STUDY PROTOCOL

Yoga for Active Duty Military with CLBP and/or CNP

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Sponsored by: NIH/NCCIH
Grant # 5 R34 AT009073-03
07/01/2016 – 05/31/2020

UCSD IRB# 16-0341X - Approved 03/01/2019

UCSD Human Research Protections Program
New Biomedical Application
RESEARCH PLAN

Instructions for completing the Research Plan are available on the HRPP website.
The headings on this set of instructions correspond to the headings of the Research Plan.
General Instructions: Enter a response for all topic headings.
Enter "Not Applicable" rather than leaving an item blank if the item does not apply to this project.

1. PROJECT TITLE

Yoga for Active Duty Military with CLBP and/or CNP

2. PRINCIPAL INVESTIGATOR

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3. FACILITIES

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Yoga of Oceanside
1830 Oceanside Blvd., Suite E
Oceanside, CA 92054

Naval Medical Center San Diego (NMCSD)
34800 Bob Wilson Dr.
San Diego, CA 92134

4. ESTIMATED DURATION OF THE STUDY

Three years.

5. LAY LANGUAGE SUMMARY OR SYNOPSIS (no more than one paragraph)

Our primary aim is to assess the feasibility of conducting yoga research among active-duty military personnel with Chronic Low Back Pain (CLBP) or Chronic Neck Pain (CNP). In addition, we will evaluate the yoga intervention preferences and refine an existing yoga intervention to address those needs. The study will be conducted in two phases: Phase 1 involves collecting qualitative data on the style of yoga that most appeals to military personnel with CLBP, obtaining military IRB approval, and modifying the existing yoga intervention. Phase 2 includes recruitment and randomization of 60 military personnel with CLBP to active yoga or to restorative yoga. This will be conducted at two sites, one at NMCSD and one at Yoga Oceanside. **(Please note: before we begin Phase 2 we will also need to obtain IRB approval from NMCSD for activities that will take place at that site. Once we obtain IRB approval from NMCSD, we will provide a copy to UCSD's IRB prior to commencing any activities at that site.)** Participants will complete assessments at baseline and end of interventions (12-weeks). Phase 1 will be completed over the first 12 months of the 36-month project. Phase 2 will be completed over the remaining 24 months. Pain interference will serve as the primary outcome with physical function and pain severity serving as important additional outcomes. The study will

prepare us for a R01 funded pragmatic clinical trial of yoga for CLBP and CNP in active-duty military.

6. SPECIFIC AIMS

Phase 1 - includes Aims 1-3 and involves obtaining military IRB approval, using qualitative methods to understand the yoga preferences and attitudes of military personnel with CLBP/CNP, and refining the existing VA yoga intervention to better suit active-duty military personnel.

- Aim 1: Assess and navigate barriers and facilitators for obtaining IRB approval to conduct randomized controlled intervention studies with active-duty military personnel.
- Aim 2: Evaluate the acceptability of and preferences for yoga interventions among active-duty military personnel with CLBP/CNP.
- Aim 3: Modify an existing yoga intervention for the preferences of active-duty military and to address both CLBP and CNP.

Phase 2 –we will accomplish Aims 4-6 by conducting a pilot randomized control trial (RCT) of yoga and a health education self-care control intervention.

- Aim 4: Evaluate the feasibility of recruitment of active-duty military personnel with CLBP/CNP.
- Aim 5: Evaluate adherence to the yoga interventions.
- Aim 6: Obtain effect size estimates to inform power analyses for a full-scale RCT.

7. BACKGROUND AND SIGNIFICANCE

Chronic low back pain (CLBP) and chronic neck pain (CNP) are highly prevalent conditions that become chronic in 20-30% of those afflicted.[1] In addition to pain, CLBP and CNP are associated with decreased functional ability,[2] work absence,[3,4] increased psychological symptoms, (depression,[5,6] anxiety[7,8]) and higher health care costs.[9] Military personnel[10,11] and veterans[12] have higher rates of CLBP/CNP than the general US population, and CLBP/CNP are two of the most common reasons for disability among deployed personnel[11] and the military in general.[13] CLBP/CNP in military personnel are often exacerbated by co-morbidities[14,15] that pose additional challenges and can interfere with treatment. Recommended treatment for CLBP/CNP begins with medication management and self-care instruction,[16] but the limited effectiveness of these approaches and risks associated with pain medication creates a need for non-pharmacologic approaches.[17,18] Of the non-pharmacological approaches, none have large effects for CLBP/CNP. Because yoga can benefit health much more broadly and has few side effects, it is an increasingly valued care option among military personnel.[19,20]

Yoga interventions involve the integration of physical postures and movement, deep breathing, and focused attention. Thus, yoga interventions are multifaceted, with documented physical and psychological benefits including a) increased strength, flexibility, and conditioning through the performance of physical postures, and b) stress reduction/ relaxation and improved psychological functioning facilitated by deep breathing exercises, concentration/ attention, and cognitive strategies.

Although the evidence for yoga as a treatment for CLBP was rated as "fair" in 2007 clinical guidelines,[18] two more recent large RCTs provide strong evidence that yoga reduces pain and disability among persons with CLBP.[21-23] However, none of these studies were conducted in military populations. PI-Groessl has conducted preliminary studies showing that VA patients with CLBP/CNP will attend yoga sessions and that yoga improved their pain, physical function, and other outcomes.[24,25] He is currently finishing a full-scale RCT of yoga for CLBP/CNP in the VA system and collaborates on a similar NCCIH project with Dr. Rob Saper. However, military personnel with CLBP/CNP[10] are on average, much different than VA patients with CLBP/CNP[26]. They are considerably younger and more active, have different co-morbidities and career objectives, and require different treatment strategies. Creating interventions that can treat more than a single condition is also needed. Health organizations cannot easily offer a long menu of yoga interventions, each designed for a specific health condition. Our pragmatic clinical trial approach will address this barrier by designing an intervention to address two common and similar spinal conditions and compare two different styles of yoga in one study.

8. PROGRESS REPORT

N/A

9. RESEARCH DESIGN AND METHODS

Overall

This is a pilot study with an objective to examine the feasibility and acceptability of conducting a yoga RCT among active-duty military personnel with CLBP/CNP in military and community settings. The subject population will consist of 80 adults, 70-75 active-duty military personnel with chronic low back pain (CLBP) or chronic neck pain (CNP) and 5-10 yoga instructors or healthcare providers who have provided yoga or care for active-duty military personnel with CLBP or CNP. The study will be conducted in two phases: Phase 1 will involve obtaining IRB approval to conduct research in military settings, collecting qualitative data from stakeholders on attitudes and preferences for yoga interventions, and refining the existing Yoga for CLBP intervention for the needs of active-duty military and persons with CNP. Phase 2 will recruit and randomize 50 military personnel with CLBP or CNP to either active hatha or restorative yoga. Pain interference, pain severity, physical function, opioid medication use, and mental health outcomes are of primary interest. Mechanisms will also be studied.

Phase 1

Phase 1 includes Aims 1-3 and involves obtaining military IRB approval, using qualitative methods to understand the yoga preferences and attitudes of military personnel with CLBP/CNP, and refining the existing VA yoga intervention to better suit active-duty military personnel.

Aim 1: Assess and navigate barriers and facilitators for obtaining IRB approval to conduct randomized controlled intervention studies with active-duty military personnel. To achieve Aim 1, we will partner with Dr. Ian Fowler and Dr. Jeffrey Millegan from the NMCSD as described above. Both Dr. Fowler and Millegan are researchers /clinicians with experience obtaining IRB approval at NMCSD. Dr. Fowler has a research nurse with experience assembling the required IRB documents. They will work closely with Dr. Groessl and the UCSD Project Coordinator to meet NMCSD military IRB requirements, starting as soon as the study has been funded. We expect the military IRB approval process to take approximately 6 months to complete. Yoga is not viewed as high risk or experimental given that it has been well studied elsewhere and few adverse events have been documented[21]. However, to be conservative, we have allotted up to 12 months for military IRB approval and Phase I activities can fully proceed under UCSD IRB approval.

Aim 2: Evaluate the acceptability of and preferences for yoga interventions among active-duty military personnel with CLBP/CNP. 30 total Qualitative Interviews will be conducted with military personnel with CLBP or CNP and with healthcare providers who provide yoga or other healthcare to military personnel with CLBP or CNP.

Qualitative Interview Methods:

The proposed qualitative component of the study is both exploratory and inductive in nature. Semi-structured qualitative interviews will be employed to explore the participant preferences and experiences with yoga in relation to their CLBP/CNP. This information will contribute to the refinement of an existing yoga intervention for veterans with CLBP so that it is optimal for active-duty military personnel. Interview techniques will use open-ended questions to stimulate a wider range of responses for a more complete understanding of the needs and attitudes encountered by study participants. Interviews are expected to last about 60 minutes in length. Open-ended questions during the interviews will address: 1) past experiences with non-pharmacological treatments for CLBP/CNP; 2) past experiences with yoga; 3) a brief presentation of the existing yoga program; 4) preferences in regard to the emphasis given to the various components the yoga intervention such as postures, pace of transition through poses, breathing techniques, meditation, ethical principles and spiritual aspects; 5) dosing of yoga; and 6) discussion of research participation and burden given military schedules. Interviews with yoga providers and other health care providers will follow the same set of questions but will ask for both their own preferences as a clinician and their perspective on how their patients

might typically respond. Of the 30 interviews, we will interview 8-10 participants with CLBP/CNP who have never done yoga. Those interviews will employ slightly different questions that are designed to elicit attitudes, beliefs, and perceptions about yoga as a treatment modality for CLBP/CNP in military personnel, and barriers to participation. Instead of a question about their past experiences with yoga, they will be asked to provide their perceptions of yoga as a treatment modality and any barriers or facilitators that may affect their future participation. All qualitative interviews will be digitally audio-recorded and digital tapes will be encrypted before being confidentially submitted to a transcription consultant to transcribe the audio recordings verbatim for the purpose of coding and analysis. All names and locations mentioned during the course of the interviews will also be removed from the final transcripts prior to analysis.

Qualitative Data Analysis:
A salient strength of qualitative analysis is its focus on the context and meaning of human experience for the purpose of inductive and exploratory-driven research. Qualitative methods facilitate the collection of data when exact measures do not exist. Transcribed summaries from the interviews will be analyzed using directed content analysis (DCA) to identify and categorize meaningful and detailed information about participant's opinions, perceptions and experiences participating in the mindfulness meditation intervention. Coding strategies will include highlighting passages for emergent themes and also a priori categories reflecting questions from the interviews. Through this process and the comparison of new data, a template of open codes will be constructed to analyze all of the transcripts in accordance with standard qualitative analytic convention. Verification of emergent themes from interviews will be examined through investigator discussions of the coding framework. Disagreements during theme interpretation or coding hierarchy will be resolved early on through investigator discussions before completing the qualitative analysis.

Aim 3: Modify an existing yoga intervention for the preferences of active-duty military and to address both CLBP and CNP. Based on the results of the qualitative interviews, the existing yoga intervention designed for VA patients with CLBP will be refined and adjusted to better fit the preferences of active-duty military personnel with CLBP or CNP. This process will start with the investigators and yoga experts reviewing Dr. Hurst's report of the qualitative results. The team will also independently review a current Yoga for CLBP manual being used by Dr. Groessl, the Cramer et al. manuscript which lists the 14 yoga poses they selected for treating CNP, and other yoga texts. Investigators and experts will then convene at UCSD for an extended afternoon meeting to select of a pool of possible poses. The PI will then work with orthopedic surgeon Dr. Chang and yoga expert Dr. Schmalzl to propose specific changes to the intervention. The revisions will be presented to the other collaborators for review and additional discussion. Possible examples include a slightly faster pace, adding postures for additional challenge for those with less impairment (yet easily modified to be safe for all), additional attention tasks or imagery, and further trauma sensitivity. All changes and the rationale behind them will be documented.

Phase 2

Please note: before we begin Phase 2 we will also need to obtain IRB approval from NMCSD for activities that will take place at that site. Once we obtain IRB approval from NMCSD, we will provide a copy to UCSD's IRB prior to commencing any activities at that site. In Phase 2 we will accomplish Aims 4-6 by conducting a pilot RCT with 2 yoga interventions. We will recruit 25 people at each of two sites, one in a military medical facility (NMCSD) and one in a community yoga studio (Yoga Oceanside) near a large military base for a total of 50 participants. Once 25 people have been recruited at each site, they will be randomized to attend either active hatha yoga or restorative yoga.

Screening and Inclusion/Exclusion Criteria.
50 active-duty military personnel with CLBP will be recruited and randomized to either active hatha yoga or to restorative yoga. Inclusion criteria are as follows:

Inclusion:

- Diagnosis of CLBP or CNP > 6 months
- Willing to attend a yoga program for 12 weeks
- Willing to complete 3 assessments
- English literacy
- Have had no changes in pain treatments in the past month

- Willing to not change pain treatments during study unless medically necessary
- Have not practiced yoga more than 2x in the last 12 months

Exclusion:

- Back or neck surgery within the last year
- Back or neck pain due to specific systemic problem (e.g., lupus, scoliosis)
- Severe vertebral disk problems,
- Persistent sciatica or nerve compression > 3 months
- Coexisting chronic pain problem (e.g., migraine headaches, fibromyalgia)
- Serious or unstable psychiatric illness (e.g., psychosis, mania, episode, or substance dependence)
- Major coexisting medical illness (e.g., cancer, COPD, morbid obesity)
- Positive Romberg test (with or without sensory neuropathy)

No other exclusion criteria will be employed. No special classes of subjects or other vulnerable populations will be recruited. We will make efforts to recruit at least representative proportions of women and racial and ethnic minorities. More detail is provided on the inclusion of women and minorities document in this application.

Table 4. Inclusion / Exclusion Criteria with Method used to Determine Eligibility for Study Participation

Inclusion Criteria	**Determined by:**	**Exclusion Criteria**	**Determined by:**
Active-duty military employment and age ≥ 18	screening interview; medical record	back or neck surgery within the last 1 year	screening interview; medical record
Diagnosis of chronic low back or neck pain > 6 months	screening interview; medical record	back or neck pain due to specific systemic problem (e.g., lupus)	screening interview; medical record
Willing to attend 12-weeks of yoga	screening interview; informed consent	severe vertebral disk problems	screening interview; medical record
Willing to complete 2 assessments	screening interview; informed consent	persistent sciatica or nerve compression > 3 months	screening interview; medical record
English Literacy	screening interview; informed consent	coexisting chronic pain problem (migraine headaches, fibromyalgia)	screening interview; medical record
No changes in pain treatments in the past month.	medical record; screening interview	Serious or unstable psychiatric illness (e.g. psychosis, mania)	screening interview; medical record
Willing to not change pain treatments during study unless medically necessary.	screening interview; informed consent	major coexisting medical illness (e.g., cancer, COPD, morbid obesity)	screening interview; medical record
Have not practiced yoga > 2x in the last 12 months	screening interview; informed consent	Positive Romberg test (with or without sensory neuropathy)	screening interview; medical record

Recruitment staff will meet with participants to obtain informed consent and HIPAA authorization before a screening visit. Potential participants will undergo a physician screening exam to ensure they meet the study inclusion/exclusion criteria and can participate safely. Screening will be performed by Dr. Fowler at NMCSD or by Dr. Chang at UCSD for the community site and includes a review of the patients' medical record, a brief interview, and a physical examination. Inclusion/ exclusion criteria and the sources of information used to determine them are listed in Table 4. Patients who have recently changed any professionally-delivered pain treatment (e.g., medications, chiropractic) are not eligible until their treatment has been stable for 30 days. Participants are asked to keep all pain treatments stable during the 12-week intervention period unless a change is medically necessary and their agreement and study participation are documented in their medical record. Staff will assess all treatments including non-prescription medication use and any treatment changes that do occur through self-report assessment at 4-weeks, 8-weeks, and the end of the 12 week study period. Participants are asked take their lowest usual dose of pain medications within 24 hours of each assessment. Although we will exclude those with serious or unstable psychiatric illness, we expect to enroll many patients with stable levels of depression, anxiety (including PTSD), substance use, etc. as these conditions are prevalent and contribute to disability among CLBP/CNP patients. Research suggests that yoga has beneficial effects on psychiatric symptoms. We will exclude patients who report active suicidal ideation at baseline or have recent suicide attempts.

Assessments and Randomization:

All eligible participants will be scheduled for assessments at two time points: pre (baseline) and post intervention (12-weeks). The assessments consist of a battery of 8-10 questionnaires taking about 20-30 minutes to complete. Next, physiological measurements will be conducted by a trained research assistant and will take about 10 minutes to complete. Participants will receive $30 for completing each assessments. Completed questionnaires will be coded with a study ID to protect confidentiality. All personal health information will be entered into a password protected secure server environment within UCSD-HSRC. After the baseline assessment, participants will be randomized to either the Hatha Yoga Intervention or to the Restorative Yoga Intervention. Randomization will occur through a web portal linked to a secure file providing block randomized digits that was prepared by the study statistician. There will be one block file for each site, with 30 digits in each file, allowing each site to have a balanced randomization. Research staff will not have access to the randomization file. Participants will be told of their group assignment and will be allowed to ask additional questions at that time.

Assessment Questionnaires and Measurements:

Screening: Medical record information will be used by screening physicians to complete the Back Pain History Questionnaire which will allow the investigators to assign a descriptive diagnosis based on the Quebec Nomenclature on Activity Related Spinal Disorders[104]. The measure has been used in previous VA studies[105-107]. Additional information on co-morbid diagnoses, opioid pain medication usage, and ongoing treatments will also be collected including information on TBI, PTSD and other psychological diagnoses, and substance use.

Demographics: A brief questionnaire will assess age, gender, education, race/ethnicity, employment status, military rank and duties, and combat status.

Pain interference with daily function and pain severity will be measured with the short version of the Brief Pain Inventory (BPI).[108] Pain interference will serve as the primary outcome. The BPI has been validated with CLBP.[109] The pain interference score is the mean of the 7 interference items. The pain severity score is the mean of 4 severity items. The BPI has good reliability (alpha 0.77 - 0.91).

Disability/Physical Function. The Roland-Morris Disability Questionnaire consists of 23 questions that ask about limitations experienced for a variety of daily activities. The scale has been shown to be reliable and is well validated[110]. It has been used in other studies of yoga studies[102]. The Neck Disability Index will be used to assess disability related specifically to neck pain. It is a well validate measure.[111]

Depression. Derived from the full Center for Epidemiologic Studies Short Depression Scale[112] (CES-D), the CES-D 10[113] consists of 10 items on the frequency of mood symptoms. Scores $\geq$ 10 indicate depression.

Anxiety. The Brief Anxiety Inventory (BAI) measures the severity of anxiety symptoms and consists of 21 items. The BAI was developed with psychiatric outpatients[114] and has good reliability and validity.[115]

HRQOL. The Short-form 12 (SF12) was derived the SF-36.[116] The PCS-12 and MCS-12 have been shown to be similar to the SF36 levels of precision and sensitivity to change.

Self-efficacy. Self-efficacy for managing pain reflects confidence in the ability to influence the intensity or impact of CLBP/CNP on daily life. The questions are based on items developed by Lorig et al.[117].

Fatigue. The Fatigue Severity Scale (FSS) assesses the impact and severity of fatigue with 9 items. A score of $\geq$ 4.0 constitutes severe fatigue.[118] The measure has good psychometrics for pain disorders.[118,119]

Attendance/ Home practice. Attendance of yoga sessions will be assessed using sign-in logs verified by the yoga instructor. Self-reported practice of yoga at home will be assessed using a weekly participant yoga log. The yoga log assesses the amount of time practiced, the use of instructions, the difficulty of poses, and the estimated level of exertion.

Acceptability and Satisfaction Questions. We will assess program acceptability and satisfaction using 10 questions developed and used by the investigators in previous and current yoga studies. The questions will gauge factors affecting attendance and participation levels.

Patient Expectations will be measured at baseline to determine whether the descriptions of the yoga interventions could result in different expectations for improvement. Dr. Karen Sherman will use the new patient expectation measure developed by her and her colleagues.[120]

Physical Measures. The integrity of physiological measure will be maintained by having multiple research staff trained by local UCSD experts in the use of the inclinometer, dynamometer, heart monitors, and core strength tests. Following initial training, research staff will conduct a series of 6 mock measurements to ensure reliability of measurement. Any problems will be tracked and addressed with re-training.

Spinal Range of Motion (ROM) will be measured using a digital inclinometer, which isolates lumbar

ROM (flexion and extension). The device uses a precise optical angular scanner placed along the spine. Device error is negligible with accuracy as high as 98%[121] The device has been used in other yoga interventions.[103]

Grip Strength will be measured using two trials for each hand with a hydraulic dynamometer. The best performance is selected for each side, and the average of the left and right hand is used for analysis. Painful or injured hands or wrists are not tested and the result of the good hand is used. Reliability has been shown to be high: r=0.88-0.92. Good predictive validity of grip strength has been shown for disability and mortality.[122]

Core Stabilization and Strength. Prone and supine bridge positions will assess core stabilization.[123] Participants begin on their elbows in the prone position with shoulders, hips, and ankles aligned. The supine position is tested next, with knees flexed 90 degrees and pelvis raised from the floor with shoulders, hips, and knees aligned. Assessors record length of time (120 seconds max) that each position is held in proper form.

Heart rate. Physical exertion during yoga will be measured using Polar FT4 Heart Rate Monitors. Worn on the chest, they provide aggregate summary data such as maximum and mean heart rate during a workout.

Interventions:

There will be two interventions: Hatha Yoga and Restorative Yoga. Both interventions will meet 2 times a week for 12 weeks with at least one day of rest between each class. Individual classes will be 60 minutes long and led by a certified yoga instructor. Additionally, participants will be encouraged to practice yoga at home as guided in a home practice manual.

Hatha Yoga (HY)

Using information gathered during qualitative interviews in Phase I, the yoga intervention will be tailored to our target population. However, we do not anticipate significant changes to the existing yoga protocol for CLBP that was developed for Dr. Groessl's current study, Yoga for CLBP being conducted with veterans. Our team of experienced yoga instructors will also adapt the existing CLBP yoga intervention to be safe and effective for CNP. Our team consists of co-investigator Dr. Laura Schmalzl (researcher and experienced yoga instructor), Camilla Sinclair (current instructor of Yoga for CLBP at VASD), Danielle Fowler (owner of Yoga Oceanside), and Betty Michalewicz (military yoga instructor at NMCSD Wellness Program). We will also consult *Anatomy of Hatha Yoga*[79] and *Yoga as Medicine* which has a useful section on avoiding neck injuries.[93] Poses known to put pressure on joints, muscles, or nerves in the neck such as head stands, shoulder stands including plow and other variations will not be used.

The HY intervention will be led by a certified instructor at each site. Both instructors will be trained by Camilla Sinclair who has been practicing yoga for over 16 years and has over 8 years of teaching experience and is the main instructor for Dr. Groessl's Yoga for Vets with CLBP. (NOTE: We will model the HY intervention after the current Yoga for CLBP intervention which is a classical hatha yoga with influences from Viniyoga and Iyengar yoga. Both Viniyoga and Iyengar yoga styles emphasize modifications and adaptations including the use of props such as straps and blocks in order to minimize the risk of injury and make the poses accessible to people with health problems and limitations.) The certified yoga instructors will lead participants through a series of 23 yoga poses (32 total variations) at a slow-moderate pace. Instructors will be asked to follow the manual which will help standardize the yoga intervention. The manual contains pictures and a description of how to perform each pose with typical instructor dialogue. The dialogue may be paraphrased and varied slightly, yet promotes more consistent replication and generalization of results. The manual includes some poses that could aggravate back conditions if they are not modified for some people. That is why multiple modifications are shown and many of the poses shown are only worked up to after weeks of practice and individual attention from the instructor. The more challenging poses are not included in the home practice manuals. The importance of attending all sessions will be stressed during session 1 and throughout all sessions. Participants who miss a session without notifying the instructor will be contacted to check on the reason for non-attendance. Participants will also receive a home practice manual containing some basic, safe postures that can be performed in 10-15 minutes on days they will not be attending the formal in-person sessions. Participants will be encouraged to not push themselves as much when practicing at home and to stop when pain or discomfort becomes noticeable. They will be encouraged to consult with the instructor individually before and after

class about any problems or difficulties they are encountering at home or in the formal sessions.

During the formal sessions, participants will be instructed to take slow, deep breaths in conjunction with specific phases of poses. Participants will be encouraged to emulate the optimal alignment being demonstrated by the instructor. In addition, participants will be encouraged to focus on a goal or positive direction for their yoga practice. The yoga classes are constructed to allow optimal flow from one pose to another. Each 60-minute session will begin with a few minutes of deep breathing and mindfulness/meditation followed by about 15 minutes of basic postures (Poses 1-8) to warm-up the muscles/body by increasing circulation, providing more flexibility as the class progresses. Most poses will be conducted once to each side or with the opposite foot leading. After warming-up, the instructor will lead students through a series of standing poses (Poses 9-14) which include balance for about 15 minutes. After the standing poses, the class will move into floor poses (Poses 15-22) for about 20 minutes. Each session will end with about 5-7 minutes of complete relaxation in the standard ending pose "savasana". At this time, additional positive mental suggestions/affirmations will be provided.

Restorative Yoga (RY)

RY will serve as the comparison intervention but is also of interest in itself as a possible treatment modality. For the purposes of this pilot study (R34 proposal), we are using the term "Restorative Yoga" to refer to yoga interventions that emphasize relaxation and include very little movement, and are non-strenuous. RY sessions typically include only 5-10 poses, mostly done lying down, eyes are often closed, with bolsters and/or blankets used for comfort and warmth, Because eyes are often closed, and movement is limited, the instructor typically provides more instructions on deep breathing techniques and guided imagery.

The details of the RY intervention will be developed using the expertise of our team of experienced yoga instructors and the feedback from the Phase 1 Qualitative Interviews. Our yoga experts have training and experience delivering RY sessions. The team will read and discuss *The iRest Program for Healing PTSD*,[101] a recent book that outlines the iRest approach to treating PTSD. The team will also review and discuss a RY practice manual developed for metabolic syndrome by our colleagues at UCSD and UCSF. The 42-page manual explains 5 different poses with an additional 8 modifications to those poses, and provides pictures and helpful tips. Based on these materials, our yoga experts will develop our RY intervention and create an intervention manual and a home practice manual. The intervention will occur 2x weekly for 12 weeks – each class will be 60 minutes to match that timeframe of the active yoga intervention.

Treatment Fidelity.

Instructor fidelity to the yoga intervention manual will be evaluated using video recordings of yoga intervention sessions. All yoga sessions will be recorded with a digital camcorder and tripod placed in the back of the yoga room. Instructors and participants will be aware of and consent to the recordings. We do not plan to analyze all recorded sessions, but recording all sessions will standardize the presence of the camera across all sessions and result in more rapid habituation. Of the 24 sessions videotaped at each site, we will randomly select a session from weeks 1-4, weeks 5-8, and weeks 9-12 for review by a yoga instructor from Yoga Oceanside. They will review the sessions using a manual checklist for instructor adherence to the yoga manuals, which will consist of a Yes/No, blank, and 0-10 rating scale for each procedure or instruction.

Data management. Questionnaires will be formatted by the project coordinator under the supervision of Dr. Groessl (PI). Formatting will be designed to reduce recording errors and facilitate computer scanning and verification. Forms will be de-identified to protect confidentiality, and data will be scanned and verified by the data manager (and project coordinator). 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. Data will be stored on a password protected secure network server at UCSD. Access privileges are limited to essential staff.

Statistical Management and Analysis: Qualitative data will be managed and analyzed by Co-I Hurst. Results will be presented to the research team and additional sub-analyses will be conducted as needed before the intervention is modified. Health outcome data and mediational variables will be collected directly before and after the 12-week yoga program using physiological assessments and questionnaires. We will assess the effect size of the difference in change in health outcomes (pain interference, pain severity, and physical functioning) from pre- to post-intervention between

intervention groups using a linear random effects model. We will assess clustering by site with a likelihood ratio test. The point estimate of difference in change score between two groups and the 95% confidence interval for the estimated difference will be provided. We will also perform multivariate analysis and an adjusted effects size (with 95% CI) by including baseline characteristics that are significantly imbalanced between two groups as covariates in the random effects model. Analyses will be conducted by the biostatistician (Dr. Liu). The effect size estimates (and CI width) will help inform power calculations for the subsequent R01 submission. R software packages will be used for all statistical analyses.

10. HUMAN SUBJECTS

The subject population will consist of 80 adults, 70-75 active-duty military personnel with chronic low back pain (CLBP) or chronic neck pain (CNP) and 5-10 yoga instructors or healthcare providers who have provided yoga or care for active-duty military personnel with CLBP or CNP.

In Phase 1:
30 qualitative interviews will be conducted. 20-25 active-duty military personnel and 5-10 yoga instructors or healthcare providers who have provided yoga or care for active-duty military personnel with CLBP or CNP will participate in the interviews. Inclusion criteria for the qualitative interviews includes being active-duty personnel in the U.S. military, and having a self-reported history of CLBP or CNP. Inclusion criteria for instructors/providers includes having self-reported experience teaching yoga or providing other pain treatments for active-duty military personnel with CLBP or CNP.

In Phase 2: 50 active-duty military personnel with CLBP will be recruited and randomized to either active hatha yoga or to restorative yoga. Inclusion criteria are as follows:

Inclusion:

- Diagnosis of CLBP or CNP > 6 months
- Willing to attend a yoga program for 12 weeks
- Willing to complete 3 assessments
- English literacy
- Have had no changes in pain treatments in the past month
- Willing to not change pain treatments during study unless medically necessary
- Have not practiced yoga more than 2x in the last 12 months

Exclusion:

- Back or neck surgery within the last year
- Back or neck pain due to specific systemic problem (e.g., lupus, scoliosis)
- Severe vertebral disk problems,
- Persistent sciatica or nerve compression > 3 months
- Coexisting chronic pain problem (e.g., migraine headaches, fibromyalgia)
- Serious or unstable psychiatric illness (e.g., psychosis, mania, episode, or substance dependence)
- Major coexisting medical illness (e.g., cancer, COPD, morbid obesity)
- Positive Romberg test (with or without sensory neuropathy)

No other exclusion criteria will be employed. No special classes of subjects or other vulnerable populations will be recruited. We will make efforts to recruit at least representative proportions of women and racial and ethnic minorities. More detail is provided on the inclusion of women and minorities document in this application.

11. RECRUITMENT AND PROCEDURES PREPARATORY TO RESEARCH

Phase 1: Qualitative Interviews
We will recruit a total of 30 stakeholders to participate in qualitative interviews. Of the 30 participants, 20-25 will be military personnel with CLBP and/or CNP and 5-10 will be clinicians who provide yoga or other clinical care to military

personnel with CLBP or CNP. Of the 20-25 participants with CLBP/CNP, we will enroll at least 8-10 participants who have not done yoga before to explore reasons or perceived barriers to yoga participation. Recruitment will primarily occur through the posting of flyers and word of mouth with our military and community partners. A full Military IRB approval is not required to post flyers at the military facility or to conduct qualitative interviews at community locations off-base. Once we obtain permissions from the appropriate Public Affairs Office for the base, we will post flyers on military bases. For the 5-10 instructors/healthcare providers, we will recruit using connections with our military/community partners, and if needed, our contacts with additional healthcare providers in the San Diego area including UCSD and VA San Diego. Participants will receive a $30 gift card for participating in a qualitative interview.

Phase 2: Yoga Classes

(Please note: before we begin Phase 2 we will also need to obtain IRB approval from NMCSD for activities that will take place at that site. Once we obtain IRB approval from NMCSD, we will provide a copy to UCSD's IRB prior to commencing any activities at that site.)

Recruitment for Phase 2 will occur primarily through our military and community partners. However, we will use qualitative interview data to steer and refine our recruitment methods. The NMCSD is our military research partner and they provide care to over 100,000 active-duty military personnel each year. With an estimated 25% of the general population having chronic low back pain at any one time, and higher rates among military personnel, the pool of potential participants can safely be placed at over 20,000. Some will not meet study criteria for various reasons, but a large number will be eligible. Once military IRB approval is obtained, Dr. Fowler and staff can post the study flyer and information on a research opportunities website, request inclusion in widely distributed e-mails, notify primary care physicians, pain management staff, and other healthcare providers, and they can post flyers on medical center posting boards. Recruitment will also occur at Yoga Oceanside and through the Connected Warriors organization. Flyers will be posted within their facilities and announcements will be at the end of classes. They will both use social media (e.g. Facebook) to communicate these research opportunities to their communities (CW has 1600+ followers, and Yoga Oceanside has 500+). If needed, the study will also advertise the study in local military newspapers including three online publications from Echo Media (Miramar Flight Jacket, Navy Compass, Camp Pendleton Scout) which have a weekly readership of 88,000 and/or the Military Press publication (bi-weekly readership of over 100,000 active-duty military).

12. INFORMED CONSENT

Prior to participation in this project, participants will be thoroughly apprised of study considerations and will undergo an informed consent process. We will emphasize the key elements of the informed consent procedure: 1) the research status of the study; 2) the prospect of physical or psychological risk and the provisions for it; 3) the lack of guarantee of benefit from participation; 4) the confidentiality of the participant's responses; 5) the voluntary nature of the study; and 6) the freedom to withdraw from the study or to refuse to answer specific questions at any time. Only individuals who consent to all study conditions will be enrolled. The participant will complete the informed consent process with the RA and will be given a copy of the signed document for his or her records.

Trained research staff, who are experienced in recruitment for clinical trials and medical research, will facilitate the consenting for the qualitative interviews in Phase 1 and before the screening appointments in Phase 2. Prior to beginning the study, the PI will ensure compliance with IRB requirements and protections by obtaining approval from University of California San Diego and the Naval Medical Center San Diego (for procedures done at that facility) and will insure all protections are followed.

13. ALTERNATIVES TO STUDY PARTICIPATION

The alternative to participation is not to participate.

14. POTENTIAL RISKS

In the focus groups of Phase 1, research staff will explore the thoughts, experiences, and opinions of participants with respect to CLBP and yoga as a treatment for CLBP. They will also discuss perceptions of different aspects of a yoga intervention regarding their desirability, acceptability, and efficacy, none of which are anticipated to produce negative emotional reactions. However, participants will be given contact information for sources of help that they can contact if they are feeling distressed or desire help.

Phase 2 will involve participants attending two different yoga programs. Minor physical risks are always possible in yoga classes, although the frequency of injury has been low for CLBP and CNP patients in major studies. A small possibility also exists for injury during the physiological assessments, where someone may be asked to stand on one foot, hold a plank position, bend forward, or squeeze a dynamometer. In the event that someone is injured, the usual procedure followed at that particular facility will be followed. For example, active-duty military doing yoga at NMCSD will receive care at NMCSD. Participants doing yoga through Yoga Oceanside and the Connected Warriors program can get free care through UCSD. These organizations require instructors to be fully insured through the Yoga Alliance.

Summary of safety information. Like other exercise activity, the risks of injury from improperly performing yoga postures vary depending on how, where, and with whom the yoga is practiced. The initial practice of yoga under the direction of experienced yoga instructors, following a program that has modifications for people with limitations, and consulting a physician before starting a yoga program are all recommendations24 that will be followed in the proposed study. Data from RCTs of yoga for adults with CLBP reveal that the 3 serious adverse events among 309 persons doing yoga in these studies were all related to herniated discs, and at least one of these was found to be unrelated to yoga practice.22,23,102,103 Disc problems are common in this population in the absence of yoga practice, and thus yoga does not appear to greatly increase that risk. Among the 63 people with CNP who did yoga in two RCTs, no serious adverse events occurred. So despite popular media reports of the dangers of yoga, no specific data or evidence of risk has been presented. The poses specifically cited as being dangerous, usually head and shoulder stands and their variations probably do present some risk for novices, and are not being used in the proposed study. By screening out patients at greater risk, placing emphasis on slowly building a safe yoga practice, and hands on instruction from experienced instructors will be used to ensure that the yoga is practiced in the safest possible manner throughout the study.

In both Phase 1 and Phase 2, there is a risk of loss of confidentiality. No physical, legal, or social risks are anticipated as a result of participating in other phases or aspects of this study. The assessment questionnaires ask participants to consider and/or report health symptoms and functioning, and medication use which are not anticipated to cause negative emotional reactions. However, participants in each phase of the study will be given contact information for sources of help that they can contact if they are feeling distressed or desire help.

15. RISK MANAGEMENT PROCEDURES AND ADEQUACY OF RESOURCES

All participants will be provided the Principal Investigator's and Project Coordinator's phone numbers, whom they can contact if they have questions or need assistance. All participants are made aware that they can discontinue participation at any time. The PI and program staff will assist the participant in obtaining a referral to a mental health professional if requested or indicated. Risks to subject confidentiality will be addressed by identification of subject information only through code numbers: Data stored in the computer will only be identified with a code number. A separate file with corresponding identifying information and contact information will be kept in a separate computer file that will be password protected. Only the appropriate research staff will have access to specific subject information.

Adverse events: The investigators will track adverse events and report these on a daily basis to the Principal Investigator. Serious adverse events will be immediately reported by phone and in writing to the IMC and to the Institutional Review Board of the University of California San Diego, or relevant military IRB. Serious adverse events include death, substantial risk of dying, hospitalizations, disability, or emergency medical intervention attributable to participation in the study (http://www.fda.gov/medWatch/report/DESK/advevnt.htm). We will conduct weekly research team meetings. Once a month at these research team meetings, all adverse events occurring over the previous month and over the course of the study will be reviewed. Serious adverse events will be reviewed immediately and reviewed again at the monthly meeting. All reported adverse events will be reported to the IRBs at that site as well as the University of California San Diego IRB, which will be the primary IRB of the study.

Additional precautions: Any adverse events or protocol deviations by the PI or research assistant will be reported within 72 hours of its coming to the PI's attention. We will take regular precautions to protect human research participants during the course of the study. The investigators will be in regular contact on a daily or weekly basis by e-mail or phone so urgent problems will be addressed in a timely manner. The PI or other key personnel will inform the PI or research team about any vacation or absences so that coverage of study duties can be arranged.

If this study is funded and carried out, we will assemble an Independent Monitoring Committee (IMC) to monitor the progress and safety of the study as it proceeds. The PI will recruit 3 content or scientific experts who are not involved with this grant to serve on the IMC. One person will be a clinical psychologist or psychiatrist who specializes in diagnosing and treating psychological disorders among active-duty military; another will be an orthopedist or orthopedic surgeon; the third will be a statistician. The IMC will review the study protocol prior to activation and develop an IMC plan. The IMC will evaluate the data on an ongoing basis and assure participant safety and study integrity. The IMC will be responsible for monitoring data and for making recommendations based on the data regarding appropriate protocol and any operational changes. The committee will meet every 6 months to review progress, preliminary data, and any adverse events. They will meet with the PI to make recommendations regarding the progress of the study and will be able to report to the Institutional Review Board of the University of California San Diego. Following review, the IMC will write a report outlining recommendations. These recommendations will be forwarded to the Principal Investigator (Dr. Groessl) at the University of California San Diego and the IRB Chair at the University of California San Diego.

16. PRIVACY AND CONFIDENTIALITY CONSIDERATIONS INCLUDING DATA ACCESS AND MANAGEMENT

All signed consent forms, HIPAA forms, and the video and audio recordings for Phases 1 and 2 will be transported directly to Dr. Groessl's office at the UCSD Health Services Research Center at 5440 Morehouse Dr. #3500 San Diego, CA, 92121 where they will be stored in a locked file cabinet within the locked office. All questionnaires and other data recording forms will be pre-labeled with the participants' ID # and stored at the UCSD Health Services Research Center. The key connecting participant identifiers with the ID number is also kept in a locked cabinet and on password protected computers that reside within a firewall and data security system.

For all phases of the project, a secure, password protected encrypted database will be constructed for the names and contact information of participants that contact the Project Coordinator during recruitment. This information will be stored on a secure network server and password protected. Only the Project Coordinator and one trained research staff will have access to this database. Each participant will be assigned a study ID # which will be used for all assessment materials. All assessment information (questionnaires and measurements) will only labeled with the study ID. No names or other identifiers will appear on assessment materials. A separate database will be constructed containing the de-identified data. No identifying information will be linked with respondent answers.

Additionally, for Phases I and II, participants are informed that audio-/video-recordings may be stopped at any time and that portions and/or the entire tape may be erased at the participant's request. Also, notes and audio-recordings will be anonymously transcribed. Following transcription, the audio-recordings will be destroyed.

17. POTENTIAL BENEFITS

The primary purpose of the study is to examine feasibility of yoga research and refinement of a yoga intervention for active-duty military personnel. Thus, no direct benefit to participants is anticipated. Yoga has been shown to improve health outcomes in other populations with CLBP/CNP, and may help some individuals, but our study is not powered to make scientific conclusions regarding efficacy. Results of the study will provide important information that will prepare study investigators to conduct a full-scale randomized controlled trial of yoga for military personnel with CLBP/CNP.

The results of this study will provide essential information for medical and mental health professionals who treat veteran and active-duty US military regarding the dimensions of yoga perceived as most helpful and well-received for different conditions, and will guide future research asking specific questions regarding efficacy and effectiveness of specific interventions.

18. RISK/BENEFIT RATIO

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 in previous studies with similar populations are low, and appear no higher than natural rates of injury in this population.

Yoga has been shown to improve health outcomes in other populations with CLBP/CNP, and may help some individuals.[22-23]
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.

19. EXPENSE TO PARTICIPANT

The only expense to the subjects would be transportation costs to travel to the yoga classes. Time is required for them to complete the questionnaires. Some active duty military personnel may be unable to receive compensation for completing assessments, and would have to donate their time.

20. COMPENSATION FOR PARTICIPATION

Phase 1: Qualitative Interviews – 30 participants will receive a $30 gift card to Trader Joes for participating in a 60 minute interview.

Phase 2: Yoga Interventions – 50 participants will receive 24 free 1-hour yoga classes (12 weeks of 2 classes per week), plus a $30 gift card to Trader Joes for each assessment attended ($30 x 2 assessments = total of $60 in gift cards).

21. PRIVILEGES/CERTIFICATIONS/LICENSES AND RESEARCH TEAM RESPONSIBILITIES

Principal Investigator: Erik Groessl, Ph.D.
Dr. Erik Groessl has a Ph.D. in Clinical Psychology and has conducted research at UCSD and the VA for over 12 years. He has conducted and published yoga research at the VA San Diego and has extensive experience with health measurement. Erik Grossel, Ph.D. is a psychologist and a faculty member in the Department of Family and Preventive Medicine, UCSD. Dr. Groessl will assist in overall study administration, oversee data collection, and perform analysis and report writing.

Co-Investigator: Crystal Park, Ph.D.
Dr. Crystal Park is a Psychologist who has done extensive yoga research. Dr. Park will assist in all phases of the study design, implementation, analysis and interpretation. In year one of the project, Dr. Park will work closely with PI Groessl and staff to assist in successful launch. She will travel to San Diego to meet with the study team. In years two and three, Co-I Park will assist in interpretation and preparation of new grant proposals. Throughout the project, Dr. Park will have regular conference calls with the study team and be available for discussing issues and problems as they arise.

Project Coordinator – Danielle Casteel has a M.A. in Psychology (with an emphasis in Physical and Mental Health) from San Diego State University - May, 2015. She has been working in human subjects research for 4 years and has experience providing informed consent, conducting participant assessments, data entry, data cleaning, and data analysis.

Site Principal Investigator: Dr. Ian Fowler, MD
Dr. Fowler is the Director of the Pain Management Center at Naval Medical Center, San Diego (NMCSD). He will serve as the site Principal Investigator at NMCSD. He will work closely with the Wellness program at NMCSD, to screen and refer patients to the study. He will assist with obtaining military IRB approval and conducting all aspects of research and at NMCSD.

Dr. Douglas Chang, MD, PhD, Co- Investigator is Chief of Physical Medicine and Rehabilitation and Assistant Professor in the Department of Orthopaedic Surgery at the University of California San Diego. He also has a PhD in bioengineering from UCSD. Dr. Chang is a researcher and clinician who specializes in orthopedic surgery of the spine, and treatment of chronic low back pain. Dr. Chang will advise the research team concerning diagnostic/screening and

inclusion/exclusion criteria issues, and will assist with screening examinations as needed. He will meet with the research team on a regular basis and will contribute to the dissemination of results, and subsequent preparation for a full-scale R01 study.

Qualitative Expert: Samantha Hurst, PdD, MA received her Ph.D. in Biological Anthropology from the University of Tennessee, Knoxville and did her Post-Doctoral Fellowship training as a Medical Anthropologist in the Alcohol Research Center at The Scripps Research Institute in La Jolla. Dr. Hurst has extensive experience conducting qualitative interviews and analyzing qualitative data.

Consultant: Laura Schmalzl, Ph.D.
Laura Schmalzl received her Ph.D. in Cognitive Science from Macquarie University in Sydney, Australia. Additionally, her contribution to the current project as a co-investigator is the combination of clinical, scientific, and Yoga related trainings. Laura trained and practiced as a Clinical Neuropsychologist, followed by a PhD and Post-doctoral work in Cognitive Neuroscience. In addition, she is a Yoga Alliance Registered Yoga Teacher (500-hour level).

Yoga Instructor / Yoga Instructor Trainer: Camilla Sinclair
Camilla Sinclair, RYT 500 is a certified yoga instructor who has been practicing yoga for over 16 years and has over 8 years of teaching experience. She taught the VA Yoga for CLBP for over 5 years and helped design the intervention. Ms. Sinclair will assist Dr. Schmalzl and Bettey Michalewicz with adapting the intervention in Phase 2 of the study based on results from Phase I. She will also assist with training instructors for the active yoga program.

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23. FUNDING SUPPORT FOR THIS STUDY

Financial support for the study is pending NCCIH Council Review. This submission is part of the standard JIT process.

24. BIOLOGICAL MATERIALS TRANSFER AGREEMENT

N/A

25. INVESTIGATIONAL DRUG FACT SHEET AND IND/IDE HOLDER

N/A

26. IMPACT ON STAFF

N/A

27. CONFLICT OF INTEREST

None of the investigators have conflicts of interest with any aspect of the study.

28. SUPPLEMENTAL INSTRUCTIONS FOR CANCER-RELATED STUDIES

N/A

29. OTHER APPROVALS/REGULATED MATERIALS

N/A

30. PROCEDURES FOR SURROGATE CONSENT AND/OR DECISIONAL CAPACITY ASSESSMENT

N/A