Study Protocol and Analysis Plan

Yoga Plus Mantram Repetition to Reduce Chronic Pain in Veterans with PTSD: A Feasibility Trial

Document Date: 03/28/2019

This study is registered at www.clinicaltrials.gov; # NCT03816007

Human Protocol (Version 1.18)

General Information

***Please enter the full title of your study::**

An Enhanced Mind-body Intervention to Reduce Disability and Pain in Veterans with PTSD

***Please enter the Study Number you would like to use to reference the study:**

Yoga and Mantram for Chronic Pain in PTSD
* This field allows you to enter an abbreviated version of the Study Title to quickly identify this study.

Add departments

and Specify Research Location:

Is Primary?	Department Name
◉	**VASDHS** - VASDHS

Assign key study personnel(KSP) access to the study

***Please add a Principal Investigator for the study:**

Groessl, Erik J., PhD

3.1 If applicable, please select the Research Staff personnel

A) Additional Investigators

Ayers, Catherine R., PhD
Co-Investigator
Lang, Ariel J., PhD
Co-Investigator
Liu, Lin, PhD
Co-Investigator
Rutledge, Thomas R., PhD
Co-Investigator

B) Research Support Staff

Casteel, Danielle Lyn, MA
Research Associate
Hafey, Carol-Luanne
Study Coordinator
McCarthy, Adhana, MPAS

Research Associate
Prado-Nava, Miguel Angel, BS
Research Associate
Zamora, Tania
Research Associate

***Please add a Study Contact**

Groessl, Erik J., PhD
Hafey, Carol-Luanne

The Study Contact(s) will receive all important system notifications along with the Principal Investigator. (e.g. The project contact(s) are typically either the Study Coordinator or the Principal Investigator themselves).

VASDHS IRB
Human Subjects Protocol
v20190121

Section 1 - Preliminaries

Principal Investigator:

Erik J. Groessl, PhD

Protocol Title:

An Enhanced Mind-body Intervention to Reduce Disability and Pain in Veterans with PTSD

IRB Protocol Number:

H190004

Protocol Nickname:

Yoga and Mantram for Chronic Pain in PTSD

Form Template Version:

v20150115

Date Prepared:

04/02/2022

Please be advised that this protocol application form has changed as a result of the 2018 Common Rule. There are new questions and sections, and you may be required to provide additional information to previous sections.

1a) Is this study considered human research?

- (●) Yes
- ( ) No
- ( ) I don't know

1b) Please select:

- ( ) This is an application for a NEW human subject research protocol
- (●) This is a revision of an existing protocol

Was this study initially approved prior to January 21, 2019?

( ) Yes (●) No

Were you instructed to convert to the 2018 Common Rule Requirements?

○ Yes ◉ No

Section 2 - Research Subjects

2a) What is the total planned number of VA-consented subjects?

Include the total number of subjects who will prospectively agree to participate in the study (e.g., documented consent, oral consent, or other).

32

2b) What is the total number of VA subjects who WILL NOT be consented?

Include the total number of subjects that will be included without consent (e.g., chart review). *Note: Data about people are still considered "human subjects" by the IRB, so even if you do not intend to contact the patients whose charts you will review, you still should enter the number of charts as your "planned subjects."*

0

Section 2.1 Consented Subject Groups

2.1) For each of the subject categories listed below, indicate whether or not these subject groups will participate in the study:

2.1a) Children under the age of 18
Note: If neonates or children will be involved in this study, certification by the Medical Center Director will be required. Only minimal risk research may be performed with children. Only non-invasive monitoring and/or prospective observational and retrospective record review studies that are minimal risk can be conducted in VA involving neonates.

○ Yes ◉ No

2.1b) Pregnant women

◉ Yes ○ No

2.1c) Individuals with cognitive/decisional impairment

○ Yes ◉ No

2.1d) Non-English-speaking individuals

○ Yes ◉ No

2.1e) Prisoners of War (explicitly targeting this group)

○ Yes ◉ No

2.1f) Non-Veterans (Note: Justification for inclusion of non-Veterans will be required)

○ Yes ◉ No

2.1g) Incarcerated individuals (Note: VA CRADO approval will be required)

○ Yes ◉ No

2.1h) VA employees - including VA paid, IPA, or WOC (Note: Union review and authorization may be required)

◉ Yes ○ No

2.1i) Students of the institution (e.g., resident trainees) or of the investigator

○ Yes ◉ No

2.1j) Patients with cancer (or high cancer risk) [explicitly targeting this group]

○ Yes ◉ No

Section 3 - Study Features (these items default to "No" for convenience)

3) This section consists of several Yes/No questions addressing protocol characteristics. Click on *Save and Continue*.

Section 3.1 Protocol Basics

Select all that apply

3.1a) The research **intends to change** the participant.

◉ Yes ○ No

3.1b) **Interactions** with living participants to collect data or specimens with no intent to change them.

○ Yes ◉ No

3.1c) This is a study that **never** has any **subject contact and does not collect subject identifiers**

○ Yes ◉ No

3.1d) This is a **chart review** study involving retrospective or prospective medical records.

○ Yes ◉ No

3.1e) This is a **multi-site** study occurring in-part or in-full at other locations.

○ Yes ◉ No

3.1f) There is an **international** component to this research. *International research includes sending or receiving human derived data or specimens (identifiable, limited data set, coded, or deidentified) to or from an international source. International research does not include studies in which VA is only one of multiple participating sites where the overall study-wide PI is not a VA investigator.*

○ Yes ◉ No

3.1g) This study includes **off-station activity** (not including VA-leased space or CBOC clinics) conducted under VASDHS IRB approval. *Note: this does not include research conducted by a collaborator at their home institution under their institutional approval.*

○ Yes ◉ No

3.1h) VA subjects will **participate** in part or in full **at other locations** (not including VA-leased space or clinics) under VASDHS IRB approval. *Note: if this study involves remote participation of subjects, please indicate "no" and describe their remote participation in section 9 of the application. This question is intended to understand whether participants must physically go to a non-VA location to participate in this VA research study.*

○ Yes ◉ No

Section 3.2 Specimen Use and Data Repository

Indicate whether or not each of the following applies to this protocol

3.2a) Involves specimens that are left over from pathological or diagnostic testing (**non-research specimens**)

○ Yes ◉ No

3.2b) Involves **specimens collected for research** purposes **only**

○ Yes ◉ No

3.2c) This study includes **specimen banking** (specimens are retained for use outside of the purposes of this protocol)

○ Yes ◉ No

3.2d) The study involves **DNA** genotyping or other **genetic analysis**

○ Yes ◉ No

3.2e) Biological **specimens/material** will be sent outside of the VA.

○ Yes ◉ No

3.2f) A **data repository** is maintained (data are retained after completion of the protocol for other uses, IMPORTANT: see **?** before checking "yes")

○ Yes ◉ No

3.2g) **Data will be shared outside** of the VA (identifiable, coded, limited data set, or deidentified)

◉ Yes ○ No

Section 3.3 Treatment and Clinical Trials

Indicate whether or not each of the following applies to this protocol

3.3a) Includes a **treatment** component (a research treatment)

◉ Yes ○ No

3.3b) Study is a **clinical trial.** *Note: A clinical trial is a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.*

◉ Yes ○ No

3.3c) Has a data safety monitoring board (**DSMB)** or data safety monitoring committee.

○ Yes ◉ No

3.3d) Has a **data safety monitoring plan** (but not a DSMB) (this is not the data security plan, it is a safety plan).

◉ Yes ○ No

Section 3.4 Drugs and Devices

Indicate whether or not each of the following applies to this protocol

3.4a) **Drugs** that require **FDA** action such as an Investigational New Drug (IND) approval or exemption or 510 (k) approval.

○ Yes ◉ No

3.4b) Other drugs, supplement, etc. that **do not require FDA** action for inclusion in the study.

○ Yes ◉ No

3.4c) Medical **devices requiring FDA** IDE approval or waiver

○ Yes ◉ No

3.4d) **Other** medical **devices**

○ Yes ◉ No

Section 3.5 Risk and Hazards

Indicate whether or not each of the following applies to this protocol

3.5a) Study places subjects at **greater than minimal risk** (do not include risks that are due to standard care)

○ Yes ◉ No

3.5b) Human subjects are exposed to **radioisotopes** (do not include standard care).

○ Yes ◉ No

3.5c) Subjects have other **radiation exposure** (e.g., x-rays) (do not include standard clinical use).

○ Yes ◉ No

3.5d) Target population has psychiatric diagnosis or behavioral complaint.

◉ Yes ○ No

Section 3.6 Clinical Facilities and Standard Care

Indicate whether or not each of the following applies to this protocol

3.6a) Study **uses VA clinical services** (e.g., adds required tests run in the VA lab for study purposes; research procedures concurrent with clinical care)

○ Yes ◉ No

3.6b) Includes procedures or drugs that will be considered **part of standard care.**

◉ Yes ○ No

3.6c) Involves **lab tests done for research** purposes.

○ Yes ◉ No

Section 3.7 Subject Expenses and Compensation

Indicate whether or not each of the following applies to this protocol

3.7a) There may be expense or added **costs to the subject** or the subject's insurance.

○ Yes ◉ No

3.7b) This is a **qualifying cancer treatment trial** and subjects may be billed for study drugs or procedures.

○ Yes ◉ No

3.7c) This is a cancer treatment trial but **subjects will not be billed** for study drugs or procedures.

○ Yes ◉ No

3.7d) Subjects will be **compensated** (either in cash or other means such as a gift certificate).

◉ Yes ○ No

Section 3.8 Subject Activities

Indicate whether or not each of the following applies to this protocol

3.8a) Involves **surveys or questionnaires** completed by subjects

(•) Yes ( ) No

3.8b) Includes the use of **recruitment materials** such as flyers, advertisements, or letters

(•) Yes ( ) No

3.8c) Involves facial **photographs** or audio or video **recordings** of **patients**

(•) Yes ( ) No

Section 3.9 Sponsors and Collaboration

Indicate whether or not each of the following applies to this protocol

3.9a) This research is a funded research project **(commercial (industry) sponsor, NIH, VA, other).**

(•) Yes ( ) No

3.9b) Other **commercial (industry) non-financial support** is provided (e.g., drugs or supplies).

( ) Yes (•) No

3.9d) The protocol has **Department of Defense** involvement (e.g., subjects or funding).

( ) Yes (•) No

3.9c) The PI or other study staff member has a financial interest or other **real or potential conflict** related to this study.

( ) Yes (•) No

3.9e) This study involves **collaborative** research activities (research conducted at other institutions under the authorities or approvals of the other institution/s). *Note: this may include other VA and/or non-VA institutions, but does not include off-site VA research.*

(•) Yes ( ) No

Section 4 - Estimated Duration

4) What is the estimated duration of the entire study? (From IRB approval to IRB closure)

5 years

Section 5 - Lay Language Summary

5) Provide a summary or synopsis of the proposed study using non-technical language (not more than 1 paragraph)

PTSD is prevalent among Veterans and is associated with physical and functional impairments in addition to PTSD symptoms. Veterans with PTSD experience more chronic pain and pain-related functional limitations than Veterans without PTSD. Mind-body interventions such as yoga and meditation are non-pharmacological options for treating both chronic pain and PTSD. This pilot study will add an existing mantram repetition (MR) component designed for Veterans with PTSD to an active yoga intervention known to improve function in chronic back pain patients. The study will examine the acceptability of the interventions, adverse events, and the feasibility of recruitment, attendance, retention, treatment fidelity, and assessments by recruiting and randomizing 32 VA patients with PTSD to either yoga plus MR or to a relaxation/health education control. Health outcomes including pain-related function, pain, and PTSD symptoms will be measured. If feasible, the data will be used to plan a full-scale trial of enhanced yoga for pain in VA patients with PTSD.

Section 6 - Specific Aims

6) Provide a statement of specific aims and hypotheses that serve as the basis for this protocol. Emphasize those aspects that justify the use of human subjects.

In preparation for a full-scale study via a subsequent Merit Review IIR proposal, our overall study objective is to adapt and combine two existing interventions for a new population, and to examine the feasibility and acceptability of conducting a randomized controlled trial of an enhanced yoga + MR mind-body intervention for reducing pain-related disability and pain while improving function in Veterans with PTSD. The study will be conducted in two phases: the first phase will involve adapting and combining two existing mind-body interventions for Veterans with PTSD and chronic pain and creating instructor and home practice manuals for the intervention. The second phase will recruit and randomize 32 military personnel with chronic pain and PTSD to either enhanced yoga (yoga plus MR training) or a relaxation/health education (R /HE) comparison group.

The specific aims are as follows:
Aim 1: Expert collaborators will refine and combine the existing Yoga for cLBP and/or chronic neck pain (cNP) intervention with a shorter version of Dr. Bormann's Mantram, Repetition Program (MRP).
Aim 2: Create revised instructor and home practice manuals.
Aim 3: Examine the feasibility of recruitment, retention, assessments, randomization, adverse events, and acceptability of an enhanced yoga intervention for reducing disability and chronic pain among Veterans with PTSD via a pilot randomized controlled trial.

Section 7 - Background and Significance

7) Provide a succinct discussion of relevant background information to justify performing the proposed study.

Post-traumatic stress disorder (PTSD) afflicts thousands of Veterans and is associated with a broad array of impairments including physical and functional limitations in addition to PTSD-specific symptoms.[1,2] Recent research also indicates that Veterans with PTSD are also more likely to report the presence of chronic pain,[3] and they report greater pain severity and pain-related disability than those without PTSD.[4] Mild traumatic brain injury (mTBI) often co-occurs with PTSD and chronic pain,[5,6] creating complexity for treatment, and more risk of substance use[7] including high-risk opioid use.[8]

Musculoskeletal disorders are the most common type of chronic pain conditions reported by Veterans and chronic low back pain (cLBP) and chronic neck pain (cNP) are two of the most common reasons for disability among deployed personnel[9] and the military in general.[10] Although medications were often a front-line option for pain,[11,12] the higher risk of addiction in this population and subsequent adverse outcomes including overdose deaths[13] that characterize the US opioid epidemic, have led to increased efforts to study[14] and provide non-pharmacological pain treatments,[15] and reduce long-term opioid therapies in the VA system.[16] Other research points to the potential of treating co-occurring pain and PTSD in the same intervention.[17]

Mind-body interventions are a subset of the non-pharmacological treatment options for pain and PTSD with a growing evidence-base and very few side effects. Considerable evidence suggests that interventions such as Mindfulness Based Stress Reduction (MBSR),[18,19] and mantram repetition (MR) [20-22] are effective treatment options for Veterans with PTSD. MBSR has also been shown to reduce disability and improve function in adults with cLBP. Yoga has an even stronger evidence-base for treating CLBP in both Veterans[23] and non-Veterans,[24-26] and building on preliminary data, is being actively studied as a treatment for PTSD in VA RR&D (Davis) and CSR&D trials (Lang).

Thus, given the enormous health burden of co-occurring pain and PTSD and problems with opioid therapies, we plan to develop a hybrid mind-body intervention to improve function and reduce pain-related disability among Veterans with pain and PTSD in the absence of opioid therapies. The intervention will consist of an established yoga therapy program combined with MR training. MR was specifically chosen because it offers a user-friendly, portable tool for reducing PTSD-related stress and emotional discomfort, and improving function in daily life. Yoga can effectively reduce pain and stress, but is less portable or easily used in public situations such as on public transportation, during traffic challenges, or at the grocery store. MR also adds a personalized spiritual phrase that is not frequently taught in secular yoga or other mind-body programs.

Another study innovation is the inclusion of cLBP and cNP. Previous studies rarely combine different pain conditions because the mechanisms of pain may differ and/or too much noise may

be introduced. However, it is increasingly apparent that VA facilities will rarely be able to offer a separate yoga program for each type of pain. Thus, it is increasingly important to study interventions that include more than one type of pain to approximate what will occur in future clinical settings.

Section 9 - Design and Methods

9) Describe the research design and the procedures to be used to accomplish the specific aims of the project. Provide a precise description of the planned data collection (include what systems or databases will be used/accessed to gather data), analysis and interpretation. For chart review studies, include the timeframe of collection. Address sample size, inclusion of women and minorities. Define in clear terms exactly what will be done to the human subjects.

C1. Study Design. The study has three aims. In Aim 1, study investigators will collaboratively modify two existing interventions and combine them into the enhanced yoga intervention. In Aim 2, manuals will be created for both the enhanced yoga intervention and the relaxation/health education (R/HE) control. In Aim 3, we will conduct a preliminary clinical trial to obtain data on the feasibility of recruitment, retention, assessments, randomization, safety, and acceptability of an enhanced yoga intervention for reducing disability and chronic pain among Veterans with PTSD. The proposed study design was chosen in preparation for a full-scale clinical trial. If the interventions are established as safe, acceptable, and it is feasible to conduct necessary study procedures, we will propose a similar design in a subsequent RR&D IIR proposal. The R/HE control was chosen to provide an active control in which participants are exposed to a similar amount of interaction with peers and health professionals, yet the outcomes of interest are not expected to be impacted.

Table 3. Study timeline (months)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
Materials, contracts, etc.	■	■																				
Intervention adaptation		■	■																			
Create revised manuals			■	■																		
Train instructors				■	■																	
Recruit participants				■	■	■	■	■	■	■	■	■	■	■	■							
Assessments							■	■	■	■	■	■	■	■	■	■	■	■				
Conduct interventions								■	■	■	■	■	■	■	■	■	■					
Qualitative interviews											■	■					■	■				
Data Management										■	■	■	■	■	■	■	■	■	■	■		
Data Analysis																	■	■	■	■	■	■
																		■	■	■	■	■

Results dissemination																							
Prepare & Apply for IIR																							

C1.1. Aim 1 & 2: The interventions will be adapted in four main ways; a) to safely benefit cNP patients; [b) to ensure it is trauma-sensitive; c) includes additional emphasis on relaxation and stress reduction; and d) to include shorter MRP training sessions. Aims 1 and 2 will leverage ongoing work from the PI's current NCCIH-funded R34 in which the yoga for cLBP intervention is being adapted to benefit cNP patients. To ensure trauma-sensitivity, study investigators will build on an intervention designed by co-inv. Lang and other study RR&D-funded protocols (Drs. Davis and Bayley) to align the intervention with principles out lined by Emerson et al.[71] The additional relaxation and stress reduction emphasis is designed to alleviate PTSD symptoms in addition to chronic pain.] The MRP will be shortened to an initial 30-minute training followed by 15-minute brief interventions sessions and home practice assignments by Dr. Bormann who has done preliminary work on adapting MRP for briefer sessions and delivery by phone or Internet. Study investigators will review literature, other protocols, and the revised MRP prior to participating in a half-day intervention refinement conference at VASD. Further intervention refinement will occur at project meetings and a manual will be produced.

C1.2. Aim 3: [we will recruit and randomize 32 VA patients formally diagnosed with PTSD and chronic cLBP and/or cNP to enhanced yoga or the R/HE control. We plan to recruit starting in month 4, and will begin randomizing when we reach enrollment of 16, which is expected by month 6-7. The first set of interventions will start in month 8 and run for 12 weeks. We will repeat this process with ongoing recruitment of another 16 participants between months 8-12, with interventions running months 13-16. Participants will complete physiological and self-reported outcomes assessments at baseline, 12 weeks, and 18 weeks after enrollment. Assessments will take about 40 minutes each and participants will be compensated $40 for each completed assessment. We will also conduct qualitative interviews with 7-8 yoga participants and 4-5 R/HE comparison participants to obtain in-depth feedback on satisfaction and areas that could be improved before a larger trial is conducted.] If feasibility, acceptability, and safety are established, the primary health outcome of interest for a subsequent trial is pain-related disability/ functioning (Roland Morris Disability Questionnaire (RMDQ)).

C2. Recruitment. We will recruit a total of [32 Veterans] over the course of 8 months. Co-I Ayers serves as Director of Outpatient Mental Health at the Medical Center and meets regularly with providers and the directors of the other mental health clinics, and will orient them to study goals. Dr. Heppner is Director of the Behavioral Medicine Service and part of the Mental Health Integration Team. She serves as a liaison between mental health clinics and primary care, and also treats and evaluates chronic pain patients. Dr. Heppner will alert primary care and mental health providers to study goals and criteria. Dr. Groessl also has experience recruiting chronic pain patients with the help of Dr. Jim Michelsen in primary care clinics and through Dr. Ahadian of the Pain Management service. VA patients will be directly targeted via flyers posted in common areas of VA facilities. In sum, study investigators have extensive experience recruiting PTSD and chronic pain patients at VASD, where ~ 40,000 Veterans have chronic pain, 10-15,000 have PTSD, and 5-6,000 have both conditions. *In-person recruitment will be limited and conducted following RAMP up guidelines, including social distancing, the use of PPE, COVID-19 consent addendum, and COVID-19 symptom screening.*

C3. Screening and Inclusion/Exclusion Criteria. Recruitment staff will conduct a brief pre-screen by phone and schedule interested patients for a screening visit to obtain informed consent and HIPAA authorization. Inclusion/exclusion criteria will be applied using a chart review of the VA medical record, a standard medical history interview, and the screening measures described below. English literacy is required. Participants are asked to not perform other mind-body therapies during the study. *Due to COVID-19 pandemic, procedures have been developed to conduct the formal study clinical screening remotely whenever possible to limit in-person research activities. In-person screening for subjects at normal risk will be conducted following RAMP up guidelines, including social distancing, the use of PPE, COVID-19 consent addendum, and COVID-19 symptom screening.*

C3.1. Inclusion Criteria: age ≥ 18, current diagnosis of PTSD in the VA medical record and PCL-5 score of 25 or higher, score of ≥ 25 on Montreal Cognitive Assessment (MoCA), willing to reduce or cease opioid medications, willing to attend 12-weeks of yoga and complete 3 assessments. *Due to COVID-19 pandemic, inclusion criteria will be temporarily modified to be age 18 or greater, but less than 65 years of age. Persons 65 or over meeting other inclusion and exclusion criteria will be kep on an list for future consieration but will not be enrolled under current guidance (8/31/20) because of high risk and intervention is not linked to clinical care services.*

C3.2. Exclusion Criteria: serious or unstable psychiatric illness (e.g. psychosis, mania), suicidal or homicidal ideation, < 3 months since major trauma event, moderate or severe cognitive impairment, practiced yoga > 2x in the last 6 months, coexisting medical illness with

yoga contraindicated, *affirmative response to any questions on the COVID-19 Pre-Visit Screening Tool.*

C3.3 PCL-5. The PCL-5 is a 20-item self-report measure assessing 20 DSM-5 symptoms of PTSD. [88]

C3.4. MoCA is a brief screen for cognitive impairment. We will include those with a score of ≥ 25, based on the Youdon index[73] [to ensure that participants are able to understand the informed consent document, their rights as a participant, the assessments, and the intervention instructions.]

C3.5. VA comprehensive suicide screen. Participants will be asked about suicidal thoughts, intent, and behavior, as well as assessment of risk and protective factors as outlined in VA guidelines.[74]

C4. Randomization. After the initial assessment, participants are randomized to either enhanced yoga or the R/HE intervention. Randomization will occur via a web portal linked to a secure file containing two blocks of 20 randomized digits to provide balanced randomization. Research staff will not have access to the file.

C5. Yoga intervention. The existing evidence-based yoga intervention[23,75] will be adapted to benefit Veterans with cNP, to be more trauma-informed,[71] and to include added relaxation components expected to reduce stress and psychological symptoms of PTSD. Yoga/MR sessions will occur 1x weekly for 12 weeks and the importance of session attendance is emphasized. Participants receive a home practice manual (Appendix 4) containing basic, safe postures that can be performed in ~20 minutes. Instructors can be consulted before or after class about any problems or difficulties encountered. The yoga intervention will be led by Ms. Sinclair who has 10 years of yoga teaching experience, with 7 of those at VASD. [Ms. Sinclair has attended multiple trainings (58 hours) on trauma-sensitive yoga instruction principles, which are a set of adaptations to enhance the comfort of trauma survivors. Trauma sensitive practice includes using invitatory (as opposed to commanding) language, providing a space where clients feel less vulnerable (e.g., lighting should not be too dark), allowing patients to opt out of postures, and minimizing physical assists until trust is established.[71]] The yoga intervention is classic hatha yoga with Iyengar influences. It uses multiple pose modifications and props to make poses accessible to those limited by health problems and to minimize injury risk.[76] The intervention includes 23 yoga poses performed at a moderate pace. The instruction manual (Appendix 5) has pictures and describes how to perform each pose with typical instructor dialogue. Participants are instructed to take slow, deep breaths in conjunction with specific poses and movement and emulate the postural alignment modeled by the instructor. Each session begins with breathing and meditation followed by 15 minutes of basic postures (Poses 1-8) to warm-up, increase circulation, and increase flexibility. This is followed by a series of standing poses (Poses 9-14) for about 20 minutes. Next, the class transitions to floor poses (Poses 15-22) for about 15-20 minutes. Each session ends with about 10 minutes of relaxation in a supine resting pose or "savasana".

C6. The Mantram Repetition Program (MRP) is a portable meditation-based intervention that has been shown to be effective for treating PTSD and other psychological symptoms/disorders. MRP teaches a set of portable tools, including a) repeating a self-selected "mantram": a word or phrase that provides spiritual strength or meaning for that individual; b) slowing down: refers to slowing down thoughts and raising awareness; also setting priorities so one is not rushed; and c) one-pointed attention: refers to concentrating on one thing at a time instead of "multi-tasking", thereby staying in the present moment and conserving energy. These three tools work together to interrupt negative thoughts and emotional states such as anger, irritability and hyper-arousal, and in turn, improve quality of life. The spiritual focus of the mantram is designed to create personal meaning and inspiration by tapping into inner spiritual resources when the phrase is used. However, religiosity is not emphasized, and participants can choose any phrase that inspires them. The MRP has been manualized (Appendix 6), and the condensed MRP will be taught over the course of 12 weeks. Week 1 will include 30 minutes of MR training, followed by 45 minutes of yoga. Week 2-12 will include about 15 minutes of MR training and dialogue, followed by 60 minutes of yoga. Participants are strongly encouraged to practice MR during daily life, and are asked to self-monitor their use of MR.

C7. Summary of safety information. In multiple full-scale trials of cLBP,[23,77,78] and in a broader review of yoga trials,[70] including trials of yoga for cNP, very few adverse events (AEs) have been reported. In studies of yoga for PTSD, no AEs were found when clearly reported.[79-81] MR studies have not found any AEs attributed to the intervention.[20,22,82] If the instructor or research staff become concerned that any participant is at risk of harming him/herself or others, a comprehensive suicide assessment will be performed. If a Veteran is deemed high risk, he/she will be escorted to the walk-in mental health clinic for further treatment

C8. Relaxation/Health Education intervention. The comparison intervention will be a PTSD health education intervention with added emphasis on specific relaxation techniques. The intervention will be adapted from the Veteran calm (VC) "mind-body intervention" used by co-I Lang.[83] VC was derived from work by Taylor et al.[84] with adaptations to increase its appeal to Veterans. The 12 weekly 75-minute sessions feature psychoeducation about PTSD and the

rationale for relaxation therapy, relaxation techniques (progressive muscle relaxation, imagery), sleep hygiene, applied relaxation, and in-session relaxing experiences (self-massage, chair stretching, sensory experiences). Sessions will be led by experienced health educator.

C9. COVID-19 and Intervention Locations. ***Group intervention will not occur in Phase Orange. They will only commence if we are moved to Phase Yellow.*** *The Yoga + MR intervention is scheduled to be held in the back of the VASD chapel area on Wednesdays afternoons from 2-3:30PM. When chairs are cleared, this area is approximately 40 ft x 50ft or 2000 square feet area. This has been approved by Chaplain Larry Taylor.This large area allows for social distancing of 10 feet or greater between participants. With two cohorts, 8 participants are randomized to each intervention at a time. Attendance is expected to be 6-8 subjects each session. The Relaxation class intervention will also be held in the same space. Subjects at normal risk will be allowed to attend following RAMP up guidelines, including social distancing, the use of PPE, COVID-19 consent addendum, and COVID-19 symptom screening.*

C10. Measures, Measures will include questionnaires and two physiological measures. Questionnaires are described in section 9.8 *To reduce in-persn cntact during the COVID-19 pandemic, we will allow participants to complete follow-up assessments be mail if they cannot be scheduled for an in-pseron assessment, or if their status changes from normal risk to higher risk, or if they become infected. If this occurs, we will forego the physiological assessments below.*

Physiological measures include grip strength and a one-leg balance test.

Grip Strength*. Grip strength in both hands of each participant will be measured using an adjustable, hydraulic grip strength dynamometer (Jamar Hydraulic Hand Dynamometer, Model No. BK-7498, Fred Sammons, Inc. Burr Ridge, IL). Two trials will be conducted for each hand. In cases of current pain flare-ups or recent procedures to a hand or wrist, the affected area is not tested, and the result of the one good hand is used. The best performance of two trials will be selected for each side, and the average of the left and right hand will be used for analysis. Reproducibility for grip strength assessment has been shown to be high: r=0.88-0.92. Predictive validity of hand grip strength has been shown previously for both disability and mortality[80].*

One-leg Stance *- Balance was evaluated using the unipedal stance test, aka the single leg stance. Which is a frequent measure of fall-risk in older adults,[17] but is also frequently used in back pain research. It has been validated[18,19] and has referenced norms across all adult age groups.[20] The test was administered by research staff with calibrated stopwatches. The participant was instructed to alternately stand on one leg for as long as they could with both eyes open for a maximum of 60 seconds. They were then instructed to repeat the test with both eyes closed.*

C11. Data Analytic Methods. Because our aims focus on acceptability, feasibility, fidelity and AEs in preparation for a larger RCT, tests of statistical significance are not required. Intervention acceptability and the feasibility of conducting a full-scale RCT will be evaluated using recruitment rates, recruitment to enrollment ratio, intervention attendance rates, retention rates at 12-week assessment, participant satisfaction, serious and non-serious AE rates, participant assessment burden, and instructor fidelity. Mean differences from baseline to follow-up scores will be calculated for outcome measures.

C11.1. Data management. Questionnaires will be formatted by the project coordinator to reduce recording errors and facilitate computer scanning and verification. The project coordinator will monitor the quality of the questionnaire data as soon as they are collected to achieve prompt resolution of errors and omissions. Forms will be coded to protect confidentiality. *Coded forms will be transported by study staff to the University of California Health Services Research Center (UCSD-HSRC) for processing. UCSD-HSRC is a recharge unit within UCSD that provides research services to outside entities. They are located at 5440 Morehouse DR. San Diego, CA 92121. An approved Authorization to Transport (ATT) form will be used and on file for staff transporting the paper copies. All identifiers will be removed from the form except a subject ID code. Data will include sociodemographic data, coded interview transcripts, and health outcome data, but will not contain age, birthdate, or any of the 18 patient identifiers. The key to the coded data is kept on the PI's private folder on the VA research network on the VA server. In addition, the key linking names to ID numbers will be stored in a locked file cabinet within a locked research office in Bldg. 13 of VASDHS. UCSD-HSRC will scan and conduct quality review of data. They will manage clean data and prepare a data set for analysis. The data file will be password protected and transported back to VA by study staff or sent by MS Azure if under 40Mb.*

Audio recordings of qualitative interviews will be transcribed by a VA service. The service is VA Salt Lake Centralized Transcription Services Program, a program that was created to provide VA researchers nationwide with transcription and qualitative analysis services. Identifiable voice data will not leave the VA secure IT enviroment. It will be transferred via a secure VA Sharepoint folder. Transcripts with study ID codes will be returned to PI-Groessl via VA Sharepoint. The

Centralized Transcription Services Program will not use the data for any other purposes and is only providing transcription as a paid service.

C11.2. Data Analysis and Feasibility Criteria. Recruitment rates will be compared to the specified goal of a mean of 4 enrolled participants per month. We expect to need 5 screened eligible participants per month because some fail to follow through and enroll. If rates remain below 50% of the goal, feasibility will not be established for a full-scale RCT. Attendance rates in many mind-body intervention studies range between 50-80%.[78,94,95] For this study, attendance of 50% or higher will be required to support further research on either intervention. A retention rate of 80% or higher is considered an adequate retention rate at a post-intervention assessment for an RCT.[96] Thus, we will use a slightly more lenient 75% or higher retention to indicate feasibility to proceed. Participant satisfaction rates of 75% or higher (measured as % of participants checking agree or strongly agree) will be used to indicate acceptability of the interventions, with little or no modifications needed prior to a larger study. AEs will be evaluated in collaboration with the VASD IRB and the DSMC. In general, any more than 1-2 serious AEs attributed to either intervention among the 20 participants assigned to each would give cause for pausing the intervention until obvious solutions and modifications were identified. Mean time to complete the questionnaires is estimated at 40 minutes. Mean time of 80 minutes or more would indicate burden issues and review of the battery and/or compensation level. Instructor fidelity of under 75% will indicate a need for retraining and/or clarifications of the instructor manual. Finally, mean changes on outcome measures will be compared to minimum clinically important differences where established.

Section 9.1 Clinical Procedures

9.1) Differentiate research procedures (or any procedures done for research purposes only) from clinical procedures (procedures that are done as part of standard care).

(Note: this differentiation should be clear in the consent form as well)

All of the procedures will be considered research procedures. Mantram Repetition classes are offered at VASD as a clinical intervention, but when shortened and combined with yoga for this intervention, it will be considered research.

Section 9.8 Questionnaires & Surveys

9.8) Provide the name and a reference for questionnaires/surveys that are standard or identify them here and attach a copy of the questionnaire/survey. ***Questionnaires or surveys that are not clinical standard references must be uploaded. Reference the help link for additional information related to surveys administered to VA personnel and approved platforms for web-based surveys.***

C9. Measures. Medical records will provide information on co-morbid diagnoses, medication usage, and ongoing treatments for screening and to further describe participant characteristics.

C9.1. Feasibility of recruitment and retention. We will track and document the date that each recruitment method begins and the date each person is recruited. We will ask each potential participant to identify the recruitment source that led to their inquiry about participation. We will track retention rates, reasons for not completing the follow-up assessment and acceptability of the assessment procedures.

C9.2. Acceptability, Attendance, and Adherence will be assessed using sign-in logs verified by the instructor. Self-reported practice of yoga and MR will be assessed with weekly logs. The yoga log is shown in Appendix 7 and a draft of the MR log is shown in Appendix 8. Participants will be called to document reasons for non-attendance. We will assess program satisfaction using questions developed and used by the investigators in previous studies. (Appendix 9). We will also conduct qualitative interviews with 7-8 participants of the enhanced yoga group and 4-5 participants of the R/HE comparison group to obtain in-depth feedback on satisfaction and areas that could be improved before a larger trial is conducted. Semi-structured qualitative interviews lasting ~ 45 minutes will utilize open-ended questions to address: 1) past experience with mind-body interventions; 2) their experience with the enhanced yoga program; 3) recommendations for changes; 4) feedback on dosing and logistics of the program; and 5) thoughts on research participation and assessment burden. Transcribed interviews will be analyzed using directed content analysis (DCA) to identify and categorize meaningful and detailed information about participant's opinions, perceptions and experiences. Verification of emergent themes and

disagreements during theme interpretation or coding hierarchy will be resolved through investigator discussions before completing the qualitative analysis.

C9.3. Adverse Events: AE information will be collected via a weekly log. (Appendix 10) Participants are instructed to contact intervention instructors or study staff if they experience any health problems possibly related to the interventions. AEs will be assessed by phone if intervention sessions are missed. Medical records will be reviewed if patients cannot be contacted to complete assessments or assess absences. We will establish a Data Safety Monitoring Committee (DSMC) at start-up.

C9.4. Treatment Fidelity: Instructor fidelity to the enhanced yoga interventions will be evaluated by review of video recordings of intervention sessions. Intervention instructors will be video-recorded. Instructors and participants will be aware of and consent to the recordings. Of the 12 videotaped sessions, one session from weeks 1-4, weeks 5-8, and weeks 9-12 will be randomly selected for review by an expert yoga instructor. They will review the sessions using a manual checklist for instructor adherence to the yoga manuals.

C9.5. Health Outcomes. Outcomes measures anticipated for use in a full-scale study will be administered to gauge participant burden and observe changes. We will assess basic socio-demographics along with military rank and duties, type/date of trauma, and combat status.

C9.5.1 Pain-related Function. The RMDQ has 23 questions asking about limitations experienced with daily activities. The scale is reliable and well validated85. It has been used in other yoga studies.86 Questions will be worded to include limitations related to chronic back or neck pain.

C9.5.1a. Neck Disability Index - A validated index with 10 questions about neck pain-related functioning.

C9.5.2 Pain severity and interference will be measured with the Brief Pain Inventory (BPI).87

C9.5.3 PCL-5. The PCL-5 is a 20-item self-report measure assessing 20 DSM-5 symptoms of PTSD. 88

C9.5.4 Traumatic Brain Injury. Presence and severity of TBI will assessed and classified as either mild or moderate/severe, using four screening questions. Mild TBI is defined as: Loss/alteration of consciousness < 30 minutes, Glasgow coma scale of 13-15 (if known), and post-traumatic amnesia of < 24 hours.89
C9.5.4a The PHQ-9 contains 9 questions about depression and mental health. It is a vaidated measure.

C9.5.5 The Insomnia Severity Index (ISI) is a 7-item instrument that assesses the impact of insomnia.90

C9.5.6 Health-related Quality of Life will be measured with the SF-12, a descriptive measure with two domains of HRQOL. Reliability and validity are well established. The EQ5D will also be used as a validated measure of preference-based quality of life.

C9.5.7 Alcohol Use. AUDIT-C is a 3-item screen for problem drinking and will refer to alcohol use over the past 3-month period. The measure has questions on typical consumption and binge drinking frequency.93

C9.5.8 Non-VA Medications/Treatments. We will assess medications and self-care treatments used outside of VA via a questionnaire used in other VA studies. (Appendix 11)

C9.5.9 The Philadelphia Mindfulness Index has 20 question that ask about awareness of the present moment, and acceptance of current situations. It is a validated measure.

C9.5.10 The Fatigue Severity Scale is a validated measure of fatigue symptoms. It has 9 questions.

C9.5.11 The Self-Efficacy for cLBP scale is a validated scale with 6 questions about one's confidence in their ability to manage their cLBP.

C9.5.12 Program Evaluation - Here we ask 10 questions about participant satisfaction with the interventions.

Section 9.9 Data Safety Monitoring Board or Plan

9.9) Provide a Data Safety Monitoring Plan (DSMP) or the details of a Data Safety Monitoring Board; if a written plan is available, attach a copy of the plan to the submission form.

The study is a pilot intervention that will randomize 32 participants with PTSD to either yoga plus Mantram repetition or to a relaxation comparison group. Study investigators will review all adverse events on a weekly basis and report them as appropriate to the IRB according to established requirements. Drs.Lang and Ayers have clinical and research expertise with PTSD. If the rate of serious adverse events attributed to either intervention results in an imbalanced SEA rate between the two study arms, or is higher than clinically expected, the study will be stopped to assess safety. If adjustments to the intervention to remedy the problem are not obvious or easily made, the study intervention(s) will be discontinued.

Research activities will cease if any participant or study staff member that had recent study interactions with study staff or other participants tests positive for COVID-19 within 3 weeks of those interactions. All at risk persons will be notified of their risk at that time.

Section 9.11 Pictures and Audio/Video Recordings of Patients

9.11) Describe the purpose of photographs (facial), or audio, or video recordings of patients. Describe whether the recordings will contain, or potentially contain, identifiers. ***Note: use of photographs or recordings must be covered in the informed consent process and documented consent documents (e.g., consent form, information sheets, telephone screen scripts).***

Qualitative interviews will be audio-recorded so that they can be professionally transcribed before being analyzed. This is necessary to conduct high quality research.

The yoga and mantram interventions will be video-recorded to assess instructor fidelity. The camera is fixed and focused on the instructor, but may show the back or part of the participants, and may be identifiable.

Section 10 - Human Subjects

10) Describe the characteristics of the proposed subject population. Include age, gender, ethnicity, and health status as appropriate. ***Note: Data about people are still considered "human subjects" by the IRB, so even if you do not intend to contact the patients whose charts you will review, you still describe the characteristics related to the subjects whose charts you will review.***

- **Provide inclusion and exclusion criteria as appropriate. Provide a statement how non pregnancy is confirmed if pregnancy is an exclusion criteria.**
- **For multisite studies, provide the total number of subjects from all sites and include description of the local site's role as a coordinating center if applicable.**
- **Indicate the number of VA participants to be studied.**
- **Indicate the estimated number of consented subjects that will fail the screening process, if any.**

Human Subjects Involvement and Characteristics. The study will recruit 32 patients from the VA San Diego Healthcare System with a diagnosis of PTSD, and a diagnosis of chronic low back pain (cLBP) and/or chronic neck pain (cNP).

Inclusion Criteria: age > 18, PTSD Checklist (PCL-5) score of ≥ 25, score of ≥ 25 on Montreal Cognitive Assessment (MoCA), willing to reduce or cease opioid medications, willing to attend 12-weeks of yoga and complete 3 assessments.

Exclusion Criteria: serious or unstable psychiatric illness (e.g. psychosis, mania), suicidal or homicidal ideation WITH active plan and/or intent, < 3 months since major trauma event, moderate or severe cognitive impairment, practiced yoga > 2x in the last 6 months, coexisting medical illness with yoga contraindicated.

Screening Measures

Medical History Interview. All participants will complete a standard interview regarding medical history and functioning. In addition, a chart review of the VA patient record will be conducted to assess medical status.

C3.3. The PCL-5 is a 20-item self-report measure assessing 20 DSM-5 symptoms of PTSD. It has been validated in Veterans.
C3.4. MoCA is a brief screen for cognitive impairment. We will include those with a score of ≥ 25, based on the Youdon index to be inclusive, yet ensure that participants are able to understand the informed consent document, their rights as a participant, the assessments, and the intervention instructions.
C3.5. Columbia Suicide Severity Rating Scale. Participants will be asked about suicidal thoughts, plan, intent, and behavior, as well as assessment of risk and protective factors.

Based on data from a previous study, only about 25% or less failed the screening exam. Thus we expected to screen about 44 patients and that 12 or less will fail screening.

Qualitative Interviews (QI) will be conducted with a subset 12 of the 32 participants recruited using the criteria above. Participants will be invited to participate in the QI if they had challenges attending, asked to withdraw from the study, or if they have low satisfaction with the program. However, we will also interview at least 4 participants who attended well and were satisfied with the interventions and study.

Inclusion of Women and Minorities
Women and minorities will be included in this study. The nature of the research does not pertain specifically to either women or minorities but we will encourage their participation as much as possible in order to generalize results where possible. Less than 10% of VA patients served at the VASDHS are women, but pilot data from the VA San Diego and other non-VA studies suggest that women may be more receptive to yoga and/or MR interventions and may be overrepresented as a proportion of VA patients. Thus, we will have a recruitment target of 20% women. Ethnic minorities were also well represented in our previous VA yoga and MR studies. We will have a target of recruiting at least 30% racial or ethnic minorities for this study.

Children will not be recruited since they are not patients at the VA San Diego.

Section 10.2 Pregnant Women

10.2a) Are pregnant women the focus of the research?

○ Yes ◉ No

10.2b) Provide the justification for including pregnant women and address any special risks, protections, and safeguards.

VA patients with PTSD who are women and are pregnant still require treatment of their chronic pain. Pregnant women who qualify on all other aspects of the
study will be allowed to participate in yoga if their primary care physician provides written approval.

Section 10.6 Avoiding coercion of students or employees

10.6) Indicate how coercion of students and/or employees will be avoided:

Many VA patients are also VA employees. Their status as students or employees will in general not be known to study staff. The voluntary nature of participation will be emphasized in the informed consent process and throughout the study. Students or employees will not be targeted in any way. They may respond to flyers or be told about the study by clinicians in their role as patients. If it becomes known to study staff that an enrolled participant or an individual considering participation is a student or employee, they will be told that participation or non-participation will not affect their student or employee status in any way.

Section 11 - Recruitment

11) Describe, step-by-step, the plans for recruitment of subjects (or selection of subjects as in record review).

This description must include how, when, and where potential subjects are approached as well as procedures for identifying potential participants (through medical records, physician referral, third-party sources, etc.). Include how selection is equitable. Indicate if vulnerability to coercion may be present and if so plans to ensure voluntary participation.

Recruitment will occur through flyers posted through VA medical centers, and through clinical providers. Clinical providers will be briefed on the study goals and procedures, risks, and potential benefits. During the enrollment period, clinical providers will personally invite and refer patients to participate, and when appropriate, direct patients to speak with study research staff, who will be available during clinics. Patients who speak with research staff will be given a clear description of all aspects of study participation, including randomization, collection of electronic data, and incentives. Those who wish to enroll and meet entry criteria above by self-report will undergo signed informed consent, after which electronic medical records will be reviewed to confirm, document, and record eligibility criteria.

Section 11.1 Recruitment Materials

11.1) Identify all recruitment materials (flyers, advertisements, letters, etc.) that will be used; include the web address for any web-based advertisements. The text of all communications with prospective participants must be reviewed and approved by the IRB before it can be used. You will be reminded to attach copies of recruitment materials to the initial submission packet. ***Note: Posting of flyers with pull tabs is not permitted within VASDHS (including the VMRF building). However, you may request to advertise on the e-boards (located at the elevators and throughout the facility) or on the VASDHS Research Opportunities web-page.***

Flyers, posting on monitors in waiting rooms.

Section 12 - Informed Consent

12) Indicate whether or not each category of consent is involved in this study:

12a) Will the study team obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without (or prior to) obtaining informed consent of the prospective subject or the prospective subject's LAR?

○ Yes ◉ No

12b) **Signed** informed consent

◉ Yes ○ No

12c) Waiver of documented consent (e.g., **oral** consent) for all or part of the study.

○ Yes ◉ No

12d) Request for a **waiver** of consent for all or some study activities.

○ Yes ◉ No

12e) Alteration of **other required elements** of consent.

○ Yes ◉ No

12f) **Child** assent to participate (Director approval will be required)

○ Yes ◉ No

12g) Will any language **other than English** be used by those obtaining consent and understood by the prospective participant or the legally authorized representative?

○ Yes ◉ No

12h) **Decisional Capacity Assessment** to determine if participants have the capacity to consent for themselves.

◉ Yes ○ No

12i) **Surrogate** consent (legally authorized representative)

○ Yes ◉ No

Section 12.1 Informed Consent Process

12.1a) Will consent be obtained before any study procedures are performed (including screening procedures except screening procedures with Consent and/or HIPAA waiver when required)?

◉ Yes ○ No

12.1b) Will the information being communicated to the participant or legally authorized representative during the consent process include exculpatory language through which the participant or legally authorized representative is made to waive or appear to waive any of the participant's legal rights or release or appear to release the Researcher, Sponsor, the VA or its agents from liability for negligence.

○ Yes ◉ No

12.1c) A master list of all VA subjects consented (written or not) under this protocol will be maintained.

◉ Agree ○ Disagree

12.1d) Identify the circumstances under which consent will be obtained including where the process will take place; any waiting period between describing the research and obtaining consent including sufficient time for the prospective participant to consider participation, and any steps taken to minimize the possibility of coercion or undue influence.

The study coordinator or research staff will describe the study, requirements of participation, and inclusion/exclusion criteria via telephone for any prospective participants that inquire. If they remain interested, they will be scheduled for the informed consent process at a mutually available time, either in-person or through an online process described below. They will be allowed to have another person present if they would like. The consent form and study procedures will be fully explained at the appointment. The voluntary nature of participation will be emphasized. They will be given additional time to make a decision as needed.

For remote online consenting, we will use traditional mail or encrypted Azure email to send prospective participants a packet containing: 1) the approved Informed Consent and HIPAA document; 2) the CA Experimental Subjects Bill of Rights, and 3) the COVID-19 consent addendum. We will then arrange an appointment that will use Veteran Video Connect to complete the informed consent process, explain the HIPAA Authorization, the COVID-19 addendum, in-person procedures, and CA Experimental Subjects Bill of Rights. The staff member will witness the signing of the forms and will instruct the participant to provide documentation of written informed consent by taking a screenshot while they hold up the signed forms to the camera (approval date and signature must be clearly visible). These electronic documents will be stored electronically separate from study data in the PI's study folder on the R: drive, and the participant will retain their copies.

Section 12.6 Decisional Capacity Assessment

12.6a) Describe the method(s) for determination of decisional capacity: (see ? for guidance) ***Please note that documentation of the assessement is required.***

Decisonal capacity will be assessed with the Montreal Cognitive Assessment (MoCA), which is a brief screen for cognitive impairment. We will include those with a score of ≥ 25, based on the Youdon index to ensure that participants are able to understand the informed consent document, their rights as a participant, the assessments, and the intervention instructions.

12.6b) If subjects with limited decisional capacity will be enrolled, describe methods for obtaining subject

assent or why they are not indicated:

They will not be enrolled.

12.6c) If subjects with limited decisional capacity will be enrolled, describe procedures for respecting subject dissent and any additional safeguards or why these features are not needed:

They will not be enrolled.

12.6d) If subjects with limited decisional capacity will be enrolled, describe the risk and, if greater than minimal, the relation to potential benefits:

They will not be enrolled.

12.6e) If subjects with limited decisional capacity will be enrolled, describe the justification for the inclusion of any incompetent persons or persons with impaired decision-making capacity:

They will not be enrolled.

Section 12.9 HIPAA Authorization

For each category below, indicate whether or not this study involves the indicated process:

12.9a) **Signed** HIPAA Authorization. ***New Template is available in the ? Help section***

(•) Yes ( ) No

12.9b) HIPAA waiver to cover the entire study

( ) Yes (•) No

12.9c) HIPAA waiver for recruitment, screening, and/or for a portion of the study.

( ) Yes (•) No

12.9d) HIPAA Authorization or waiver is **not required** for some or all of the study subjects (e.g. no health data).

( ) Yes (•) No

Section 13 - Alternatives to Participation

13) Describe the alternatives to participation in this research study (see ? for guidance)

The Alternative to participation is to not participate. Clinical care will not be affected.

Section 14 - Potential Risks

14) Describe any potential or known risks or discomforts and assess their likelihood and seriousness (see ? for guidance)

The main risk to participants is the potential loss of confidentiality. It is also possible that a patient could injure themselves doing yoga, or experience some discomfort from mantram repetition practice or the relaxation intervention. There could also be discomfort from answering questions containing personal information during qualitative interviews or while completing questionnaires. Since research staff will access patient medical records and their name will appear on the first page within the assessment packet, this research could involve a loss of privacy. All of the research information will be kept as confidential as possible. Yoga could

propose a potential risk to pregnant women. The yoga being studied is of mild to moderate intensity and designed to be safe for a wide range of conditions but is not specifically designed to be safe for pregnant women.

It is possible that a participant could contract COVID-19 as a result of study participation. There is no known increase to their risk above community risks.

Section 15 - Risk Management

15) Describe the procedures for protecting against or minimizing any potential risks/discomforts, and the adequacy of resources for conducting the study and resources participants may need as a consequence of the research. When applicable, include detail of the following safety measures: (a) The type of safety information to be collected, including AEs; (b) Frequency of safety data collection; (c) Frequency or periodicity of review of cumulative safety data; (d) Statistical tests for analyzing the safety data to determine if harm is occurring; and (e) Conditions that trigger an immediate suspension of the research. See ? for further requirements.

Overall, the study poses minimal risk to the study participant. The research team is experienced in the protection of privacy and maintaining confidentiality. Based on medical literature and clinical experience at VA San Diego, the risk of being injured doing yoga or of experiencing discomfort from MR, relaxation, or completing questionnaires appears to be very small. The intervention instructors will be required to have at least 2 years teaching experience and have attended some trauma-sensitivity training. If a patient is injured or experiences sever psychological discomfort, the instructors have access to a house phone and can call for immediate help. The intervention rooms are located on the 1st floor of the hospital and can be reached by emergency staff very quickly. Staff administering the questionnaires and conducting the physiological assessments are well trained in providing informed consent and participants can refuse to answer any questions that make them uncomfortable without any consequences.
Patients will be reassured that their data will only be used for the objectives of this research project and that all of the research information will be kept as confidential as possible. All health information will be labeled with a number code, and not names. A master list linking the codes to actual names will be kept in a locked file cabinet inside a locked office. Names will not be used in any reports about the study. All of the study results are reported for groups of patients and not for individuals.
Participants will be notified that yoga may pose a potential risk for pregnant women, and women who may become pregnant or women who know they are pregnant should consult with a physician before participating. The yoga will be conducted in the VASD Medical Center and yoga instructors and research staff will call emergency medical staff if ever needed.

To reduce risk of COVID-19 transmission, study staff will strictlyfllow all approved guidance and procedures to conduct research activities remotely when possible, and follow RAMP up guidelines, including social distancing, the use of PPE, COVID-19 consent addendum, and COVID-19 symptom screening.

Section 17 - Potential Benefits

17) Discuss benefits that may be gained by the subject as well as potential benefits to society in general (see ? for guidance)

Prior studies have found that yoga can reduce disability and pain in Veterans with chronic low back pain. Yoga has also been shown to help chronic neck pain. Mantram Repetition (MR) has been shown to alleviate PTSD symptoms in Veterans, and yoga may also help PTSD symptoms in some populations. In addition,
yoga has been shown to improve pain, depression, physical functioning, sleep, and quality of life in people with other medical conditions. The yoga and MR intervention may benefit VA patients with PTSD in a similar manner. The
study will provide data on the feasibility of conducting a full-scale trial of yoga and MR for pain in PTSD. If the intervention is shown to improve pain and PTSD symptoms in VA patients, the intervention is likely to be adopted in more VA facilities and could then benefit many VA patients with PTSD.

Section 18 - Risk/Benefit Analysis

18) Discuss why the risks to subjects are reasonable in relation to the anticipated benefits to subjects and in relation to the importance of the knowledge that may reasonably be expected to result.

The investigators believe that it is unlikely that confidentiality concerning personal medical information will be breached given the security plan. It is also unlikely that patients will suffer serious emotional discomfort because they are fully informed about what will happen during the study and have sufficient time to prepare and decline participation if necessary. They also can stop participating at any time without penalty. Rates of physical injury and adverse events from yoga and MR in previous studies with similar populations are low, and appear no higher than natural rates of injury in this population. Therefore, the investigators believe that the potential benefits to participants and the potential of obtaining new scientific information and designing new interventions for people with chronic low back pain outweigh the potential risks.

Section 20 - Compensation for Participation

20) Provide all details and justifications of the compensation plan. See ? for detailed requirements.

Participants will receive $40 for completing each assessment and up to $120 for completing all assessments. 12 participants will also receive $40 for completing a qualitative interview. Participants can also receive up to $60 for attending all intervention sessions ($5 per session)

Section 21 - Responsibilities and Qualifications

Here are the identified study staff members

Erik J. Groessl, PhD

Ariel J. Lang, PhD, Catherine R. Ayers, PhD, Lin Liu, PhD, Thomas R. Rutledge, PhD, Carol-Luanne Hafey, Adhana McCarthy, MPAS, Danielle Lyn Casteel, MA, Miguel Angel Prado-Nava, BS, Tania Zamora

21) For each staff member listed above, describe their role and qualifications. Also indicate which of the study staff are authorized to obtain consent, when applicable to the study.

Dr. Erik J. Groessl (PI) will actively participate in all aspects of the project and will be responsible for overall management. Dr. Groessl will collaborate with Drs. Lang, Ayers, Rutledge, Liu, and intervention instructors on adapting the MR and yoga interventions.

Carol Hafey will serve as a main Contact and Study Coordinator. She will assist with IRB submissions, recruitment, informed consent, data entry, and assessments.

Danielle Casteel will assist with IRB submissions, recruitment, informed consent, data entry, data management, and assessments.

Adhana McCarthy will assist with IRB submissions, recruitment, informed consent, data entry, data management, data analysis, and assessments. She will also lead one of the yoga sessions and assist with intervention refinement. Ms McCarthy is a Certified Yoga Therapist with 1000 hours of training. They will attend project meetings as needed.

Miguel Prado-Nava is the co-research assistant with WOC approval. He will assist in recruitment, consents, assessments, and data management.

Tania Zamora will assist Rahil with administrative issues as needed, and may assist with assessments or scheduling.

Dr. Ariel Lang will advise Dr. Groessl on design issues, adapting the intervention, and recruitment. She will attend project meetings on a regular basis at the beginning of the study and as needed during later stages.
Dr. Tom Rutledge will assist Dr. Groessl with adapting the intervention, and recruitment. He will attend project meetings on a regular basis at the beginning of the study and as needed during later stages.

Dr. Catherine Ayers will assist with intervention design and facilitate recruitment of PTSD patients thought out the VASD Mental health clinics. She will attend project meetings as needed. Dr. Lin Liu will advise Dr. Groessl on data analysis issues and dissemination.

Section 22 - Bibliography

22) List relevant articles that the IRB can use to provide necessary background for the protocol. Do not include an extensive NIH-grant-style bibliography. (Up to 5 recommended, but use more if needed to support the protocol or citations above.)

Groessl EJ, Liu L, Chang DG, Wetherell JL, Bormann JE, Atkinson JH, Baxi S, Schmalzl L. Yoga for Military Veterans with Chronic Low Back Pain: A Randomized Clinical Trial. Am J Prev Med. 2017 Jul 17.

Groessl EJ, Weingart KR, Aschbacher K, Pada L, Baxi S. Yoga for veterans with chronic low-back pain. J Altern Complement Med. 2008 Nov;14(9):1123-9.

Groessl EJ, Weingart KR, Johnson N, Pada L, Baxi S. The benefits of yoga for women veterans with chronic low back pain. J Altern Complement Med. 2012 Sep;18(9):832-8. Epub 2012 Jul 19.

Bormann, J. E., Thorp, S. R., Wetherell, J. L., Golshan, S. & Lang, A. J. (2013). Meditation-Based Mantram Intervention for Veterans with Posttraumatic Stress Disorder: A Randomized Trial. Psychological Trauma: Theory, Research, Practice and Policy. 5(3):259-267, doi: 10.1037 /a0027522

Bormann, J. E., Hurst, S. & Kelly, A. (2013). Responses to mantram repetition program from veterans with posttraumatic stress disorder: A qualitative analysis. Journal of Rehabilitation Research and Development, 50(6), 769-784. doi:10.1682/JRRD.2012.06.0118

Section 23 - Sponsors and Collaborators

23) Clarify any industry financial or other support (e.g., NIH funds the study or Company X provides the assay kits). Identify non-VA Research collaborators and their role in this protocol, including whether or not they have access to subjects or identified data.

VA RR&D is the funding agency.

Camilla Sinclair will lead the yoga intervention as an instructor and will assist with refinement and manualization of the yoga intervention components. Ms. Sinclair is RYT-500 certified and has 10+ years experience teaching yoga at VASD.

In the submission form, upload a copy of the grant, subaward, CRADA, etc. as appliable to the study.

Section 27 - Privacy, Confidentiality, and Information Security

27a) Provide a brief description of how participant privacy and confidentiality will be protected in this study. Describe the circumstance under which it may be possible for a research team member to identify subjects and any related protections or assurances to prohibit or avoid identification. Describe how the number of people with access to identifiers for research purposes is limited in order to protect a participant's privacy.

Data Security Plan.
• The particular sensitive information (SI) that will be used in this study includes the following data extracted from VA medical records: medical diagnoses, medications prescribed; medical co-morbidities, appointment attendance.
• Questionnaire data will be coded after completion by separating the top page and assigning a study ID number.
• Qualitative interviews will be audiotaped, and transcribed by VA Salt Lake through VA Sharepoint. Transcribed text files will be labeled with a study ID code, and no other identifiers.

• SI will be used by approved study personnel only.
• In the event of a real or suspected breach of security, the VA Police, the VA Information Security Officer, and the VA Privacy Officer will be notified.

All research records will be kept confidential. SI is stored both electronically and as a hardcopy. Hardcopy SI is stored in the locked study office of Dr. Groessl. Electronic data extracted from the VA San Diego medical record will be kept in locked file cabinets located at the VA San Diego Healthcare System, Building 13, Room 215. Data will be collected on consented patients and stored on a VA secure server. In concordance with VA policy and IT security guidelines, digital video files and electronic files with patient identifiers (name, social security, address, telephone) will only be kept on a VA secure server. These files will not be kept on VA or non-VA laptops, non-VA PCs, discs or memory storage devices. Access to medical records is password protected (requiring prior authorization from the VA to review records for research purposes on consented participants only). Coded forms will be transported by study staff to the University of California Health Services Research Center (UCSD-HSRC) for processing. UCSD-HSRC is a recharge unit within UCSD that provides research services to outside entities. They are located at 5440 Morehouse DR. San Diego, CA 92121. An approved Authorization to Transport (ATT) form will be used and on file for staff transporting the paper copies. All identifiers will be removed from the form except a subject ID code. Data will include sociodemographic data, coded interview transcripts, and health outcome data, but will not contain age, birth date, or any of the 18 patient identifiers. The key to the coded data is kept on the PI's private folder on the VA research network on the VA server. In addition, the key linking names to ID numbers will be stored in a locked file cabinet within a locked research office in Bldg. 13 of VASDHS. UCSD-HSRC will scan and conduct quality review of data. They will manage, clean and prepare the coded data set for analysis. The data file will be password protected and transported back to VA by study staff or sent by MS Azure if under 40Mb.

Audio recordings of qualitative interviews will be transcribed by a VA service. The service is VA Salt Lake Centralized Transcription Services Program, a program that was created to provide VA researchers nationwide with transcription and qualitative analysis services. Identifiable voice data will not leave the VA secure IT environment. It will be transferred via a secure VA Sharepoint folder. Transcripts with study ID codes will be returned to PI-Groessl via VA Sharepoint. The Centralized Transcription Services Program will not use the data for any other purposes and is only providing transcription as a paid service.

We anticipate collecting data and keeping the study protocol active for at least four years. VHA requires compliance with Records Control Schedule (RCS-10) for retention of electronic and hard copy records. Following study closure, these temporary records must be retained for six years and then destroyed.

27.b) Entry of a CPRS Research Informed Consent Note is required when subjects will be admitted as inpatients or treated as an outpatients for research *and* the study involves research medical care or may affect medical care.

- ***If a Research consent Note is required, then a Research Progress Note should also be entered for each procedure or intervention.***
- ***Scanning the Consent and HIPAA Authorization into CPRS is not required. Linking the Consent to the Research Informed Consent Note may be permitted and can be useful for trials involving the Research Pharmacy or when research will be performed in conjunction with clinical procedures.***
- ***For Non-Veterans, if Research Informed Consent Notes are entered, then the NOPP Acknowledgment must be scanned into the record. Otherwise a copy of the signed NOPP must be retained with the Investigator's research records and a copy sent to the Privacy Officer; see the ? Help for more information.***

27.b1) Is entry of CPRS notes required based on the above criteria?

- (•) CPRS notes are needed for ALL subjects
- ( ) CPRS notes are needed for SOME subjects
- ( ) CPRS notes are NOT needed for any subjects

27c) Select the VA Sensitive Information (VASI) use category

- ( ) This study does not collect or use any VASI
- ( ) This study uses but does not save, collect, copy, or record VASI

(•) This study does collect or record VASI

Section 27.1 VA Sensitive Information (VASI)

27.1a) For each type of VASI, indicate all that apply:

Indicate which of the following will be collected/recorded:

- [x] Protected Health Information (PHI)
- [x] Names
- [ ] Device identifiers and serial numbers
- [ ] E-mail addresses
- [ ] Medical record numbers
- [ ] URLs (Universal Resource Locator)
- [x] All elements of dates (except year) or any age over 89
- [ ] Health plan beneficiary numbers
- [ ] IP Addresses (Internet Protocol)
- [x] Telephone numbers
- [ ] Account numbers
- [ ] Biometric Identifiers including finger and voice print
- [ ] Fax numbers
- [ ] Certificate or license numbers
- [x] Full face photographic images and comparable images
- [ ] All geographic subdivisions smaller than a state
- [ ] Vehicle ID and serial numbers including license plate numbers
- [x] Social security numbers or scrambled SSNs (describe below)
- [x] Other unique identifying number, characteristic, or code (describe below)

27.1a1) Describe why SSN are needed for this study

SSNs are need to compensate participants for their time. The last 4 SSN digits will also be used to access medical records and enter CPRS notes during the study.

27.1a2) Identify the specific other identifier/s that will be used or recorded

Audio voice recordings of interviews.

27.1b) Consent Forms and/or HIPAA Authorization

(•) Yes ( ) No

27.1c) Images with personal identifiers are used for this study (x-rays, MRI images with patient names, record numbers, dates, etc.)?

( ) Yes (•) No

27.1d) Photos with faces or audio video recordings are used for this study.

(•) Yes ( ) No

27.1d1) Identify the device or devices that will be used to take/make the photographs or recordings.

Videocameras record yoga sessions but are positioned to focus on the instructor to assess intervention fidelity. If a participant moves or turns around it is possible their image would be captured.
Audio voice recordings of interviews using VA authorized recorders. Devices used to record audio or video are the Canon FS31 digital recorder. New devices will be purchased if needed.

27.1d2) Identify where images will be stored (e.g., in the medical record, with study hardcopy records, with study electronic VASI records

Images will be stored on the R drive in the PI folder - R01SDCHSM02.R01.MED.VA.GOV\Groessl\Yoga and CAM Research\PTSD - Yoga\Yoga and MR for pain in PTSD

27.1e) Biological specimens with identifiers are used for this study.

○ Yes ◉ No

Section 27.2 Data Collection, Tools, and Resources

27.2a) Will any specially obtained software be used?

○ Yes ◉ No

27.2b) Will any mobile devices (laptop, tablet, portable hard-drive, etc.) be used in support of this study?

○ Yes ◉ No

27.2c) Does the study require use of an electronic data capture system?

○ Yes ◉ No

27.2d) Will any other web-based applications be used (e.g., for recruitment, completing online questionnaires, or processing data)?

○ Yes ◉ No

27.2e) Will coded data that excludes personal identifiers be used? Coded data excludes *all* HIPAA identifiers (per VHA Handbook 1605.1 Appendix B), including dates

◉ Yes ○ No

27.2e1) Identify where the code key is stored and in what format (electronic, paper).

Code key is stored in a locked file cabinet in Rm, 215, Bldg 13, VASDMC. It will also be stred electronically at R01SDCHSM02.R01.MED.VA.GOV\Groessl\Yoga and CAM Research\PTSD - Yoga\Yoga and MR for pain in PTSD.

Section 27.3 Data Sharing and Transportation

27.3a) Does this study involve collecting, sharing or transporting any type of data outside of the local VA?

(●) Yes ( ) No

27.3b) This study collects VASI outside of VA (i.e., at a non-VA location).

( ) Yes (●) No

27.3c) VASI is transported outside of VA for any purpose other than sharing.

( ) Yes (●) No

27.3d) PHI may be disclosed to monitoring/auditing agencies by HIPAA Authorization. ***Note: The Research Office must be notified when monitors come to audit***

(●) Yes ( ) No

27.3e) Data may be shared with collaborators or others in the conduct of this protocol.

(●) Yes ( ) No

27.3e1) Describe the data to be shared or disclosed, the entities to which the data are to be disclosed, how the data are to be transmitted, and how the transmitted data will be stored, retained, destroyed, and/or further disclosed and to whom. This includes data from individual subjects as well as other data developed during the research such as the analytic data and the aggregate data. For PHI and VASI, indicate the authority/ies permitting the sharing or disclosure of data (HIPAA Authorization, Limited Data Set, Data Use Agreement, VA Form 10-5345-Request for and Authorization to Release Health Information., etc.).

As authorized by participants in the consent and HIPAA forms, coded forms will be transported by study staff to the University of California Health Services Research Center (UCSD-HSRC) for processing. UCSD-HSRC is a recharge unit within UCSD that provides research services to outside entities. They are located at 5440 Morehouse DR. San Diego, CA 92121. An approved Authorization to Transport (ATT) form will be used and on file for staff transporting the paper copies. All identifiers will be removed from the form except a subject ID code. Data will include sociodemographic data, coded interview transcripts, and health outcome data, but will not contain age, birth date, or any of the 18 patient identifiers. The key to the coded data is kept on the PI's private folder on the VA research network on the VA server. In addition, the key linking names to ID numbers will be stored in a locked file cabinet within a locked research office in Bldg. 13 of VASDHS. UCSD-HSRC will scan and conduct quality review of data. They will manage, clean and prepare the coded data set for analysis. The data file will be password protected and transported back to VA by study staff or sent by MS Azure if under 40Mb.

Audio recordings of qualitative interviews will be transcribed by a VA service. The service is VA Salt Lake Centralized Transcription Services Program, a program that was created to provide VA researchers nationwide with transcription and qualitative analysis services. Identifiable voice data will not leave the VA secure IT environment. It will be transferred via a secure VA Sharepoint folder. Transcripts with study ID codes will be returned to PI-Groessl via VA Sharepoint. The Centralized Transcription Services Program will not use the data for any other purposes and is only providing transcription as a paid service.

Section 27.4 Research Record Storage and Retention

For each type of record, indicate whether it is collected for this study

27.4a) Hardcopy records/data (includes paper, pictures, film, etc.)

(•) Yes ( ) No

27.4a1) Identify precisely where hardcopy data will be stored to include physical site, building, and room number, etc. For each location identify whether VASI or non-sensitive information is stored at that location. For VASI, identify how the data is secured.

Hardcopy data is stored in a locked file cabinet in Rm, 222, Bldg 13, VASDMC. It is locked and only PI or study Coordinator has the key.

27.4a2) Are all of the above locations at VA?

(•) Yes ( ) No

27.4b) Electronic study records (includes computer files, removable disk files, digital files, etc.).

(•) Yes ( ) No

27.4b1) Identify precisely where ***non-sensitive*** electronic records/data will be stored to include the full map drive, network location/server name, etc., and a brief description of what data/information is stored at each location.

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27.4b2) Identify precisely where ***VASI*** electronic records/data will be stored to include the full map drive, network location/server name, etc., and a brief description of what data/information is stored at each location.

If no VASI is collected or recorded for this study, simply indicate that the "Study does not collect or record VASI".

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27.4b3) Are any of the locations described in 27.4b outside of the VA Secure Network? *Note: this includes storage on a computer local hard drive.*

○ Yes ◉ No

27.4c) Record Retention - VHA requires compliance with Records Control Schedule (RCS-10) for retention of electronic and hard copy records. Following study closure, these temporary records must be retained for six years and then destroyed. Longer retention may be permitted if requred by other Federal regulations or requirements. Will RCS-10 requirements be followed (i.e., 6-year retention)?

◉ I will adhere to VHA Records Control Schedule-10 requirements
○ I request an exception to RCS-10 requirements

Section 27.5 Additional Privacy or Information Security Details

Provide any other privacy or information security details here.

Section 27.6 Attestations

In the event of real or suspected breach of security, the Information Security Officer, Privacy Officer, VA Police (if appropriate), and the individual's supervisor will be notified within one hour of learning of the event.

◉ Agree ○ Disagree

Study staff will be up to date on any required VHA Privacy Policy and Information Security training or they will not be allowed access to VA Sensitive Information.

◉ Agree ○ Disagree

Access to research sensitive information, if any, will be removed when study personnel are no longer part of the research team.

◉ Agree ○ Disagree

At least one copy of all study records (whether sensitive or non-sensitive) will be retained under VA control and only destroyed in compliance with the approved Records Control Schedule

◉ Agree ○ Disagree

The VA retains ownership of the research data. Should the investigator leave the VA, custody of the research records will be assigned to another investigator and the Research Service notified in writing, or custody of the research records will be transferred to the Research Service.

◉ Agree ○ Disagree

Section 28 - Protocol Association to New or Existing Project

28) Is this a new R&D Project? Before you go on to complete the *Initial Review Submission Form* (which is used for attachments), please address the association of this Protocol to an R&D Committee Project. This Protocol may represent a new R&D Project, or it may be an additional Protocol under an existing R&D Project (such as when a single grant supports multiple Protocols). Will this Protocol be submitted to the R&D Committee as a new Project?

○ Yes ◉ No

Section 29 - Existing Project Association

29) The associated R&D Project should already exist in the database. Identify the R&D Project(s) that correspond to this protocol.

Project Status	Proposal Number	Project Title	Principal Investigator
No Projects are Linked to this Study			

The Protocol Application is now complete for a Protocol attached to an existing Project.

Next you will go on to the Initial Review Submission Form. This form is used to collect the Application and any other needed attachments for submission to the IRB for review.

Press *Save and Continue*