-item self-report measure that examines the extent to which participants catastrophize pain in the forms of rumination, magnification, and helplessness[40].	X	X	X	X	
PTSD checklist for DSM-5. A 20-item self-report measure that examines symptoms of DSM-5 posttraumatic stress disorder criteria over the past month[41, 42]. [Aligns with CDE Domain: Neuropsychological[35]]	X	X	X	X	
Insomnia severity index. A 7-item self-report measure that is used as a brief screen of insomnia symptoms and is sensitive measure of change in perceived sleep difficulties[43]. [Aligns with CDE Domain: Sleep[35]]	X	X	X	X	
PROMIS self-efficacy for managing symptoms short form. An 8-item self-report measure that examines elements of self-care[44].	X	X	X	X	
PROMIS global health scale short form. An 8-item self-report measure that examines physical function, fatigue, pain, emotional distress, and social health[45]. [Aligns with CDE Domain: Quality of Life[35]]	X	X	X	X	
Chronic pain self-efficacy scale. A 22-item self-report measure that examines perceived self-efficacy to cope with components chronic pain such as pain management, physical function, and coping with symptoms[46].	X	X	X	X	
West Haven-Yale multidimensional pain inventory. A 52-item self-report measure that examines experiences with chronic pain and engagement in everyday activities[47]. [Aligns with CDE Domain: Pain[35]]	X	X	X	X	
Mindful attention awareness scale. A 15-item self-report measure that assesses participants' openness towards, awareness of, and attention to the present. This scale can reveal information about one's self-regulation and well-being[48].	X	X	X	X	
Seven-day physical activity recall. A variable-length measure that is administered by the study staff in an interview format. Examines participants' recall of the amount of time they engaged in moderate, hard, and very hard physical activity and time spent sleeping each day over the past week[49]. [Aligns with CDE Domain: Post-Exertional Malaise[35]]	X	X	X	X	
Measures of Feasibility and Acceptability					
Client satisfaction questionnaire. An 8-item self-report measure that examines participants' satisfaction with services provided[50].		X			
Qualitative Interview. A variable-length, semi-structured interview developed for this study that gathers qualitative information about the participants' experience with the content and modality (telehealth group format) of the intervention and that is audio recorded with participant consent.		X	X	X	
Tai Chi Home Practice Log. Number of days per week and minutes per practice session are recorded weekly during treatment.					X
Weekly Wellness Goals Log. SMART Goals and progress ratings are recorded weekly during treatment.					X

Measure	Pre	Post	3-Mo	9-Mo	Weekly During Tx
Group cohesiveness scale. A 7-item self-report measure that examines group cohesion within a therapeutic atmosphere[51].					X
Measure of Distress Related to COVID-19 and Social Distancing					
Epidemic – pandemic impacts inventory. A 92-item questionnaire. Designed to learn about and describe the impact of the coronavirus disease pandemic on various domains of personal and family life, including employment, education, home life, social life, economic, physical health, infection experiences, and positive changes[52].		X	X	X	
Descriptive Measures					
Demographics: A 12-item self-report measure that examines age, years of education, gender, sex, race, ethnicity, relationship/marital status, employment status, current living situation, number and age of children (if any), and internet accessibility. [Aligns with CDE Domain: Baseline/Covariate[35]]	X				
The Kansas Gulf War experiences and exposures questionnaire part 1. A 32-item self-report measure that queries about chronic symptoms and diagnoses required to ascertain Kansas and Chronic Multi-symptom Illness (CMI) case status [1]. [Aligns with CDE Domain: Baseline/Covariate[35]]	X	X	X	X	
The Kansas Gulf War experiences and exposures questionnaire part 2. A 36-item self-report measure that queries about demographics such as military rank and current military status, GW duty service (active vs. reserve/National Guard), military and deployment history, and exposures[1]. [Aligns with CDE Domain: Baseline/Covariate[35]]	X				
Health symptom checklist. A 34-item self-report measure that examines health and mental health symptoms over the past 30 days. The symptoms assessed fall under the following categories: cardiac, pulmonary, dermatological, gastrointestinal, genitourinary, musculoskeletal, neurological, and psychological[7, 53]. Within this measure there are 5 embedded items that address malingering behaviors[54]. [Aligns with CDE Domain: Baseline/Covariate[35]]	X	X	X	X	