Study Protocol and Statistical Analysis Plan

Mindful Action for Pain: An Integrated Approach to Improve Chronic Pain Function

Document Date: 12/12/2023

NCT03800654

Human Protocol (Version 1.31)

General Information

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

Mindful Action for Pain: An Integrated Approach to Improve Chronic Pain Function

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

MAP
* 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:**

Herbert, Matthew S., PhD

3.1 If applicable, please select the Research Staff personnel

A) Additional Investigators

Afari, Niloofar, PhD
Co-Investigator
Backhaus, Autumn L., PhD
Co-Investigator
Lang, Ariel J., PhD
Co-Investigator

B) Research Support Staff

Fishbein, Joel N., PhD
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***Please add a Study Contact**

Herbert, Matthew S., PhD
Salamat, Jennifer S.

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:

Matthew S. Herbert, PhD

Protocol Title:

Mindful Action for Pain: An Integrated Approach to Improve Chronic Pain Function

IRB Protocol Number:

H180175

Protocol Nickname:

MAP

Form Template Version:

v20150115

Date Prepared:

12/12/2023

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).

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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."*

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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, behavioral complaint, or chronic pain.

◉ 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)

6 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)

The gold standard psychosocial intervention for chronic pain, Cognitive Behavior Therapy (CBT),

is not universally effective and does not produce reliable increases in functional improvement. An emerging scientific model that holds promise for improving functional outcomes in chronic pain is the psychological flexibility (PF) model. Acceptance and Commitment Therapy (ACT) is the best known treatment from the PF model, but like CBT, ACT falls short on achieving meaningful changes in function for individuals with chronic pain. Nonetheless, there is empirical support that improvements in pain outcomes are mediated by PF treatment processes, giving support to this model and suggesting that identifying alternative ways of increasing PF may lead to significant increases in functional improvement. There is compelling empirical rationale that the mechanisms underlying formal mindfulness meditation, a practice used to train non-judgmental awareness and attention to present-moment experiences, will bolster PF processes and, in turn, facilitate functional improvement. To test this rationale, the PI has developed a novel 8-week group-based intervention, Mindful Action for Pain (MAP). MAP is distinct from ACT in that formal mindfulness meditation practice, which has never been tested within the PF model, is a principal treatment method, and it is integrated with experiential methods from different evidence-based treatment approaches (ACT, Dialectical Behavior Therapy) to address the key psychological barriers to optimal functioning.

In phase 1, the initial MAP protocol will be executed with participants with chronic pain and iteratively refined based on participant feedback.

In phase 2, we will complete a pilot randomized controlled trial comparing MAP to CBT that will allow us to estimate initial treatment effects and determine if a future, large-scale trial is warranted.

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.

This proposal seeks to develop and initially evaluate an integrated, model-driven mindfulness-based intervention for chronic pain, Mindful Action for Pain (MAP), designed to help Veterans with chronic pain achieve sustained functional changes driven by personal values. To accomplish this, we have chosen the psychological flexibility (PF) model. PF refers to the ability to behave consistently with one's values even in the face of unwanted thoughts, feelings, and bodily sensations such as pain. The PF model is especially applicable to chronic pain because of its ultimate goal of supporting increased engagement in meaningful life activities. MAP is unique in that it integrates evidence-based treatment methods from Mindfulness-Based Stress Reduction (e.g., formal mindfulness meditation), Acceptance and Commitment Therapy (metaphors and experiential exercises), and Dialectical Behavior Therapy (e.g., informal mindfulness techniques) within a group-based delivery approach that is guided by the PF model. This application seeks to develop MAP (Phase 1) and conduct a pilot randomized trial of MAP vs. CBT for chronic pain (CBT-CP) (Phase 2).

Aim 1: Fully develop MAP in a population of Veterans with chronic pain (Phase 1).

Aim 2: Evaluate the feasibility of a future randomized efficacy trial of MAP vs. CBT-CP (Phase 2).

Hypothesis 1: MAP and CBT-CP will be feasible to deliver, as evidenced by attainment of recruitment goals, retention rates > 80%, and high credibility and expectancy ratings.

Aim 3: Estimate the preliminary impact of MAP and CBT-CP to determine if a future efficacy trial is warranted.

Aim 4: Explore the relationship between meditation adherence and treatment outcomes.

Aim 5: Explore objective measures of physical activity (actigraphy) at baseline and post-intervention as a potential future index of functional outcomes.

Section 7 - Background and Significance

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

According to the Veterans Health Administration, the goal of pain treatment is to improve physical and psychological functioning, emphasizing non-pharmacological approaches to target psychosocial factors that maintain disability (Department of Veterans Affairs, 2009).

Unfortunately, the gold standard psychosocial intervention for chronic pain, Cognitive Behavior Therapy for chronic pain (CBT-CP), is not universally effective and does not produce reliable increases in functional improvement (Eccleston, Williams, & Morley, 2009). Veterans with chronic pain would greatly benefit from innovative, theoretically-grounded alternative interventions that accomplish the goals set forth by the VHA. An emerging scientific model that holds promise for improving functional outcomes in chronic pain is the psychological flexibility (PF) model.

The PF model consists of six interrelated processes that are targeted in treatment: present moment contact, acceptance, cognitive defusion, self-as-context, values, and committed action. Briefly, present moment contact refers to voluntary attention to the present as opposed to dwelling in the past or future. Acceptance is the willingness to openly experience unpleasant internal stimuli (thoughts, emotions, memories, etc.) when doing so is helpful for moving in a desired life direction. Cognitive defusion refers to the ability to see thoughts as a passing experience and to have experiences without being dominated by one's appraisal of them. Self-as-context, sometimes called self-as-observer, refers to a perspective of the self that remains stable as one's circumstances change. Values are desired qualities of ongoing action that are rooted in the one's personal sense of meaning and purpose. Committed action is the flexible and persistent approach towards chosen goals. These processes are often grouped into acceptance processes (present moment contact, acceptance, cognitive defusion, and self-as-context) and change processes (values, committed action) that work in concert to decrease maladaptive behaviors and increase adaptive behaviors, respectively. An impressive feature of the PF model is its trans-diagnostic nature. Indeed, there is evidence that the PF model is applicable across a range of conditions beyond chronic pain, including depression, anxiety, psychosis, diabetes, epilepsy, smoking cessation, and stigmatizing attitudes.

Similar to CBT-CP, the best known treatment from the PF model, Acceptance and Commitment Therapy (ACT), falls short on achieving meaningful changes in function for individuals with chronic pain (Hughes et al., 2016). However, there is empirical support that improvements in pain outcomes are mediated by PF treatment processes, giving support to this model and suggesting that identifying alternative ways of increasing PF may lead to significant increases in functional improvement. The most compelling treatment method that has never been tested within the PF model is formal mindfulness meditation. Although ACT is considered a "mindfulness-based therapy," the ACT approach emphasizes "informal mindfulness" techniques, not formal mindfulness meditation (Hayes, Strosahl, & Wilson, 2012). Formal mindfulness meditation entails concentrating on one primary object (typically the breath) until attention is stable and then expanding awareness to include all physical and mental events with the intention of developing non-judgmental awareness of moment-to-moment experience (Kabat-Zinn, 1982). Unlike informal mindfulness techniques, which is difficult to precisely define, formal mindfulness meditaiton is a practice, and like any type of practice, demonstrates practice effects. For example, several studies show a dose-response relationship between formal mindfulness meditaiton practice and improvements in physical and mental health. Further, neuroimaging has provided strong evidence of biological changes associated with formal mindfulness meditation. In a 2016 meta-analysis, formal mindfulness meditation was consistently associated with increased activation in neural areas associated with interoception (insula), and with voluntary regulation of thought and action (left inferior frontal gyrus, supplementary motor area, premotor cortex) (Fox et al., 2016). Finally, and importantly, there is evidence that formal mindfulness meditation targets core PF treatment processes (Bieling et al., 2012; Carmody et al., 2009).

The proposed project aims to maximize functional improvement in Veterans with chronic pain, a goal that has largely remained elusive with existing treatment approaches. MAP seeks to accomplish this by using the PF model to guide the integration of formal mindfulness meditation practice and other evidence-based techniques to address key psychosocial barriers to optimal functioning. Being a trans-diagnostic concept, increasing PF holds promise to simultaneously decrease pain-related barriers to functional improvement as well as barriers related to common comorbidities (e.g., anxiety, depression, PTSD). By increasing engagement in valued life activities despite pain, Veterans may find greater quality of life and be able to achieve higher levels of functioning. This reduction in disability holds promise to reduce the healthcare and societal costs associated with chronic pain.

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.

*******Please scroll down to see temporary measures to be implemented during COVID social distancing requirements*******

Approach

This proposed project consists of two phases across the 5-year award perioid: 1) development and refinement of MAP and 2) a pilot randomized trial to evaluate feasibility and estimate the preliminary impact of MAP vs CBT-CP.

Procedures: Phase 1, Protocol Refinement (years 1 - 2)

Potential participants will be recruited primarily from the Behavioral Medicine and Primary Care clinics at the VASDHS (other recruitment strategies are discussed in 11 Recruitment). Participants recruited through Behavioral Medicine and Primary Care clinics will give permission to their provider for the study coordinator to contact them. The study coordinator will perform a telephone screening to discuss the study and initial eligibility. Participants that appear eligible and are interested in participating will be invited for an in-person visit to obtain informed consent and and complete the Mini International Neuropsychiatric Interview (see *Measures*) to confirm eligibility. After consent is obtained, the participant will complete measures before, during and after the intervention. Participants will receive a payment of $40 for the baseline assessment, $40 for the post-intervention assessment, and $40 for a 3-month follow-up assessment. The 3-month follow-up assessment will occur either in person or by phone, whichever is most convenient for participants. Additionally, participants will receive $20 for the mid-treatment qualitative phone interview and $20 for a post-treatment qualitative phone interview (described below).

The initial protocol for MAP is based on a transdiagnostic mindfulness group protocol developed by the PI and offered clinically at VASDHS 2016 - 2018, called Mindful Living (pain was not the focus). The initial refinement of the 8-week MAP protocol will be done to assure that the material is accessible to Veterans seeking treatment for chronic pain. Based on feedback from each MAP session and the two qualitative phone interviews, the PI will refine the approach with his study team to accomplish the aims of the intervention. The subsequent MAP group will be run incorporating potential improvements identified using the refinement strategies discussed below.

Number of Visits: Visit 1: Consent, MINI, baseline measures and actigraphy; Visits 2 - 4: MAP sessions 1 - 3; Visit 5: MAP session 4 and mid-treatment qualitative phone interview; Visit 6 - 9: MAP sessions 5 - 8; Visit 10: Posttreatment measures, actigraphy, posttreatment qualitative phone interview; Visit 11: 3-month follow-up measures (may be done by phone).

Subject Educational Materials: Educational materials will be printed for participants. Guided meditation CD recordings will be provided to participants, in-person or mailed, or accessed through the LifeData app. Based on participant feedback during Phase 1, we may alter the guided meditation instructions to best fit the needs of participants prior to Phase 2, in which guided meditation instructions will no longer be altered. Participants may also request a CD if they do not have easy access to a computer with internet capabilities.

Participants: Participants in both phases will be Veterans with chronic pain who are able to consent and willing to participate (refer to Human Subjects for detailed inclusion/exclusion criteria). Co-occurring disorders such as depression, anxiety, and PTSD are permitted provided that chronic pain is the primary presenting complaint.

Sample Size: Based on Dr. Lang's (co-investigator) past experience in intervention development, it is estimated that 4 MAP groups of 5 participants per group will be needed to achieve Phase 1 refinements with a total sample size of 20 Veterans.

Refinement Strategies: Each MAP cycle will be refined based on qualitative and quantitative feedback from study participants. Participants will be informed of the goal of refining the intervention, and will be encouraged to provide honest feedback about their experience. Initially we will focus on the extent to which participants understand and believe in the approach, and challenges in establishing a daily meditation practice. Starting at the 2nd session, each participant will complete a brief questionnaire after each session to assess their understanding of material and satisfaction with treatment delivery. Examples of questions participants would compete after each MAP session include: Did you understand today's topic? (Yes/No; If no, please briefly explain); Did you understand the exercises and examples used in today's group? (Yes/No; If no, please briefly explain); Were you satisfied with the way facilitator explained today's topic (Yes /No; If no, please briefly explain); Is today's topic applicable to your life (Yes/No; If no, please briefly explain).

Further, at mid-treatment (between session 4 and 5) and post-intervention, Dr. Backhaus (co-investigator and co-mentor on CDA award) will administer a 15-20 min phone interview with each Phase 1 participant. The purpose of these phone calls is to determine 1) overall satisfaction with and perceived benefit of MAP, 2) the performance of the facilitator (the PI) and any positive or negative feedback to explore the relationship between leader characteristics and treatment effects, 3) understanding and adherence to the formal meditation practice, and 4) the ability to relate mindfulness with PF processes. Phone calls will be audiotaped in order to collect and score qualitative data. The qualitative questions were developed with input from Dr. Backhaus (co-mentor) and Dr. Hurst (qualitative methodology consultant) and can be found in the *27. Attachments* of this application. As themes are identified in the responses, subsequent questioning may be refined to try to elicit types of feedback that will further develop our understanding of the participants' experience and how to best achieve the goals of MAP.

The PI will meet regularly with the research team during Phase 1. In these meetings, we will discuss feedback from participants and what modifications are in order. In particular, the research team will be looking for any difficulty in understanding the concepts being presented (different approach? more or less time for discussion?), the perceived appropriateness of exercises /metaphors (did participants relate personally? do they fit with military/veteran culture?), challenges in engaging in meditation practice (to what extent did participants engage in practice outside the session? any observable discomfort or lack of engagement in the class setting? Do our measures seem to be capturing actual behavior?). Based on that material, we will modify that session in the protocol and plan for the next class session (e.g., choosing to explain again material that was not well understood, to give an alternative metaphor to assist in understanding a concept, or to modify a practice). Adjustments made to the original protocol will be incorporated into the manual and reviewed by the research team for use in the next MAP group. Decisions about protocol changes will be made by consensus among the primary research team (the PI and co-investigators). We will allow 1 month between MAP cycles to review and make refinements to the protocol. This period of time will also be used to recruit for the next group.

Procedures: Phase 2, Feasibility of MAP vs CBT-CP

In Phase 2, we will conduct a pilot randomized trial consisting of 12 groups, randomly assigning 6 groups to receive MAP or CBT for chronic pain (CBT-CP; see Description of CBT-CP below for rationale of comparison group). As in Phase 1, potential participants will be recruited primarily from the Behavioral Medicine and Primary Care clinics at the VASDHS, and other clinics as needed. Groups will be randomly assigned to MAP or CBT-CP in a 1:1 ratio based on a computer-generated randomization table produced by Dr. Golshan (biostatistician consultant). The refined procedures from Phase 1 will be followed for securing consent, conducting assessments and providing compensation for participation, and the same eligibility criteria will apply. However, participants in Phase 2 will not complete weekly post-session questionnaires or mid-intervention /post-intervention qualitative phone interviews.

Sample size for Phase 2: In Phase 2, we will conduct 12 groups (6 MAP and 6 CBT-CP) with 7 - 8 Veterans in each group to examine the feasibility of a future RCT and preliminary response to MAP (year 3 = 4 groups; year 4 = 6 groups; year 5 = 2 groups). Anticipating up to a 20% attrition rate, 86 participants will be recruited for Phase 2.

Number of Visits: Visit 1: Consent, MINI, baseline measures and actigraphy; Visits 2 - 9: MAP or CBT-CP sessions 1 - 8; Visit 10: Posttreatment measures, actigraphy; Visit 11: 3-month follow-up measures (may be done by phone); Visit 12: 6-month follow-up interview using Microsoft Teams.

Interventions. An overview of the MAP intervention is described below, as well as the CBT-CP intervention. Both groups use an 8-week, 90-minute session protocol. The MAP intervention will be delivered solely by the PI. The PI is a licensed clinical psychologist with several years of experience conducting group and individual therapy for chronic pain using mindfulness-based techniques. For the CBT-CP intervention (Phase 2 only), we will use a manualized protocol developed at the VASDHS used in previous research (Wetherell et al., 2011). In the second half of Year 2 of the award, a part-time study therapist will be hired and trained to deliver the CBT-CP intervention. This therapist will be required to have graduate (at least master's level) training in psychology, and will be recruited within the expansive VASDHS and UCSD communities. The study therapist will be supervised by Dr. Backhaus (co-investigator), who is a certified CBT-CP VA provider and the current supervisor for trainees in the Behavioral Medicine clinic that provide group-based CBT-CP at the VASDHS. Dr. Backhaus will train the study therapist and ensure competency prior to the start of Phase 2. The study therapist will have weekly check-ins with Dr. Backhaus via in-person or telephone while facilitating CBT-CP groups to ensure minimal drift from the protocol and to answer any questions that arise.

Description of MAP

In MAP, participants are first exposed to mindfulness (paying attention in a particular way: on purpose, in the present moment, without judgement) and instructed how to engage in formal practice (session 1). Similar to other formal mindfulness meditation interventions, MAP consists primarily of two principal techniques: sitting meditation and body scan meditation. Briefly, sitting meditation consists of focusing attention on the sensations of breathing, noticing when the mind has wandered from the breath, briefly noting the source of wandering (e.g., "pain in shoulder," "thinking," etc.), and returning attention back to the sensation of breathing. The body scan meditation entails sustaining and moving attention around specific body parts starting at the toes and ending at the head (or vice versa). Similar to sitting meditation, when the practitioner notices the mind has wandered, the source of wandering may be briefly noted and attention is returned to the body. Starting after the 1st session, Veterans are expected to engage in daily formal mindfulness meditation, at first using provided audio recordings and later without recordings, and complete a daily meditation diary. Home meditation practice will follow a similar protocol as other meditation-based interventions at the VA. Specifically, Veterans will have access to audiotapes that vary in duration (5 - 20 minutes) via the Lifedata application or audio CD if preferred for the sitting and body scan meditations. Audio instructions are provided by Dr. Herbert and links to publicly available guided meditations. This will enable the most control over meditation instruction and allow alterations to instructions during Phase 1. Sample meditation scripts are provided in *27. Attachments*.

Topics for sessions 2 through 8 address PF processes (present moment contact, acceptance, cognitive defusion, self-as-context, committed action, and values) using experiential methods from ACT and DBT, scaffolded on the formal mindfulness meditation practice to support values-based living. For example, in the "Tug-of-War" exercise, which targets the acceptance process, a Veteran from the group is asked to engage in a tug-of-war (using an actual rope) with the group facilitator. The Veteran is asked to imagine the facilitator represents his pain, and between them is a fiery pit. The Veteran and facilitator (i.e., pain) proceed to engage in a tug-of-war to try to win the tug-of-war. The take home message of the exercise is that when engaged in a tug-of-war with pain, one is bound to pain and unable to engage fully in other activities, and when one drops the rope (i.e., acceptance), there is increased ability to move freely, even though the facilitator (i.e., pain) remains. This naturally leads to a group discussion of how acceptance of pain can help one move towards values-congruent goals despite pain. In MAP, Veterans will be subsequently asked what the relationship between mindfulness and the "Tug-of-War" exercise (e.g., having the ability to notice when a tug-of-war with pain is occurring in real time and how to proceed), being prompted as needed. DBT methods, primarily participate and one-mindfulness skills, are particularly helpful in this exercise to promote engagement in values-based action. The facilitator will then engage in a question and answer session with the group about the practical utility of formal mindfulness meditation (e.g., during formal mindfulness meditation, we practice "dropping the rope" with pain by noticing when it distracts from the practice and allowing it to be there (i.e., dropping the rope), and then choosing to return to the object of focus).This same process is repeated in each session to continuously reinforce the relationship between formal practice and PF processes. Because values, operationalized as desired qualities of ongoing action, serve as the context for behavior change within the PF model, values are introduced early to provide maximal time during MAP to help Veterans clarify values and values-based action, as well as the relationship between mindfulness and values-based action. This is accomplished through in-session experiential exercises, discussions, and homework. Each MAP session is 90 minutes and begins with a formal mindfulness meditation practice (10-15 mins), a review of homework and previous topics (10 – 15 minutes) experiential exercises and discussions of a treatment topic (35-45 minutes), and closes with an informal mindfulness exercise and formal mindfulness meditation sitting (10-15 minutes).

Description of CBT-CP

As aforementioned, the CBT-CP comparison group will use an 8-week, 90-minute session, manualized protocol developed at the VASDHS and used in previous research (Wetherell et al., 2011). This protocol is based on the three-component CBT model (thoughts, feelings, behaviors) with the rationale that controlling some of the factors that contribute to pain can lead to a decreased subjective experience of pain. CBT-CP focuses on training participants to manage their pain using a variety of techniques, including pain monitoring, pacing, increasing pleasant activities, progressive muscle relaxation, thought challenging, and problem skills training. The net results of these strategies is to control pain by changing its physical, cognitive, behavioral, and emotional precursors, leading to reduced pain severity and resulting beneficial consequences on pain interference, quality of life, and physical activity. Similar to MAP, CBT-CP emphasizes the importance of at-home practice assignments to develop skills taught in session.

Treatment Fidelity

Treatment fidelity is essential to the reliability and validity of study findings as well as the eventual large-scale trial and dissemination of MAP. We will employ several strategies recommended by the National Institutes of Health Behavior Change Consortium to develop a

treatment fidelity checklist for MAP during the proposed project (Bellg et al., 2004). Treatment dose across both treatment groups will be equivalent. I will conduct all MAP sessions during both phases, and the part-time study therapist will administer all CBT-CP sessions in Phase 2. Using different therapists for the MAP and CBT-CP interventions will maximize treatment adherence and minimize contamination across groups. To ensure my competency, a portion of the time during weekly meetings with Dr. Afari (co-investigator and primary mentor on CDA) will be reserved to minimize drift from the MAP protocol.

In order to ensure that treatment is delivered consistently throughout Phase 2, all treatment sessions will be audiotaped. A random sample of 10% of all treatment sessions, divided equally across type of intervention, will be reviewed by Dr. Backhaus. For the CBT-CP groups, tapes will be coded for therapist competence as well as adherence to the CBT model using a similar rating system use for a previous CBT for chronic pain trial at the VASDHS (Wetherell et al., 2011). Dr. Backhaus also will evaluate MAP sessions based on the treatment fidelity checklist we develop to test for feasibility of fidelity tracking. Undertaking treatment fidelity evaluations in this manner will allow me to develop the necessary skills and documents necessary to ensure treatment fidelity in future trials.

Data and Data Analysis

Phase 1: Analyses for Aim 1 will be directed toward the development of MAP and collection of data to inform modification of the treatment. Qualitative and quantitative data will be collected and analyzed to achieve this. The purpose of the qualitative data is to synthesize the information and present it to the research team in order to make modifications to the approach. Drs. Hurst (qualitative methodologist consultant) and Backhaus have extensive experience with qualitative methods and will provide guidance for conducting these analyses. Qualitative data will be analyzed using atlas.ti, a qualitative data analysis software package frequently used by Dr. Hurst. Qualitative data analysis starts with coding, a process in which quotes are marked and labeled. The labeled quotes are then sorted and grouped, so that categories, then concepts, then themes can be developed. As is often standard practice for qualitative data analysis, analysis will be concurrent with data acquisition. Quantitative data (see *Questionnaires*) will be collected to test for feasibility of assessments and to compare with qualitative data. We will first examine the data for missing values. Descriptive statistics will be used to summarize the outcomes and detect and analyze outlies, data errors, and data distribution.

Phase 2: Data from subject tracking logs will be used to determine the proportions of Veterans 1) who agree to be contacted out of the number approached about the study (general interest in the study), 2) who consent out of the number contacted (willingness to participate in the trial), 3) who attend the initial group meeting out of the number consented (enrollment), 4) who attend each class and complete the intervention out of the number who began (retention), and 5) reasons given for discontinuation. The number of contacts based on various recruitment strategies also will be recorded. Additional feasibility data includes: rate of missing data between treatment groups and per time point; differences in retention rate between treatment groups; factors influencing retention rate and their impact on study outcomes; completion of study measures and homework; and participants' satisfaction with study procedure and treatment delivery method. Further, age, gender, race/ethnicity, medications (including pain and other medications), and changes to medications/chronic pain treatments (TENS, injections, etc.), as well as pain etiologies (collected via chart review) will be explored within and between groups as they relate to study measures. This information will be helpful for assessing the feasibility of MAP and future hypothesis generation.

Additionally, we will examine the preliminary impact of MAP on pain interference (primary outcome), as well as pain acceptance, trait mindfulness, and pain catastrophizing (secondary outcomes). Other questionnaires that will be measured are listed in the *Questionnaires* section. Changes on these measures as well as participant satisfaction would also serve as indicators that MAP may be worthy of a future large-scale RCT.

Initially, chi-squares and Analysis of Variance will be used to assess the effectiveness of the randomization procedures by comparing participants in each treatment condition on baseline variables. Within-group change will be assessed separately in MAP and CBT-CP groups on the primary (pain interference) and secondary clinical outcomes (pain acceptance, trait mindfulness, pain catastrophizing). We will plot means and standard deviations overtime to examine them visually, and determine the percentage of participants in each group that achieve minimally clinically important change on the BPI Pain Interference scale (1-point change, etc.). Additionally, we will use linear mixed-effects (LME) models to explore preliminary estimates of treatment effects. Time will be added as fixed effects in models, and the intercept will be added as a random effect. Effect size for within-group change will be calculated according to procedures described by Cohen, and interpreted with caution and in the context of the 95% confidence interval that surrounds it. The preliminary within-group treatment effects of MAP will help determine our future directions. For example, medium-large treatment effects would provide signal for future testing

whereas small treatment effects would suggest a need for additional development. Within the CBT-CP group, treatment effects will be examined in relation to findings from other published pain trials with similar Veteran populations to ensure adequacy of CBT-CP delivery.

We will also conduct preliminary between-group comparisons on the BPI Pain Interference measure to better understand if continuing to pursue evaluation of MAP is warranted. Given that functional improvement is the ultimate goal of this research, we chose pain interference as the key outcome for the preliminary between-group analyses and power calculations because it is a proxy for functional improvement and one the most commonly used outcome measure in psychosocial intervention trials of chronic pain. Group comparisons will be examined via LME with group (MAP vs. CBT-CP), time (10-total time points: baseline [1 time point], weekly during sessions [8 time points], post-intervention [1 time point]), and the treatment by time interaction added as fixed effects. The intercept will be added as a random effect. Effect size for the difference between groups will be calculated according to procedures described by Cohen. Effect size will be interpreted with caution, and in the context of the 95% confidence intervals that surrounds it.

Average time spent per week in meditation practice will be calculated from the LifeData mobile application or daily weekly diaries. The relationship between meditation practice time and study measures will be explored by adding the adherence rate to LME models as a covariate.

The actigraphy outcome will be the total activity count from each active interval, averaged across each 7-day observation period, excluding periods of missing data that occur due to temporary removal of the device. We will exclude participants that wear the Actiwatch < 5 valid days, with valid days defined as periods with < 4 hours of missing data. Participants will be instructed to press the event marker button on the Actiwatch to denote the times they get into and out of bed. Rest intervals (analogous to time in bed) will be scored manually using event markers, activity, and light, following the methodology of Patel et al. (2015) , which takes into account that participants sometimes forget to press the event marker. Actigraphy data will be explored visually and via LME for trends of increased activity levels from baseline to post-intervention within group (Phase 1 and 2) and between groups (Phase 2) with guidance from Dr. Golshan (statistical consultant), who has previous experience analyzing actigraphy data.

Data collection and quality control. Data management and statistical analysis will be supervised by the study statistician, Dr. Shahrokh Golshan. Dr. Golshan will oversee the development of the study database, which will be maintained on the secure VA research server. Participant names will be held separate from data. Subjects will be assigned a unique ID number, and the single name-to-ID relational file will be kept in an encrypted form electronically and in a locked filing cabinet physically. Data for this study will be entered into Excel. Statistical analysis will be conducted using SPSS, R and SAS software packages. Prior to inferential analyses, data will be examined for missing values and statistical outliers. All statistical transfer routines are inherently secure via their operating platform and they contain no patient names or personal data.

The assessment and questionnaires to be used are described in Secion 9.8

Timeline and feasibility.

The major study activities are outline in the table below.

	Year 1	Year 2	Year 3	Year 4	Year 5
Phase 1					
Hire research coordinator	x				
Recruit, conduct groups, modify protocol	x	x	x		
Data management and analysis		x	x		
Finish MAP refinement			x		
Phase 2					

Hire research assistant and study therapist	x						
Pilot study: Recruit, conduct groups, collect data		x	x	x	x	x	
Data management and analysis		x	x	x	x	x	x
Manuscript preparation					x	x	x

NOTE: Due to COVID-19 concerns, session 7 and 8 (slated to occur on 3/17/2020 and 3/24 /2020) of cohort 3 may be conducted via the secure VANTS (VA National Teleconferencing System) line. Participants will be asked to give verbal consent and will be asked to be in a secure location during the teleconference to minimize breach of confidentiality.

UPDATED measures due to COIVD-19 social distancing requirements (5/18/2020)

The following are temporary procedures to allow for participation in this research protocol while maintaining social distancing due to the COVID-19 pandemic.

The protocol remains as approved with the following exceptions:

Consenting

If a Veteran is potentially interested in participation after initial contact, we will send an encrypted email (using VA Azure RMS) containing (1) the approved ICF, (2) the approved HIPAA document, (3) the CA Experimental Subjects Bill of Rights and arrange a telehealth meeting (using VA approved secure Telehealth communications software such as Veteran Video Connect, VA-approved Cisco Webex, etc.) to complete the informed consent process, explain the HIPAA Authorization and CA Experimental Subjects Bill of Rights. The staff member will witness the signing of the ICF and HIPAA Authorization and will instruct the potential participant to provide documentation of written informed consent by either returning images of the documents through MyHealtheVet or by allowing a screenshot of the signed documents (approval date and signature must be clearly visible). These electronic documents will be stored electronically separate from study data on the Investigator's R-drive, and the participant will retain their copies. Participants may also fax (secure landline) the consent and HIPAA documents which will be stored per the usual protocol after obtaining hardcopy consents.

Eligibility Assessment

Initial eligibility will continue to be determined through the pre-approved HIPAA-waived screening form during initial contact. Once documentation of written consent is received, research staff will conduct the MINI (mental health assessment) administered by a study clinician to further determine eligibility. This will be conducted by telephone appointment or through a telehealth meeting, again using one of the approved systems above (Veteran Video Connect, VA-approved Cisco Webex, etc.)

Research Assessment/Data Collection

Once eligibility has been confirmed, the participant will complete study research assessments including data collection via questionnaires. These questionnaires will be administered and collected by the following methods: (1) Study participants are sent a link to a Qualtrics survey by study staff and can complete their survey on any internet-connected device with an internet browser, (2) through telephone where research staff will contact participants to collect responses to questionnaires, or (3) by sending an encrypted email (using VA Azure RMS) containing a password-protected fillable pdf of the questionnaires that the participant will return by one of three methods: (1)via encrypted email to a staff VA email account, (2) by fax (secure landline), or (3) via MyHealtheVet.

Group Treatment

Participants will engage in group treatment with the research study clinician via an arranged telehealth meeting (using Veteran Video Connect). Should technical difficulties arise using this method, teleconferencing (non-video) will be available through the VA Nationwide Teleconferencing system (VANTS line). Participants will be reminded of limits of confidentiality during these sessions.

Section 9.5 Data Banking

9.5) Provide details about the data repository for example,

- **Identify what information will be retained.**
- **Whether participation in the repository will be optional or required.**
- **Whether or not identifiers are included with the banked data,** ***Note: If banking is optional and identifiable information will be retained, then the combined consent/HIPAA form may not be used. Please use the single consent and HIPAA form 10-0493.***
- **Provide future use examples.**
- **Indicate how the study will comply with VHA Handbook 1200.12.**

All data obtained as part of this study including, but not limited to, sociodemographic information, medical history, and psychosocial functioning, will be retained for future use in analysis not yet determined. Identifiers will be retained and this is stated in the consent form. The data repository will be established after closure of the protocol outlined in this application. The establishment and management of the data repository will comply with VHA Handbook 1200.12.A repository SOP will be submitted prior to creation of the repository.

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.***

See also attachment for tables of assessments by visit.

Eligibility:
- The PEG (Krebs et al., 2009) is a brief pain screening instrument developed from the Brief Pain Inventory (described below). The PEG contains one item that assesses pain intensity (P), and two items that assesses pain interference: interference with enjoyment of life (E), and interference with general activity (G). In order to be eligible for the study (both phases),

participants must score >4/10 on both pain intensity and one or both of the pain interference items.
- Mini International Neuropsychiatric Interview (MINI; Lecrubier et al., 1997): 15 - 30 minute interview used to identify the exclusionary conditions of current psychosis, mania, substance abuse within the past year, and suicidality. It also will be used to determine current and lifetime major depression, generalized anxiety disorder, and PTSD for descriptive purposes. The MINI will be administered only at the baseline assessment by the PI.

Phase 1 Only:
-Reactions to class material and practices (logic, understandability, applicability, and self-efficacy)

All Phases:
- Demographics: age, gender, race/ethnicity, relationship status, years of education, SES/income /living situation, occupation/work status, branch of service/highest rank
- Credibility/Expectancy Questionnaire (CEQ; Borkovec & Nau, 1972), given at end of 1st session to assesses how logical the treatment seems to the participant and how much they expect to benefit from it
- Client Satisfaction Questionnaire (CSQ-8; Larsen et al., 1997) 8-items
- Practice diary to determine average time spent per week in meditation practice (MAP group only). Participants will have option of using LifeData app to record daily meditation).
- Brief Pain Inventory (BPI; Cleeland & Ryan, 1994). The BPI consists of two subscales: pain severity (4-items) and pain interference (7-items). This questionnaire will be administered at the baseline assessment, weekly during the intervention (using the Polls function on WebEx), and at the post-intervention assessment. The Polls function on WebEx allows for participants to complete the BPI at the beginning of the session. Participants cannot see the responses of others. The Polls are saved on the PI's R drive located behind the VA firewall.
- Chronic Pain Acceptance Questionnaire (CPAQ; McCracken, Vowles, & Eccleston, 2004). 20-items
- Pain Catastrophizing Scale (PCS; Sullivan Bishop, & Pivik, 1995). 13-items
- Medical Outcomes Study 12-Item Short Form Health Survey (SF-12; Ware, Kosinski, & Meller, 1996). 12-items
- Patient Health Questionnaire (PHQ-9; Spitzer, Kroenke, & Williams, 1999). 9-items
- PTSD Checklist for DSM-5 (PCL-5; Bovin et al., 2016). 20-items
- Mindful Attention and Awareness Scale (MAAS; Brown & Ryan, 2003). 15-items
- Adverse Childhood Experience Questionnaire (ACE; Centers for Disease Control and Prevention, 2008). 10-items
- Injustice Experience Questionnaire (IEQ; Sullivan et al., 2008). 12-items
- Cognitive Fusion Questionnaire (CFQ; Gillanders et al., 2014). 7-items
- Insomnia Severity Index (ISI; Morin, 1993). 7-items
- Chronic Pain Values Questionnaire (CPVQ; McCraken & Yang, 2006). 12-items
- Medication will be recorded at the baseline (Visit 2) and post-intervention assessments (Visit 11). Participants will be asked to have all medication bottles, including over-the-counter medications and dietary supplements, available at their assessment appointments.
- Medication/treatment changes and adverse events will be assessed weekly. Participants will be asked if they made any medication/treatment changes over the last week and if any adverse events occurred.
- Actigraphy. The Actiwatch Spectrum PRO (Phillips Respironics, Bend, Oregon) will be used as an objective measure of physical activity. The Actiwatch Spectrum PRO will be worn continuously on the non-dominant wrist for two one-week periods at baseline and post-intervention in both phases by all participants.
-6-month interview questions:
Example questions:
1. What has been the most helpful part of the group for your pain?
2. When engaging in day-to-day activities, how are you able to manage pain?
3. What influence has the intervention had on your amount of physical activity?
4. What strategies did you learn from the group that you are currently using?
5. How has your relationship with pain changed since being in the group?

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 Data Safety and Monitoring Board (DSMB) is comprised of Drs. Arpi Minassian, Fadel Zeidan, and Michael Thomas. Drs. Minassian, Zeidan, and Thomas are not associated with this research project and work independently of the PI, so they are able to monitor the trial independently.

They are qualified to review the patient safety data generated by this study because of their unique experience in chronic pain management (Dr. Minassian), mindfulness-based interventions (Dr. Zeidan), and biostatistics (Dr. Thomas).

Drs. Herbert and Golshan will report to the DSMB on an annual basis.

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).***

In Phase 1, the phone calls that occur at mid-treatment and post-treatment will be audio-recorded for qualitative data analysis purposes. Dr. Backhaus and the PI will be in charge of these analyses under the supervision of Dr. Hurst. Dr. Backhaus will complete the phone calls in her private office , and will record the conversation via a Sony ICDPX312 Digital Voice recorder by using the speaker-phone option. The Sony ICDPX312 Digital Voice recorder is compliant with VHA regulations, and often used as VASDHS for research and clinical purposes.

In Phase 2, audio-recordings will be made for all sessions in both treatment groups (MAP and CBT-CP) using the Sony ICDPX312 Digital Voice recorder. Audio-recordings of the MAP group will be used for quality control and to develop an adherence tracking form for future research, whereas Dr. Backhaus will review randomly selected recordings of the CBT-CP sessions to assure adherence to the protocol.

Recordings from both Phase 1 and 2 will be uploaded and imported from the Sony ICDPX312 Digital Voice recorder via USB to the VA secured server system that is backed by the VA firewall. The audio recordings will be saved as MPG files and stored on the VA secured network R drive. The audio recordings will be labeled with a unique ID number, and the code key kept in a separate locked cabinet. Once the audio-recordings are uploaded and saved on the VA secured server, they will be deleted from the Sony ICDPX312 Digital Voice recorder.

Recordings from Phase 2, 6-month interviews:
We will use Microsoft Teams to record this interview session. Per Research Guidance Article KB0116766, VA investigators may use VA MS Teams to conduct remote VA research subject interviews. VA investigators are allowed to record those interviews using VA MS Teams if all applicable human subject protection regulations and policies as well as all applicable privacy laws, regulations and policies are met. We also may use the Pocket Memo Voice Recorder DPM8000 to record these interviews, which allows for audio-only recording. The Pocket Memo Voice Recorder DPM8000 has been previously approved through VA IRB.

When possible, participants will not be addressed by name during interviews, and transcribed interviews used for data analysis will deidentify participants.

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.**

The study will involve ~106 Veterans in the San Diego area. We expect the demographic make-up to approximate that of the VASDHS. Inclusion criteria are: 1) diagnosis of a chronic, non-terminal pain condition, 2) pain most days (>3 days/week) for at least 6 months, and 3) average pain severity and interference with enjoyment of life and/or general activity >4/10 over the past

week, as measured by the PEG (described in 9.8 Questionnaires). The following are exclusion criteria: 1) serious or unstable medical or psychiatric illness (e.g., unmanaged psychosis, manic episode, or substance abuse within the past year) or psychosocial instability (e.g., homelessness) that could compromise study participation, 2) active suicidal ideation or history of suicide attempt within the past year, 3) current participation in group psychotherapy for pain or any type of individual psychotherapy, or 4) changes to professionally delivered pain or mood treatments (e.g., no discontinuation of a treatment; no increasing the dose of medication) one month preceding the baseline assessment.

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.

Pregnant women will not be excluded from the study as there is no known risk to the woman or fetus associated with the methods used in either intervention. No additional protections are needed.

10.2c) It is indicated that pregnant women are the focus of the research. All of the below must be certified to be true to permit enrollment of pregnant women.

1. Where scientifically appropriate, preclinical studies including studies on pregnant animals and clinical studies including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses. *A description of such studies should be included in the project application.*
2. The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important medical knowledge which cannot be obtained by any other means.
3. If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, the pregnant woman's informed consent is obtained in accordance with the informed consent provisions of 38 CFR 16.116, paragraphs 30-35 and 45 CFR 46.204(d).
4. Each individual providing informed consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus.
5. Any risk is the least possible for achieving the objectives of the research.
6. There are no inducements included in the research, monetary or otherwise, that will be offered to terminate a pregnancy.
7. Individuals involved in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy.

(•) Agree ( ) Disagree

Section 10.6 Avoiding coercion of students or employees

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

Employees or students of the study staff will not be recruited. Otherwise, student status or employment with the VASDHS does not preclude participation.

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 strategies will be the same for Phase 1 and Phase 2.

Eligible participants will contact our study in response to:
1) Referral from VASDHS clinics, including the Behavioral Medicine and Primary Care clinics
2) Flyers posted in San Diego VA hospital, including Mission Valley, Chula Vista, and Oceanside CBOCS, and
3) Research databases of Veterans who have previously consented to be contact about additional study opportunities.
4) Self-referral from the VA Research Website
5) Referrals from VHASDC PATH (Patient Assessment and Triage Hub)

Recruitment from VASDHS clinics: Potential participants will be recruited primarily from the Behavioral Medicine and Primary Care clinics at the VASDHS. Dr. Backhaus is the Clinic Coordinator at these clinics and receives approximately 20 – 25 referrals per month for chronic pain management. Thus, recruitment needs for the proposed study should be met by these two clinics. If need be, we may also recruit from the VASDHS Pain Clinic/ Anesthesiology, Physical Medicine and Rehabilitation, Urgent Care Center, and Spinal Cord Injury Unit. We will attend team meetings and network with clinicians to encourage referrals by clinicians in those sites. Veterans that are interested in the study will complete the Research Candidate Form and given a flyer about the study, with the study coordinator's information (see Attachments). For these participants, we will request a partial waiver of consent/HIPAA for screening purposes (phone screening). The nature of the study will be explained, portions repeated as necessary, and questions answered. If participants appear eligible, they will be scheduled for an in-person screening session, where informed consent and HIPAA will be completed.

Recruitment from flyers: For potential participants that call in from the flyers, we will request a partial waiver of consent/HIPAA for screening purposes (phone screening).The nature of the study will be explained, portions repeated as necessary, and questions answered. If participants appear eligible, they will be scheduled for an in-person screening session, where informed consent and HIPAA will be completed.

Recruitment from research databases: Veterans who have previously participated in research studies at VASDHS with investigators/co-investigators affiliated with the current study (e.g., Dr. Niloofar Afari's "Technology Solution to Improve OEF/OIF Intake and Assessment Porgram") that have agreed to be re-contacted about other research will be contacted by letter and/or phone after CPRS record screen if no immediate exclusion criteria is found. If the participant did not agree to initial contact by phone, a letter will be sent first (see Attachments). After a period of 2 weeks, if no contact is made by the participant, study staff will follow up by phone and request verbal permission to administer the phone screen.

Recruitment from VA Research Website: For potential participants that call in from the flyers, we will request a partial waiver of consent/HIPAA for screening purposes (phone screening).The nature of the study will be explained, portions repeated as necessary, and questions answered.

Recruitment from PATH: Study details will also appear on a current research list posted to the VHASDC Clinical Research Teams channel. Providers from the Patient Assessment & Triage Hub (PATH) can access this spread sheet and refer veterans directly to study during treatment planning.

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.***

For potential participants that call in from the flyers, we will request a partial waiver of consent /HIPAA for screening purposes (phone screening). The nature of the study will be explained, portions repeated as necessary, and questions answered. If participants appear eligible, they will be scheduled for an in-person screening session, where informed consent and HIPAA will be completed.

Additionally, we will provide Research Candidate Forms and flyers to clinicians in order to share and information about the research study, and acquire consent to be contact by phone.

See attachments for copy of Research Candidate From and flyer.

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.

Signed consent documents for VA subjects will use VA form 10-1086. Consenting will take place at the La Jolla clinic with a trained assessor/study coordinator in a private room and the participant will be given ample time to read the consent form and ask questions. At the first visit, prior to initiation of any study-related procedures, subjects will give their written consent to participate in the study after having been informed about the nature and purpose of the study, participation/ termination conditions, risks, and potential benefits. Informed consent is a process that is initiated prior to the individual's agreeing to participate in the study and continuing throughout the individual's study participation. Upon reviewing the document, the assessor will explain the research study to the participant and answer any questions that may arise. Extensive discussion of risks and possible benefits of this therapy will be provided to the participants as needed. The investigator will explain study procedures and let the participant know how many assessments he/she will be asked to complete. The participants will sign the informed consent document prior to any procedures being done specifically for the study. The participants may withdraw consent at any time throughout the course of the trial. A copy of the informed consent document will be given to the participants for their records. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

During COVID-19 pandemic restrictions for in-person research visits, participants may be remotely consented using approved Docusign as follows:
1) At the time of remote consenting, the study team member/consenter will send a DocuSign envelope (email containing links to the study documents) to the potential subject. The email will contain a reminder for the recipient to not sign the documents prior to the scheduled contact time.
2) At the scheduled time, the study team member (referred to as "consenter") will contact the potential subject via phone or using the approved video (VVC or Webex). The consenter will guide the potential subject to open the DocuSign envelope (email) and the linked study documents therein. The consenter will open a copy of the study documents on their own computer as a reference. The consenter will review the study documents with the potential subject, ask questions to gauge comprehension, and answer any questions and concerns. If the potential subject agrees to participate in the study, the consenter will guide them to fill in the fields in the study documents (e.g., "Last, First, Middle Initial" name field, Last 4 SSN field, etc.) and to sign the documents. When the subject has signed the documents, they will click "FINISH" to finalize the documents.
3) While still on the phone or video with the subject, the consenter will receive an email notification to log into DocuSign. The consenter will verify that all fields are completed accurately and, subsequently sign the document(s) (e.g., ICF). The consenter will guide the subject on how to download a copy of the signed document(s) to the subject's personal computer for their record.
4) The consenter will download a copy of the signed document(s) to a study folder in the PI's VA secure Research drive for study records.
5) The consenter will document the consenting process as a "Research/Informed Consent" note in the subject's medical record (in CPRS). The note will specify that consent was obtained over phone/video and DocuSign on the specific date.

Section 12.5 Alteration of Other Required Elements of Consent

12.5) Identify the alteration to the required elements of informed consent and the justification for this approach.

The only aspect of informed consent that will be altered will be replacing discussion of the mPRO application to with LifeData application.

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 12.10 HIPAA Waivers and Alterations

12.10a) Describe the purpose/nature of the HIPAA waiver or alteration and list specifically, what identifiers and health information are being requested under the waiver/alteration and identify whether the waiver is for access, use, and/or collection of this information.

The HIPAA waiver will be needed to screen for inclusion and exclusion criteria before in-person contact. This will include identifiers (name, SSN) and health information (diagnoses). This is used only to assess the information.

12.10b) The proposed access, use, and/or disclosure of PHI involves no more than a minimal risk to the privacy of individuals.

(•) Agree ( ) Disagree

12.10c) The plan to protect the identifiers from improper use and disclosure is adequate.

(•) Agree ( ) Disagree

Describe the plan

The only hard copy will remain in a locked cabinet. Only Dr. Matthew Herbert, PI, will have access to the identifiers.

12.10d) An adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law.

(•) Agree ( ) Disagree

12.10d2) Describe the plan:

We will follow VA guidelines for destroying identifiers at the earliest opportunity consistent with

conduct of research.

12.10e) By signing this protocol for submission, the PI is providing written assurance that the PHI will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research for which the use or disclosure of protected health information would be permitted by the Privacy Rule. 38 U.S.C. 7332 Information: If the waiver of HIPAA authorization is for the use of 38 USC 7332 information (applicable to drug abuse, alcohol abuse, HIV infection, and sickle cell anemia records), by signing this protocol for submission the PI is providing written assurance that the purpose of the data is to conduct scientific research and that no personnel involved may identify, directly or indirectly, any individual patient or subject in any report of such research or otherwise disclose patient or subject identities in any manner. (Ref: 38 U.S.C. 7332(b)(2)(B))

(•) Agree ( ) Disagree

12.10f) The research could not practicably be conducted without the waiver or alteration.

(•) Agree ( ) Disagree

12.10f2) Describe how the waiver/alteration enables the research to be conducted

The waiver will enable the study team to assess for necessary inclusion and exclusion criteria to prevent scheduling Veterans who would be ineligible for the study.

12.10g) The research could not practicably be conducted without access to and use of the PHI.

(•) Agree ( ) Disagree

12.10g2) Describe why it would be impracticable to conduct this research without the PHI described 12.10a. (v3 /8/18)

Because inclusion and exclusion criteria can be found in PHI, it important to access. This will save time and resources for both Veterans and research staff.

Section 13 - Alternatives to Participation

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

Potential participants may seek care through the VA or in the community.

Section 14 - Potential Risks

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

At the initial assessment and other assessments for enrolled subjects, the interview questions and /or questionnaires may produce discomfort or anxiety from the discussion of personal, emotional, or anxiety-provoking topics. The methods used in the MAP and CBT-CP groups have been evaluated in prior studies with patients with chronic pain, and have been shown to be well-tolerated. Patient confidentiality will be protected to the extent permitted by law; however, there is always a risk of breach of confidentiality.

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.

The following steps are taken to minimize risk.

1) To minimize the risk of patient discomfort, confidentiality will be stressed, participants will be offered breaks as needed, they will be informed that they have the right to refuse to answer questions or to terminate their participation in the study at any time without prejudice, and everyone who interacts with participants will be trained and supervised. Clinical staff will be available if immediate in-person evaluation is required for medical or mental health issues.

2) To minimize the risk of patients becoming more anxious or depressed, every patient will be given a 24-hour contact phone number to call in the event of increased depression or anxiety. If these symptoms are detected by either the research coordinator, research assistant, or the person conducting the intervention, Dr. Autumn Backhaus, licensed psychologist and co-investigator, will be available to evaluate the patient and refer to appropriate treatment and notify the patient's other health care providers. When in doubt, the decision whether continued participation in the study is safe and clinically warranted will always be on the side of patient safety. Adverse events, including those unlikely to be the result of participation in the research (e.g., hospitalization due to an automobile accident), will be monitored at every study contact, including therapy as well as assessment sessions. They will be reported to the appropriate human subjects committees as per policy and to the Data Safety Monitoring Board for this study within the required time frame.

3) Veterans that report suicidal ideation at assessment or baseline/post-treatment assessment via the PHQ-9 or verbally will be further evaluated by the PI and Dr. Backhaus. Subsequent action will depend on the level of threat presented by the Veteran and may range from making a safety plan to implementing 5150 procedures for an inpatient hold. Further, suicidal ideation will be closely monitored during treatment by clinical observation and through comprehensive suicide risk assessments, which are part of standard VA care. Participants who develop suicidality during the treatment will be evaluated by the PI and Dr. Backhaus to determine whether continued participation in the study is safe and clinically warranted. If we and the participant believe that continued participation is contraindicated, an endpoint evaluation will be done and the participant will be referred for appropriate treatment. Appropriate treatment will depend on level of threat, and may include recommending a different form of psychotherapy that more directly addresses the predominant concern (e.g., depression, anxiety, PTSD, sleep, etc.), a referral to the participant's primary care provider or psychiatrist for medication management, referral to the Suicide Prevention Program at the VASDHS for passive suicidality, and/or hospitalization for imminent threat of suicide.

4) For participants who wish to terminate prematurely, we will request a final meeting to assess clinical status and safety and to review reasons for withdrawal (if the participant is willing to share them). Referrals for alternative mental health services, including those outside this protocol, will also be provided. Participants enrolled in the study may withdraw at any time without penalty or loss of any benefits or treatment options available to them. Investigators may also withdraw a participant from the study for treatment non-compliance or a newly developed psychiatric or medical problem if, in the opinion of myself and the study team, these factors interfere with the participant's ability to participate fully in the study. If a participant discontinues the study for any reason, he/she will be offered and allowed access to any care in our clinics that any other patient not associated with the study would receive.

5) Numerous steps will be taken to protect against social risks related to confidentiality. No personally identifiable information (PII) will exist on the intervention platform, the LifeData app, or with assessment data; data will be identified via subject ID number only. In addition, the intervention platform and LifeData dashboard utilize secure servers to protect participants' coded data and do not collect IP addresses (see Section 27.2d1). The master list linking ID numbers to participants' names will be stored locally on secure, restricted-access San Diego VA research servers in a password-protected database only accessible on password protected computers. Only IRB-approved research staff that has completed training in the handling of confidential data, and re-trained at least once annually, will have access to participant data and files. Last, no individual will ever be identified by name, audio recording, or other identifiers in professional presentations or manuscripts related to this study.

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)

Veterans may experience clinical improvement from participating in either intervention group (MAP or CBT-CP).

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.

Evidence from previous studies suggests that these interventions may reduce distress and improve quality of life. Some participants may also feel that they are making a useful contribution by furthering our understanding of how to treat chronic pain. We believe the benefits from this study outweigh its risks.

Section 20 - Compensation for Participation

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

For both phases, participants will receive $40 for the baseline assessment, $40 dollars for the post-treatment assessment, and $40 for the 3-month follow-up assessment. Additionally, participants in Phase 1, but not Phase 2, will receive $20 for the mid-treatment qualitative phone interview and $20 for the post-assessment qualitative phone interview.
During Phase 2, we will also compensate participants $1 each day they log a daily homework exercise during the study. Participants will be compensated up to $50 total for logging in all 50 days of homework.

Section 21 - Responsibilities and Qualifications

Here are the identified study staff members

Matthew S. Herbert, PhD

Ariel J. Lang, PhD, Autumn L. Backhaus, PhD, Niloofar Afari, PhD, Alexandra O. Higdon, PsyD, Andrea Naomi Henneken, James Manchanda, Suzanna R. Purpura, BS, Jennifer S. Salamat, Shahrokh Golshan, PhD, Erica Martinez, Mara E. Tynan, Joel N. Fishbein, PhD, Rosi Fedra Vera

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.

Matthew Herbert, PhD (UCSD and VASDHS) is the PI for this study. Dr. Herbert will be responsible for oversight of all scientific, logistical and financial aspects of the study and for securing and maintaining appropriate approvals. Further, Dr. Herbert will be the sole facilitator of the MAP intervention during both Phase 1 and Phase 2. He is a licensed clinical psychologist and is currently in the process of securing limited clinical privileges at the VASDHS.

Niloofar Afari, PhD (UCSD and VASDHS) is the primary mentor on this CDA award project. Dr. Afari will provide mentorship during all research activities, data collection, analyses, interpretation, and treatment modification.

Ariel J. Lang, PhD, MPH (UCSD and VASDHS) is a co-mentor on this CDA award project. Dr. Lang will serve as an expert in treatment modification (Phase 1) and clinical trials (Phase 2).

Autumn Backhaus, PhD (UCSD and VASDHS) is a co-mentor on this CDA award project. Dr. Backhaus will complete the qualitative phone interviews during Phase 1 and assist with qualitative data analyses. Further, as the Clinic Coordinator for the Behavioral Medicine and Primary Care clinics at the VASDHS, Dr. Backhaus will be a key source for referrals during both phases.

Jennifer Salamat, BS (VASDHS) will be the study coordinator on this study. Ms. Salamat has many years of experience coordinating studies at the VASDHS and will be responsible for

screening, administering assessments, data entry, and other office tasks.

Shahrokh Golshan, PhD (UCSD and VASDHS) is a Project Scientist in the UCSD Department of Psychiatry and the PI and Director of the Methodology, Biostatistics and Data Management (MBDM) Unit for the Advanced Center for Innovation in Services and Intervention Research. He will be responsible for developing and executing the analytic plan.

Alexandra Higdon, PsyD (VASDHS) is a licensed clinical Psychologist who will conduct the clinical interview (MINI) with Veterans, as well run treatment groups in the study.

Mara Tynan, B.A., is a graduate student in the SDSU joint doctoral program under the supervision of the PI. She will be aiding with administrative support and study coordination.

Erica Martinez (VASDHS WOC) Her duties will include study recruitment, data management/entry /collection, and obtaining informed consent.

Ms. Andrea Henneken is a current WOC at the San Diego VA. Ms. Henneken will be assisting with study screening, data management, study procedures, and informed consent.

Mr. James Manchanda is a current WOC at the San Diego VA. Mr. Manchanda will be assisting with study screening, data management, study procedures, and informed consent.

Ms. Suzanna Purpura is a current WOC at the San Diego VA. Ms. Purpura will be assisting with study screening, data management, study procedures, and informed consent.

Dr. Joel Fishbein is a VA postdoctoral fellow a the San Diego VA that will be assisting with study procedures and dissemination of study results.

Ms. Rosi Vera is a current WOC at the San Diego VA. Ms. Vera will be assisting with data management and other study procedures.

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.)

Affairs DoV: VHA Directive 2009-053: Pain Management. 2009

Baer RA, Smith GT, Hopkins J, Krietemeyer J, Toney L. Using self-report assessment methods to explore facets of mindfulness. Assessment. 13:27-45, 2006

Bellg AJ, Borrelli B, Resnick B, Hecht J, Minicucci DS, Ory M, Ogedegbe G, Orwig D, Ernst D, Czajkowski S. Enhancing treatment fidelity in health behavior change studies: best practices and recommendations from the NIH Behavior Change Consortium. Health Psychol. 23:443-451, 2004

Bieling PJ, Hawley LL, Bloch RT, Corcoran KM, Levitan RD, Young LT, Macqueen GM, Segal ZV. Treatment-specific changes in decentering following mindfulness-based cognitive therapy versus antidepressant medication or placebo for prevention of depressive relapse. J Consult Clin Psychol. 80:365-372, 2012

Borkovec TD, & Nau, S.D. Credibility of analogue therapy rationales. Journal of Behaviour Therapy and Experimental Psychiatry. 3:257-260, 1972

Bovin MJ, Marx BP, Weathers FW, Gallagher MW, Rodriguez P, Schnurr PP, Keane TM. Psychometric properties of the PTSD Checklist for Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition (PCL-5) in veterans. Psychol Assess. 28:1379-1391, 2016

Carmody J, Baer RA, Lykins ELB, Olendzki N. An empirical study of the mechanisms of mindfulness in a mindfulness-based stress reduction program. J Clin Psychol. 65:613-626, 2009

Cleeland CS, Ryan KM. Pain assessment: global use of the Brief Pain Inventory. Ann Acad Med Singapore. 23:129-138, 1994

Eccleston C, Williams AC, Morley S. Psychological therapies for the management of chronic pain (excluding headache) in adults. Cochrane Database Syst Rev.CD007407, 2009

Fox KC, Dixon ML, Nijeboer S, Girn M, Floman JL, Lifshitz M, Ellamil M, Sedlmeier P, Christoff K. Functional neuroanatomy of meditation: A review and meta-analysis of 78 functional neuroimaging investigations. Neurosci Biobehav Rev. 65:208-228, 2016

Hughes LS, Clark J, Colclough JA, Dale E, McMillan D. Acceptance and Commitment Therapy (ACT) for Chronic Pain: A systematic Review and Meta-analyses. Clin J Pain. 2016

Hayes SC, Strosahl K, Wilson KG: Acceptance and commitment therapy : the process and practice of mindful change. 2nd edition, Guilford Press, New York, 2012

Kabat-Zinn J. An outpatient program in behavioral medicine for chronic pain patients based on the practice of mindfulness meditation: theoretical considerations and preliminary results. Gen Hosp Psychiatry. 4:33-47, 1982

Krebs EE, Lorenz KA, Bair MJ, Damush TM, Wu J, Sutherland JM, Asch SM, Kroenke K. Development and initial validation of the PEG, a three-item scale assessing pain intensity and interference. J Gen Intern Med. 24:733-738, 2009

Larsen DL, Attkisson CC, Hargreaves WA, Nguyen TD. Assessment of client/patient satisfaction: development of a general scale. Eval Program Plann. 2:197-207, 1979

Lecrubier Y, Sheehan DV, Weiller E, Amorim P, Bonora I, Harnett Sheehan K, Janavs J, Dunbar GC. The Mini International Neuropsychiatric Interview (MINI). A short diagnostic structured interview: reliability and validity according to the CIDI. European Psychiatry. 12:224-231, 1997

McCraken, L. M., & Yang, S. (2006). The role of values in a contextual cognitive-behavioral approach to chronic pain. Pain, 123, 137-145.

Patel SR, Weng J, Rueschman M, Dudley KA, Loredo JS, Mossavar-Rahmani Y, Ramirez M, Ramos AR, Reid K, Seiger AN, Sotres-Alvarez D, Zee PC, Wang R. Reproducibility of a Standardized Actigraphy Scoring Algorithm for Sleep in a US Hispanic/Latino Population. Sleep. 38:1497-1503, 2015

Sullivan MJL, Bishop SR, Pivik J. The Pain Catastrophizing Scale: Development and validation. Psychol Assessment. 7:524-532, 1995

Spitzer RL, Kroenke K, Williams JB. Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. Primary Care Evaluation of Mental Disorders. Patient Health Questionnaire. JAMA. 282:1737-1744, 1999

Wetherell JL, Afari N, Rutledge T, Sorrell JT, Stoddard JA, Petkus AJ, Solomon BC, Lehman DH, Liu L, Lang AJ, Atkinson JH. A randomized, controlled trial of acceptance and commitment therapy and cognitive-behavioral therapy for chronic pain. Pain. 152:2098-2107, 2011

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.

Samantha Hurst, PhD (UCSD) is an expert in qualitative data analysis. She will provide guidance to the PI and help oversee qualitative assessments and analyses during Phase 1. She will not have any subject contact or access to identified data.

Pollyanna Casmar, PhD (UCSD and VASDHS) will assist the PI with protocol development and strategies to maximize participants adherence to formal meditation practice. She will not have any subject contact or access to identified data.

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.

Participants will be identified by subject numbers, which will be stored separately from coded data. Research team members will identify participants for purposes of communication about the study (scheduling, assessments), documentation (e.g., CPRS notes) and safety (e.g., identifying SAEs or AEs). Only staff with direct contact with participants will have access to identifies.

Interview responses may be recorded by the assessor from a remote location in an electronic format (electronic form behind the VA firewall).

Electronic research data will include responses on self-report assessment surveys. Research data will be collected by phone or the LifeData app and will be entered into an electronic data set stored on VA secure local research servers accessible only by authorized users on password-protected computers.

LifeData
Participants will receive a unique 5-digit LifeData ID to access the LifeData application. This 5-digit ID will be separate from the participant's study ID, ensuring separation of identifiers and data. A participant crosswalk that links the study ID and 5-digit LifeData ID to the participant's name and user name will be securely stored electronically in the study directory in a password-protected Excel document. Only research staff, approved by the IRB, can access the study directory.

Participants will use the LifeData mobile app to access guided meditation recordings (in the MAP group only) and log daily practice (both MAP and CBT-CP groups). Participants will download the app on their personal mobile device. When participants log into the app on their phones, participants will be given a unique 5-digit code (LifeData ID). De-identified data collected from the app are encoded and encrypted before it is sent to an encrypted storage database located in the US. Data are encrypted before being pushed to the storage database. No data are ever stored on the server's file server but always in the database. Once in the database, data are stored in an encrypted manner. Access to data is gated so entry is only permitted to users entering through the approved route (i.e., the database cannot be hacked into by guessing at the URL).

Additional steps to ensure confidentiality include: confidentiality training for research staff; identifying subjects by an arbitrary number; filing ID number key lists separately from data; omitting participant names from any forms; using an acronym in return addresses on any correspondence to participants; storing all data in locked file cabinets; securing all computers that store data; storing electronic data on secure servers behind firewalls. This study will use LifeData's "Anonymous Mode," which does not require participants to input a valid email address or any other identifiable information. All research staff will fulfill the educational requirements set forth by VA.

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:

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

27.1a1) Describe why SSN are needed for this study

Participant payment and chart access

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

27.1c1) Identify where images will be stored (e.g., in the medical record, with study hardcopy records, with study electronic VASI records).

PI's research drive

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.

As described in section 9.11, we use the Sony ICDPX312 Digital Voice Recorder to record treatment sessions, which is compliant with VHA regulations and often used at VASDHS for research and clinical purposes.

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

PI's research drive

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

27.2b1) Provide details of the device/s. Indicate whether the device is FIPS 140-2 encryption validated and confirm that the device is listed in the VA EIL. Provide details regarding the nature of the data that will be stored or transmitted on the device and confirm whether a copy of all data will be stored on the VA network.

Participants will have the option to use the LifeData mobile app to access guided meditation recordings and log daily practice (participants will also have option to access guided meditation via CD and log using paper and pencil, if they prefer). Participants will download the app on their personal mobile device. When participants log into the app on their phones, participants will be given unique 5-digit codes (LifeData ID). De-identified data collected from the app are encoded and encrypted before it is sent to an encrypted storage database located in the US. Data are encrypted before being pushed to the storage database. No data are ever stored on the server's file server but always in the database. Once in the database, data are stored in an encrypted manner. Access to data is gated so entry is only permitted to users entering through the approved route (i.e., the database cannot be hacked into by guessing at the URL).

Participants will be provided with a unique 5-digit LifeData ID to access the application, which will be distinct from participant's study ID, ensuring separation of identifiers and data. A participant crosswalk that links the study ID and 5-digit LifeData ID to the participant's name and user name will be securely stored electronically in the study R-drive in a password-protected Excel document. Only research staff, approved by the IRB, can access the study R-drive.

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

(●) Yes ( ) No

27.2c1) Provide the web address, details regarding their security features, the nature of the data involved, and the research purpose. Also include a description of how VA retains a copy of the data entered into the system.

Data collected on the LifeData mobile application are made accessible to the researchers only by directly accessing the secure site (https://server.lifedatacorp.com) and downloading the dataset as a CSV file. Data are encrypted in transmission with TLS 1.2 or greater. Datasets are never transmitted by email. Only study personnel communicating with Veterans (e.g., providing support for the mobile app; arranging appointments) will have direct access to identifiable data. Participants will be given the option of using Qualtrics to complete baseline and post-program questionnaires. Information about Qualtrics is available here: https://www.qualtrics.com and https://vhaordfedramp.gov1.qualtrics.com. Qualtrics enables accessible and user-friendly collection of patient-reported outcome survey data for research studies using remote procedures. Study participants are sent a link to a Qualtrics survey by study staff and can complete their survey on any internet-connected device with an internet browser. Qualtrics is accredited by FedRAMP, a government-wide initiative to protect sensitive data in federal agencies, ensuring gold standard security for data collected through Qualtrics. Further information can be found at https://qualtrics.com/platform/fedramp. Researchers will access participant data using the Qualtrics dashboard, and all data will be identified through a numeric participant code only. Only approved members of the research team have access to the secure dashboard. Research team members will export participant data from the dashboard directly to secure VA research servers (i.e., the R drive).

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).

Coded key will be stored on paper in a locked cabinet in a locked office and in a file separate from data on the PI's research drive.

A participant crosswalk that links the study ID and 5-digit LifeData ID to the participant's name and user name will be securely stored electronically in the study directory in a password-protected Excel document.

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

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.

VMRF room 242 in locked cabinet

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.

R:/Herbert

Data collected on the mobile application are made accessible to the researchers only by directly accessing the secure site (https://server.lifedatacorp.com) and downloading the dataset as a CSV file. Data will then be permanently deleted from the LifeData secure server.

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".

R:/Herbert

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

27.4b4) Describe the storage method (e.g., in a VA encrypted laptop) and security details, including the device /media location and ownership; describe backup procedures; identify the web applications; security features; and the nature of the data involved. Identify the rationale for needing to store data outside of the VA Network and describe the arrangement and authority (MOU, contract, other) to permit the arrangement.

Daily tracking of homework will be collected via a mobile device and temporarily stored on the LifeData secure sever. Participants' responses are always encrypted inside the app and as they travel from the participants' phones to the LifeData server. Their responses are also encrypted in the LifeData server. All data in the LifeData server is encrypted using several techniques that include AES 256 bit encryption and TLS encryption 2.0 or greater.

Data being transmitted from the participant's phone to the LifeData server is first encoded using Base 64 and then encrypted using AES 256 bit encryption. Synchronous and asynchronous SSL encryption is used
between the LifePak Builder and Manager (https://server.lifedatacorp.com), where assessment schedules
are created. The LifePak Builder and Manager can only be accessed after supplying a verified user ID and
password.

Once downloaded to VA computers, all digital files will be stored in the study directory in the secure VA network.

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 required 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.

None

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*