University of California, San Francisco Results Record # 21-34357,
Development and Feasibility of Mindfulness Based Pain Reduction

Mehling, Study Protocol, IRB approval July 28, 2022

# Study Application (Version 1.11)

## 1.0 General Information

| *Enter the full title of your study: | | |
|---|---|---|
| Feasibility Clinical Trial of Integrated Mind-Body Therapy for Chronic Low Back Pain | | |
| ***Enter the study alias:** | | |
| MBPR - Phase 2<br>* This field allows you to enter an abbreviated version of the Study Title to quickly identify this study. | | |

## 2.0 Add departments

**2.1 and Specify Research Location:**

| Is Primary? | Department Name |
|---|---|
| ○ | **UCSF** - *784050* - PSYCHIATRY |
| ◉ | **UCSF** - *101001* - M_Osher Center |

## 3.0 List the key study personnel: (Note: external and affiliated collaborators who are not in the UCSF directory can be identified later in the Qualifications of Key Study Personnel section at the end of the form)

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

Wolf Mehling MD, MD

☐ Department Chair ☐ Resident

☐ Fellow

If the Principal Investigator is a Fellow, the name of the Faculty Advisor must be supplied below.

**3.2 If applicable, please select the Research Staff personnel**

A) Additional Investigators

Hartogensis, Wendy E PhD
Other Investigator
Hecht, Frederick MD, MD
Co-Principal Investigator
Strigo, Irina PhD, PhD
VAMC Principal Investigator

B) Research Support Staff

Goldman, Veronica M
Study Coordinator
Menon Vinodkumar, Anitha
Study Coordinator
Murphy, Emily
Study Coordinator
Rogers, Kirsten, BA
Study Coordinator

**3.3 *Please add a Study Contact**

Goldman, Veronica M
Mehling, Wolf MD, MD
Rogers, Kirsten, BA

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).

**3.4 If applicable, please add a Faculty Advisor/Mentor:**

**3.5 If applicable, please select the Designated Department Approval(s)**

Add the name of the individual authorized to approve and sign off on this protocol from your Department (e.g. the Department Chair or Dean).

## 4.0 Initial Screening Questions

**Updated May 2021 - Revised Common Rule (January 2018) Compliant / COVID-19 - v97**

**4.1 * PROJECT SUMMARY: (REQUIRED) Give a brief overview of this project (250 words or less). Tell us what this study is about, who is being studied, and what it aims to achieve. If you have an NIH Abstract, paste it here (Click on the orange question mark to the right for more detailed instructions):**

We aim to develop and test an 8-week **MBPR (Mindfulness-Based Pain Reduction)** program, which draws on intervention work and clinical experience in the investigative team to optimize a mindfulness-based intervention for individuals with chronic pain. We hypothesize that this optimized intervention will be more effective than MBSR for cLBP. The overall goal of this study is to ensure that the MBPR program has been carefully refined and manualized in an in-person setting before performing clinical trials comparing MBPR to MBSR to test whether it improves pain outcomes. This study is funded by an R34 from NCCIH

This project also includes an ancillary brain imaging study designed to build on neuroscience reports of markedly decreased brain function and structure in the insular cortex (IC) of cLBP patients. This ancillary project has the potential to reveal a potential central mechanism by which mind-body and acceptance-based approaches improve chronic pain conditions, e.g. cLBP may

reveal a new paradigm for the treatment of cLBP with key importance and consequences for future behavioral treatment studies. The brain imaging is a separately funded study element, funded by a small ancillary grant through a U19 (PI Dr. Jeff Lotz; REACH study at UCSF as part of BACPAC nationwide) from NIAMS. The brain imaging will be done pre and post intervention at the VA by VA personnel and Dr. Irina Strigo as the VA PI.

**4.2 * HUD DEVICE: (REQUIRED) Does this application involve a Humanitarian Use Device (HUD):**

- (•) No
- ( ) Yes, and it includes a research component
- ( ) Yes, and it involves clinical care ONLY

**4.3 * TYPE OF RESEARCH: (REQUIRED) Select the option that best fits your project (Click the orange question mark to the right for definitions and guidance):**

- ( ) Biomedical research (including medical records review, biospecimen collection and/or use, other healthcare or health outcomes related activities, research database, biospecimen bank, or recruitment registry)
- ( ) Social, behavioral, educational, and/or public policy research
- (•) Hybrid - includes aspects of BOTH types of research (check this option if your research is mainly social/behavioral but also involves specimen collection or blood draws to look at biological measures)

**4.4 * SUBJECT CONTACT: (REQUIRED) Does this study involve ANY contact or interactions with participants:**

- (•) Yes (including phone, email or web contact)
- ( ) No (limited to medical records review, biological specimen analysis, and/or data analysis)

**4.5 * RISK LEVEL: (REQUIRED) What is your estimation of the risk level, including all screening procedures and study activities:**

- (•) Minimal risk
- ( ) Greater than minimal risk

**4.6 * REVIEW LEVEL: (REQUIRED) Requested review level (Click on the orange question mark to the right for definitions and guidance):**

- ( ) Full Committee
- (•) Expedited
- ( ) Exempt

**4.7 * EXPEDITED REVIEW CATEGORIES: (REQUIRED) If you think this study qualifies for expedited review, select the regulatory categories that the research falls under: (check all that apply)**

- [ ] Category 1: Research using approved drugs or devices being used for their approved indications
- [ ] Category 2: Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture in certain populations and within certain amounts
- [ ] Category 3: Prospective collection of biological specimens for research purposes by

noninvasive means (e.g. buccal swabs, urine, hair and nail clippings, etc.)

- [x] Category 4: Collection of data through noninvasive, routine clinical procedures (e.g. physical sensors such as pulse oximeters, MRI, EKG, EEG, ultrasound, moderate exercise testing, etc. - no sedation, general anesthesia, x-rays or microwaves)
- [ ] Category 5: Research involving materials (data, documents, records, or specimens) that have been or will be collected solely for nonresearch purposes
- [x] Category 6: Collection of data from voice, video, digital, or image recordings made for research purposes
- [x] Category 7: Research on individual or group characteristics or behavior or research employing survey, interview, oral history, focus group, program evaluation, human factorsevaluation, or quality assurance methodologies

**4.9 * DATA/SPECIMEN ANALYSIS ONLY: (REQUIRED) Does this study ONLY involve records review and/or biospecimen analysis (do not check 'Yes' if this is a registry, research or recruitment database, or biospecimen repository):**

○ Yes ◉ No

**4.10 * CLINICAL TRIAL: (REQUIRED)**
**Is this a clinical trial:**

**According to The World Health Organization (WHO) and the International Committee of Medical Journal Editors (ICMJE) a clinical trial is:**

- Any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes.

ICMJE requires registration of a clinical trial in a public database (such as ClinicalTrials.gov) prior to enrollment, for eventual publication of results in member biomedical journals.
**Guidance:** Public Law 110-85 requires that all investigators who perform an *applicable clinical trial* must ensure that the trial is registered on a government web site called **ClinicalTrials.gov**.

**The FDA requires registration for 'applicable clinical trials,' defined as follows:**

- For any trials of drugs and biologics: controlled clinical investigations, other than Phase 1 investigations, of a product subject to FDA regulation.
- For trials of biomedical devices: controlled trials with health outcomes of devices subject to FDA regulation, other than small feasibility studies, and pediatric post-market surveillance.

For additional information on the **ClinicalTrials.gov** registration process at UCSF and the definition of a clinical trial for purposes of registration, visit the **ClinicalTrials.gov section of the UCSF Clinical Research Resource HUB.**

◉ Yes ○ No

*** Clinical Trial Registration** - 'NCT' number for this trial: **(REQUIRED)**

04980612

**4.11 * CLINICAL TRIAL PHASE: (REQUIRED) Check the applicable phase(s):**

- [ ] Phase 0
- [ ] Phase 1
- [ ] Phase 1/2
- [ ] Phase 2
- [ ] Phase 2/3
- [ ] Phase 3
- [ ] Phase 4
- [x] Not Applicable

**4.12 * INVESTIGATOR-INITIATED: (REQUIRED) Is this an investigator-initiated study:**

- (•) Yes
- ( ) No

**The UCSF IRB recommends use of the Virtual Regulatory Binder to manage your study.**

**4.13 * CORONAVIRUS RESEARCH: (REQUIRED) Does this study involve research on coronaviruses (COVID-19, SARS, MERS or other):**

- ( ) Yes
- (•) No

**4.15 * CANCER: (REQUIRED) Does this study involve cancer (e.g., the study involves patients with cancer or at risk for cancer, including behavioral research, epidemiological research, public policy research, specimen analysis, and chart reviews):**

- ( ) Yes
- (•) No

**4.16 * RADIATION EXPOSURE: (REQUIRED) Does your protocol involve any radiation exposure to patients/subjects EITHER from standard care OR for research purposes (e.g., x-rays, CT-scans, DEXA, CT-guided biopsy, radiation therapy, or nuclear medicine including PET, MUGA or bone scans):**

- ( ) Yes
- (•) No

**4.17 * SCIENTIFIC REVIEW: (REQUIRED) If this study has undergone scientific or scholarly review, please indicate which entity performed the review (check all that apply):**

- [x] Funding agency, cooperative group, study section or other peer-review process
- [ ] Cancer Center Protocol Review Committee (PRC) (Full approval is required prior to final IRB approval for cancer-related protocols.)
- [ ] CTSI Clinical Research Services (CRS) Advisory Committee
- [ ] CTSI Consultation Services
- [ ] Other:
- [ ] Has not undergone scientific/peer review

* Specify entity that provided review: **(REQUIRED)**

This study was reviewed as a R34 grant application by NIH's National Center for Complementary and Integrative Health (NCCIH)

**4.18 * STEM CELLS: (REQUIRED) Does this study involve human stem cells (including iPS cells and adult stem cells), gametes or embryos:**

- (•) No
- ( ) Yes, and requires IRB and GESCR review
- ( ) Yes, and requires GESCR review, but NOT IRB review

**4.19 * FINANCIAL INTERESTS: (REQUIRED) Do you or any other responsible personnel (or the spouse, registered domestic partner and/or dependent children thereof) have financial interests related to this study:**

( ) Yes (•) No

## 5.0 Funding

**5.1 * FEDERAL FUNDING: (REQUIRED) Is this study currently supported in whole or in part by Federal funding, *even by a subcontract*, OR has it received ANY Federal funding in the past:**

(•) Yes ( ) No

**5.2 * DoD INVOLVEMENT: Is this project linked in any way to the Department of Defense (DoD): (REQUIRED)**

( ) Yes (•) No

**5.3 SPONSORS: Identify all sponsors and provide the funding details. If funding comes from a Subcontract, please list only the Prime Sponsor:**

### External Sponsors:

| View Details | Sponsor Name | Sponsor Type | Awardee Institution: | Contract Type: | Project Number | UCSF RAS System Award Number ("A" + 6 digits) |
|---|---|---|---|---|---|---|
| ⊟ | NIH Miscellaneous Other | 01 | UCSF | Grant | P1234567 | A136426 |

| | |
|---|---|
| Sponsor Name: | NIH Miscellaneous Other |
| Sponsor Type: | 01 |
| Sponsor Role: | Funding |
| **CFDA Number:** | |
| **Grant/Contract Number:** | |
| Awardee Institution:: | UCSF |

| | |
|---|---|
| **Is Institution the Primary Grant Holder:** | Yes |
| Contract Type: | Grant |
| Project Number: | P1234567 |
| UCSF RAS System Award Number ("A" + 6 digits): | A136426 |
| Grant Number for Studies Not Funded thru UCSF: | |
| Grant Title: | grant by NIH-NCCIH |
| PI Name:<br>(If PI is not the same as identified on the study.) | |
| Explain Any Significant Discrepancy: | |

⊟ NIH Natl Inst Arthr, Musculoskel & Skin 01 UCSF P0536633 A134160

| | |
|---|---|
| Sponsor Name: | NIH Natl Inst Arthr, Musculoskel & Skin |
| Sponsor Type: | 01 |
| Sponsor Role: | |
| Awardee Institution:: | UCSF |
| **Is Institution the Primary Grant Holder:** | No |
| **if No, then who is the Primary Grantee?** | |
| Contract Type: | |
| Project Number: | P0536633 |
| UCSF RAS System Award Number ("A" + 6 digits): | A134160 |
| Grant Number for Studies Not Funded thru UCSF: | |
| Grant Title: | ancillary funding provided by U19 REACH study (part of HEAL - BACPAC initiative of NIH, PI Jeff Lotz, PhD)<br>Dr. Mehling is the PI of the ancillary study: adding brain imaging to original R34 from NCCIH |
| PI Name:<br>(If PI is not the same as identified on the study.) | |
| Explain Any Significant Discrepancy: | The U19: Core Center for Patient-centric Mechanistic Phenotyping in Chronic Low Back Pain<br>Grant Number: U19-AR076737 |

## Other Funding Sources and Unfunded Research - Gift, Program, Departmental or other Internal Funding (check all that apply):

- ☐ Funded by gift (specify source below)
- ☐ Funded by UCSF or UC-wide program (specify source below)
- ☐ Specific departmental funding (specify source below)
- ☐ Unfunded (miscellaneous departmental funding)
- ☐ Unfunded student project

## 6.0 Sites, Programs, Resources, and External IRB Review

**6.1 * UCSF AND AFFILIATED SITES (check all that apply): (REQUIRED)**

- [ ] UCSF Benioff Children's Hospital Oakland (BCH OAK)
- [ ] UCSF Cancer Center Berkeley
- [ ] UCSF Cancer Center San Mateo
- [ ] UCSF China Basin clinics and facilities
- [ ] UCSF Helen Diller Family Comprehensive Cancer Center
- [ ] UCSF Langley Porter Psychiatric Institute (LPPI)
- [ ] UCSF Medical Center at Mission Bay (Benioff Children's Hospital, the Betty Irene Moore Women's Hospital, Bakar Cancer Hospital, or outpatient clinics)
- [x] UCSF Mount Zion
- [ ] UCSF Parnassus (Moffitt-Long hospital, dental clinics or other outpatient clinics)
- [ ] UCSF Other Sites (including Laurel Heights and all the other sites outside the main hospitals and clinics)
- [ ] Fresno - UCSF Fresno OR Community Medical Center (CMC)
- [ ] Gladstone Institutes
- [ ] Institute on Aging (IOA)
- [ ] Jewish Home
- [ ] SF Dept of Public Health (DPH)
- [x] SF VA Medical Center (SF VAMC)
- [ ] Vitalant (formerly Blood Centers of the Pacific and Blood Systems Research Institute)
- [ ] Zuckerberg San Francisco General (ZSFG)

**Research involving the SF VAMC: Please thoroughly review the Working with the SF VAMC webpage and/or consult the VA Research Office (V21SFCHRPP@va.gov or (415) 221-4810 x6425) prior to submitting your application to the IRB and:**

- **If this study involves both UCSF and the VA, identify who is serving as the VA PI under 'Descriptions of Study Responsibilities' in the 'Qualifications of Investigators' section at the end of this form**
- **Include the additional required VA forms in the Study Documents section of the Initial Review Submission Packet form**

**6.2 LOCATIONS: At what locations will study visits and activities occur:**

1) UCSF Osher Center for Integrative Medicine
2) San Francisco Veterans Affairs Medical Center

The only in-person study visits will occur at the SFVA for the MRIs. All other activities will occur online organized by staff at the UCSF Osher Center Participant involvement will be mostly online, using the Zoom platform.
Recruitment, questionnaires, and curriculum review will be done remotely by UCSF staff.
Document storage, data storage, data analysis will be done at both (1) and (2).
The intervention program will occur online and will be managed from UCSF Osher Center staff.
MRI scans will take place at the San Francisco Veterans Affair Hospital (2).

**6.3 OFF-SITE PROCEDURES: Will any study procedures or tests be conducted off-site by non-UCSF personnel:**

- ○ Yes
- ◉ No

**6.4 RESEARCH PROGRAMS: Check any UCSF research programs this study is associated with:**

- ☐ Cancer Center
- ☐ Center for AIDS Prevention Sciences (CAPS)
- ☐ Global Health Sciences
- ☐ Immune Tolerance Network (ITN)
- ☐ Neurosciences Clinical Research Unit (NCRU)
- ☑ Osher Center
- ☐ Positive Health Program
- ☐ Weill Institute for Neurosciences Translational Research Unit (WIN TRU)

**6.5 * CTSI CRS SERVICES: (REQUIRED) Will this study be carried out at one of the UCSF Clinical Research Services (CRS) units or utilize CRS services:**

- ○ Yes
- ◉ No

**6.6 * MULTI-CENTER TRIAL: (REQUIRED) Is this a multi-center or multi-site research trial:**

By '**multi-center trial**' we mean a study where the protocol is developed by an lead investigator, an industry sponsor, consortium, a disease-group, etc.,and multiple sites across the nation or in different countries participate in the trial. The local sites do not have any control over the design of the protocol.

- ○ Yes
- ◉ No

**6.8 OTHER SITE TYPES: Check all the other types of sites not affiliated with UCSF with which you are cooperating or collaborating on this project:**

**Do NOT check any boxes below if this is a multi-center clinical trial, UCSF is just one of the sites, and neither UCSF nor one of its faculty-linked affiliates (SF VAMC, Gladstone, ZSFG) are the coordinating center.**

- ☐ Other UC Campus
- ☐ Other institution
- ☐ Other community-based site
- ☐ Foreign Country
- ☐ Sovereign Native American nation (e.g. Navajo Nation, Oglala Sioux Tribe, Havasupai, etc.)

**6.14 * RELYING ON AN EXTERNAL IRB: (REQUIRED) Does this application include a request to rely on an external IRB (a central IRB (other than the NCI CIRB) or an external IRB (other UC campus, commercial, or institutional):**

○ Yes ◉ No

## 7.0 Research Plan and Procedures

**7.1 HYPOTHESIS: Describe the hypothesis or what the study hopes to prove:**

We aim to develop and test an 8-week **MBPR (Mindfulness-Based Pain Reduction)** program, which draws on intervention work and clinical experience in the investigative team to optimize a mindfulness-based intervention for chronic pain. We hypothesize that this optimized intervention will be more effective than MBSR (Mindfulness-Based Stress Reduction) for cLBP. The overall goal of this R34 is to ensure that the MBPR program has been carefully refined and manualized in an in-person setting before performing clinical trials comparing MBPR to MBSR to test whether it improves pain outcomes.

There are three hypotheses for the ancillary component of this project:

**Hypothesis 1**: Baseline pain attention style, as determined by the fMRI attention task (e.g. lower IC and higher DMN activity), is associated with (higher) pain interference post-intervention.

**Hypothesis 2**: IC-ACC connectivity will trend to improve from pre to post MBPR.

**Hypothesis 3**: Increased IC-ACC activity will be associated with improved pain interference.

**7.2 AIMS: List the specific aims:**

**Specific Aim 1:** To refine and manualize an 8-week **MBPR (Mindfulness-Based Pain Reduction)** program for patients with cLBP, integrating mindfulness with (1) interoceptive awareness, i.e. cultivating a direct, non-judgmental sensory attention focus on the location of their cLBP, (2) yoga practices targeting cLBP, and (3) elements of both chronic pain education and CBT, i.e., modifying maladaptive cognition and behavior. In Phase 1 we are convening a panel of behavioral and yoga therapists with expertise in chronic pain education and management to obtain expert advice on MBSR optimization and produce a first draft of the new MBPR manual.

**Specific Aim 2:** To refine **ecological momentary assessments (EMA) measures of key pain outcomes and mobile technology measures of adherence to MBPR home practice.** EMA is emerging as a key tool for measuring pain outcomes and home practice in clinical trials, but measures are poorly standardized and validated. We will compare pain questionnaires and EMA and ensure that an EMA measure is refined and vetted before use as a clinical trial outcome. We will test a meditation timer mobile app to measure adherence.

**The aims for the neuroimaging component of this project are as follows:**

**Aim 1:** To determine if attention style at baseline predicts treatment response.

**Aim 2:** To explore, whether MBPR improves a potential new biomarker for pain attention style: IC-ACC (anterior cingulate cortex) connectivity.

**Aim 3.** To explore if there is a preliminary association between treatment-related changes in IC-ACC connectivity (or IC activity) during immediate sensory attention to pain, and pain-related outcomes (outcomes are the same as for the BACPAC REACH studies).

**7.3 DESIGN: Briefly describe the study design (e.g., observational, interventional, randomized, placebo-controlled, blinded, cross-over, cross-sectional, longitudinal, pharmacokinetic, etc.):**

interventional for 4 iterations of the intervention, the last iteration as a randomized trial.

**7.4 BACKGROUND AND SIGNIFICANCE: Briefly provide the background and significance of this study (e.g. why is this study needed) (space limit: one half page):**

If this is a first in humans study, please summarize the safety data from the animal studies. For pediatric drug or device studies, please identify if this is the first study in pediatric populations.

**Treatment of chronic low back pain (cLBP) remains a major public health challenge.** cLBP is the leading cause of disability worldwide. Medication is of limited value. Current guidelines recommend using non-pharmacologic approaches for cLBP as the first-line approach. These approaches include exercise, multidisciplinary rehabilitation, acupuncture, yoga, tai chi, Mindfulness-Based Stress Reduction (MBSR), and Cognitive-Behavioral Therapy (CBT). Traditional first-line pharmacological therapies and physical therapy exercise are not superior to these currently recommended non-pharmacological therapies. All studied interventions have shown beneficial effects in randomized controlled trials (RCT), but only of moderate efficacy and often less than minimal clinically important improvement. There is thus a strong need for more effective non-pharmacologic treatments for cLBP, as well as other forms of chronic pain.

**Treatment of chronic pain needs to address central processing of pain.** Current research clearly shows that cLBP and other forms of chronic pain are not simply the result of nociceptive pain receptors signaling tissue damage, but involve extensive central nervous system processes. cLBP is a complex condition that involves the emotional psychology of the patient and properties of the emotional learning circuits as determinants of its prognosis. The learned emotional elements of pain and other aspects of central processing of pain signals are critical targets to address in chronic pain. Cognitive Behavioral Therapy (CBT) is the best-studied behavioral intervention for chronic pain, and recommended as first line treatment. It uses a structured approach that focuses on cognitions, emotions, and behaviors related to pain. It uses cognitive restructuring to help patients to evaluate, challenge and change thought content, beliefs and behavior. Coping skills include healthy distraction. However, benefits are modest. Moreover, distraction from pain is useful for acute pain but of uncertain benefit and not recommended for chronic pain.

**Mindfulness interventions are somewhat effective for pain, but need to be better optimized for managing pain conditions.** Studies of mind-body group interventions, e.g. **MBSR**, which teaches mindfulness and aims at changing the way we relate to thoughts, have shown modest benefits, quite similar to CBT group treatment. Perhaps the most important trial of MBSR for cLBP was a trial by Cherkin and colleagues that compared three treatment arms: (1) MBSR, (2) CBT, and (3) usual care. MBSR was clearly better than usual care; clinically meaningful improvement in pain bothersomeness at 26 weeks was 43.6% in the MBSR group, compared with 26.6% in the usual care group ($p$ =.01). However, MBSR was no better than CBT, in which 44.9% had clinically meaningful improvement in pain bothersomeness. *The lack of any evidence of better outcomes from MBSR compared to CBT clearly indicates there is room to improve outcomes from a mindfulness-based intervention for cLBP. This is further underlined by the fact that over half the study population failed to have clinically meaningful improvement in pain bothersomeness.*

In summary, current cLBP management, even with recommended behavioral interventions, is of modest effectiveness. **There is a strong need to develop more effective non-pharmacologic interventions.**

**7.5 PRELIMINARY STUDIES: Briefly summarize any preliminary studies relevant to your proposed research (space limit: one half page):**

The YoMA study: In a mechanistic single-arm study ($N$ =23) of a 12-week yoga intervention designed for cLBP, we found preliminary evidence that Body Listening, measured by the Multidimensional Assessment of Interoceptive Awareness (MAIA) increased from baseline to 6 weeks and predicted improved pain at 12 weeks (post intervention) ($\beta$ =-1.18; $p$ =0.02), whereas mindfulness scores (FFMQ) did not. Body Listening is a MAIA scale and a key element of self-reported interoceptive awareness, which we aim at fostering with MBPR.

In a study of Mindfulness-Based Cognitive Therapy (MBCT) in 31 patients with comorbid chronic pain and depression we found preliminary evidence that the positive effect of MBCT on depression

severity was partially mediated by Not-Distracting, measured by a MAIA scale indicating attention towards bodily sensations. We will use the updated version of the same self-report measure (MAIA-2) in our proposed study.

**7.6 * TREATMENT PROTOCOL: Is this a treatment study, i.e. does this study intend to provide treatment to individuals with a medical or psychological condition: (REQUIRED)**

(•) Yes ( ) No

**7.7 * BILLABLE PROCEDURES: Does this study involve any procedures, lab tests or imaging studies that have a CPT code and could be billable to patients, their insurance, Medi-Cal, Medicare, or any other entity (answer 'Yes' even if the study is going to pay for all the procedures): (REQUIRED)**

( ) Yes (•) No

**If you are not sure if your study involves billable procedures, send an email to the UCSF Office of Clinical Research (OCR) for help answering this question.**

**7.8 * COMMON RESEARCH ACTIVITIES: Types of research activities that will be carried out. Check all that apply and describe in more detail in the 'Procedures / Methods' section: (REQUIRED)**

- [x] Interviews, questionnaires, surveys
- [ ] Educational or cognitive tests
- [ ] Focus groups
- [ ] Social media-based research activities
- [x] Observation
- [ ] Fitness tests or other exertion activities
- [x] Use of mobile health apps or other apps
- [ ] Collection of data from wearable tech such as Fitbit, Apple Watch, Garmin, motion actigraphs, etc.)
- [x] Non-invasive imaging or testing (MRI, EEG, pulse oximetry, etc.)
- [ ] Imaging procedures or treatment procedures that involve radiation (x-rays, CT scans, CT-guided biopsies, DEXA scans, MUGA or PET scan)
- [ ] Administration of contrast agent
- [x] Randomization to one intervention versus another
- [ ] Use of placebo
- [ ] Biopsy conducted solely for research purposes
- [ ] Sham surgical procedure
- [ ] None of the above

**7.9 * PROCEDURES / METHODS: (REQUIRED)**

Describe the research methods and study activities taking place at each site (e.g. what will participants be asked to do and what will members of the study team do?). If there will be multiple participant groups or study sites, explain what will happen with each group or study sites.

If some of the activities would occur even if the person were not in the study, as in the case of treatment or tests performed for diagnostic purposes, **clearly differentiate between those activities that will be**

**done solely for research purposes and those that are happening as part of routine care.**

Please call our office at 415-476-1814 and ask to speak to someone on the Expedited Review team if you need help differentiating between what parts are research and what parts aren't.

At UCSF:

As we described in the application for Phase 1 of this study, **MBSR** is a standardized and manualized 8-week program, delivered once a week in 2½-hour group sessions and a daylong retreat. It trains individuals in several mindfulness practices, e.g. focus on breath, varying degrees and directions of object orientation, open monitoring of awareness of intero- and exteroceptive stimuli and thoughts, de-reification (i.e. the notion that thoughts and perceptions are not always true to reality), and meta-awareness (i.e., awareness of thinking) in addition to focused attention. The program typically includes an audio-recording and a book for home practice and has shown benefits in patients with cLBP.

**MBPR** will be an optimized mindfulness program specifically designed for treating cLBP that we aim to develop and test in this project. The format is the same as MBSR: 8 weeks of weekly 2½-hour group sessions and a daylong retreat in smaller groups: 10 participants per class to allow for more individualized support. All sessions include training to enhance mindful interoceptive awareness through focused attention in the region of pain, the lower back. Key goals are to reduce avoidance, rumination, catastrophizing, and fear of movement, all key mechanisms of action in MBSR or CBT. The new elements of these classes will include more pain-specific education and key elements of CBT, enhance mindful interoceptive awareness and an expanded yoga component, for which we will provide videos for home practice.

In addition, we will identify potentially eligible participants through review of our Medical Center's electronic medical records and send *letters inviting study participation using* the UCSF CTSI. Randomization for the final cohort will be performed using a computer-based assignment program, in which study staff must enter the participant ID number before randomization is revealed; assignment is then locked into the database. It will be stratified by sex, as responsiveness to mind-body interventions varies by sex. The UCSF study site of the ongoing NIH HEAL BACPAC initiative, for which both Drs Mehling and Hecht are key personnel, will create a large cohort of patients with cLBP (recruitment started June 2021), which can be approached for advertising our study.

MBPR will be delivered by an experienced mind-body practitioner with expert skills in mindfulness, MBSR and body awareness-enhancing approaches. Phase 1 includes a 2-day training retreat for the instructor led by Dr. Mehling to prepare the MBSR instructor for the MBPR program. Home practice will be supported by audio recordings uploaded to the Insight Timer® smart phone platform. The Insight Timer application will also be used to track and record the frequency in which participants are doing a meditaton practice in combination with a physical or electronic log. The instructor will use a workbook, audio recordings of guided meditation (these are standard recordings used e.g. in MBSR classes at the Los Angeles Insight Meditation Center), *Outsmart your Pain* by Christiane Wolf, MD, PhD, a guide book for mindfulness with pain, and videos of yoga sequences (as outlined in handout, attached). Study participants will receive additional printed and audio support material.

**Schedule of Measures:** Participants will be assessed using computer-assisted questionnaires in the first and last week of the MBPR courses and will be followed up at 6 months for clinical outcomes. In addition we will use a mobile platform-based EMA, as detailed below.

**Meditation home practice adherence measure:** *Rationale:* All participants will be instructed to do daily homepractice. Benefits of any mind-body intervention may depend on applying the class teaching to practice at home. Home practice for chronic conditions may need a higher dose than e.g. for experimental pain. We will request a minimum of 30 minutes for an expected effective duration of 20 minutes (>70%) on at least 5 days per week. *Methods:* Our research team has successfully used the free downloadable mobile app InsightTimer® to monitor adherence to home practices by asking participants to use it during home practice session. It has a variety of bell sounds that can be set for desired meditation time periods. The application includes two other features we have successfully tested at UCSF: 1) It connects with the research team in our study providing data about when and for how long a participant practiced meditation. 2) The app allows guided meditation recordings that we are preparing for home practice to be uploaded and made available to participants. Participants will log in with unique pseudonyms and a participant-specific e-mail address that is created for this study only to eliminate any risk to loss of privacy, which will be discussed during the consent process. Any identification of the

participating InsightTimer user will not be possible as the app will not use the personal e-mail of the participant and only use pseudonyms.

At the VA:

This study includes a Pain Attention Task to be preformed in the fMRI that separates insula activation during experimental heat application between different pain attention conditions.

The participants will be patients with cLBP according to the definition of the NIH Task Force on Research Standards for cLBP: pain at least half the days in the past 6 months, by using 2 questions and a human figure drawing illustrating the region between the lower posterior margin of the rib cage and the horizontal gluteal fold. Participants will have an average pain intensity in the past week of at least 4 out of 10 on the numeric rating scale (NRS). They will be recruited through advertisement in newspapers, social media and fliers, and from the current UCSF Spine Center cLBP cohort (see below).

**MRI Pain Attention Task:** The paradigm has 4 stimulus conditions presented in pseudo-random order. Individually determined, moderately painful (~47.5°C) stimuli will be delivered with a $9cm^2$ thermode (Medoc) securely placed at the forearm. Subjects are instructed and trained before scanning as follows: (A: thinking) for the 'think'- condition: "think about pain stimulus and your chronic pain, it's history and impact on your life, your expectation for your future life"; (B: sensing) for the 'feel'-condition: "feel the pain stimulus, be aware about how it makes you feel, its location, intensity and quality."; (C: metacognition) for the 'reflect'-condition: "please notice whether you can observe how thoughts and emotions regarding your pain arise that may be familiar, whether they are really appropriate or not"; and (D: default) for the 'none'-condition: "do nothing specific, just wait for the stimulus to be over". The instructing cues: think, feel, reflect, and none, will be presented for 1s, followed by 20s of painful heat stimulation, followed by 39s baseline with neutral temperature to minimize habituation/ sensitization, until the start of the next trial. 7 trials of each condition will be performed for each subject. The task will be administered in four 7-min sequences.

This task has been used in prior studies without any risks for the participant.

A total of 50 participants will be enrolled into this study. 40 participants with cLBP will be enrolled into 4 consecutive MBPR classes (*n* = 10 for each course)to iteratively refine the manualized MBPR protocol through mixed-methods evaluations after each round of MBPR. 10 participants with cLBP will be in the MBSR as the control group.

The first 30 participants enrolled in the study will be assigned to MBPR classes and the final 20 participants will be randomly assign with (*n* 10) participants assigned to MBSR and (*n* 10) participants assigned to MBPR to test recruitment and randomization approaches.

**7.10 STANDARD CLINICAL PRACTICE: To what extent, if any, do the planned research procedures differ from the care that people would otherwise receive at this institution or the study site if not being done locally:**

MBPR is based on MBSR, a program that is part of the national guidelines for treating chronic low back pain. MBSR programs are currently delivered regularly at the Osher Center at UCSF. The differences are described above and do not affect the burden or safety of participating patients with cLBP. Phase 1 of the study developed the manual and support materials and nears completion with this application. This application is for Phase 2, the implementation of MBPR with patients.

**7.11 INSTRUMENTS: List all questionnaires, surveys, interview, or focus group guides that will be used for this study:**

If the instruments are not complete or not available because they will be developed as part of this study, describe the basic content or include an outline and submit the final versions to the IRB with a modification for approval prior to use.

Questionnaires are identical to required instruments in the larger BACPAC study of the NIH HEAL Initiative.

1) BACPAC Baseline Demographics *Includes HEAL required questions* (22)* only at baseline. This includes questionnaire items necessary to adjust for MRI, e.g. to fit MRI-compatible correcting eye glasses.
2) PEG scale assessing pain intensity and interference (Pain, Enjoyment, General Activity) (3)*
3) Generalized Anxiety Disorder (GAD-2) *[Kroenke et al, 2007]* (2)*
4) Patient Health Questionnaire-2 (PHQ-2) *[Kroenke et al, 2003* **(2)***
5) Tobacco, Alcohol, Prescription medication, and other Substance use (TAPS) tool (4)*
6) PROMIS Physical Functioning Short Form 6b (2 items not in PROMIS-29)*
7) PROMIS Sleep Disturbance 6a *[Yu et al, 2011]* (2 items not in PROMIS-29)*
8) Sleep Duration Question *[Kurina et al, 2013]* (1)*
9) Pain Catastrophizing Scale - short form 6 (PCS) *[McWilliams, 2015]* **(6)***
10) Patient Global Impression of Change (PGIC) (1) only at 8 weeks.
11) PROMIS-29+2 Profile v2.1 (PROPr) 02Jan2020 *[PROMIS]* (31)*
12) Charlson Comorbidity Index (CCI), *[MDCalc (**https://www.mdcalc.com/charlson-comorbidity-index-cci**)]** baseline only
13) PainDETECT Questionnaire (PD-Q) *[Freynhagen et al., 2006]* (7)*
14) Fear-Avoidance Beliefs Questionnaire Physical Activity (FABQ-PA) *[Waddell et al., 1993]* (5)*
15) Chronic Pain Acceptance Questionnaire-SF8 *[Fish et al. 2010]* (8)*
16) Multidimensional Assessment of Interoceptive Awareness (MAIA) *[Mehling et al., 2018]* (37)
17) Perceived Stress Scale *[Cohen et al., 1989]* (4)*
18) International Positive (and Negative) Affect Schedule 10-item SF *[Watson et al., 1988]* (5)*
19) PROMIS Emotional Support 4a V2 *[Tucker et al, 2014]* (4)* only baseline
20) Pain Self-Efficacy Questionnaire 4-item version (items 4, 6, 8, 9) *[Chiarotto et al, 2016]* (4)*
21) Primary Care PTSD Symptom Screener *[Prins et al, 2016]* (1)* only baseline
22) Financial Strain *[Puterman et al, 2012]* (1)* only baseline
23) Perceived Discrimination *[NIMDH]* (1)* only baseline
24) Expectation of Pain Relief *[Cormier et al, 2016]* (1)* only baseline
25) Pain Anxiety Symptoms Scale - Short Form (PASS-20) - (items 6-10, 16-20) *[McCracken et al. 2002]* (10)*
26) Five Facets Mindfulness Questionnaire (FFMQ) *[Baer et al. 2006]* (39)
27) CHILD TRAUMA QUESTIONAIRE (CTQ) – SHORT FORM [Bernstein et al.1995]
28) Ecological Moment Assessment (EMA)
29) Semi-structured exit interviews
30) Qualitative questions at 6 months, 3 items

**Attach any unpublished instruments in the 'Other Study Documents' section of the Initial Review Submission Packet form after completing the study application. Published instruments should NOT be attached.**

**7.12 * BIOSPECIMEN COLLECTION: Are you drawing any blood or collecting other biosamples (e.g. tissue, buccal swabs, urine, saliva, hair, etc.) for analysis under this protocol and/or storage for future research: (REQUIRED)**

○ Yes ◉ No

**7.13 STATISTICAL METHODS: Briefly summarize the methods and types of analyses that will be performed:**

**Overall Analysis Approach:** Preliminary analysis will be performed to confirm that key data variables are clean and complete. Many of our outcomes will involve descriptive statistics, such as proportions and means calculated using standard methods. Recognizing the challenge of *missing data*, we will take concerted steps to limit missing data. We have extensive experience in study retention; in a current mindfulness study by Dr. Hecht ( R61-33 AT009333), outcome assessment was completed in 97% of participants at 12 weeks. If indicated, we will use mixed effects models, which are robust to the effects of missing data.

**7.14 REFERENCES: List only the 5-10 most relevant references (a separate bibliography can be attached for reference purposes if this study involves novel approaches, agents, or an emerging technology that the IRB may not be familiar with):**

1. Collaborators USBoD, Mokdad AH, Ballestros K, et al. The State of US Health, 1990-2016: Burden of Diseases, Injuries, and Risk Factors Among US States. *Jama*. Apr 10 2018;319(14):1444-1472. doi:10.1001/jama.2018.0158

2. Qaseem A, Wilt TJ, McLean RM, Forciea MA, Clinical Guidelines Committee of the American College of P. Noninvasive Treatments for Acute, Subacute, and Chronic Low Back Pain: A Clinical Practice Guideline From the American College of Physicians. *Annals of internal medicine*. Feb 14 2017;doi:10.7326/M16-2367

3. Apkarian AV, Baliki MN, Farmer MA. Predicting transition to chronic pain. *Curr Opin Neurol*. Aug 2013;26(4):360-7. doi:10.1097/WCO.0b013e32836336ad

4. Hashmi JA, Baliki MN, Huang L, et al. Shape shifting pain: chronification of back pain shifts brain representation from nociceptive to emotional circuits. *Brain : a journal of neurology*. Sep 2013;136(Pt 9):2751-68. doi:10.1093/brain/awt211

5. Butler DS, Moseley GL. Explain Pain, 2nd edition. *Noigroup Publications*. 2013;ISBN: 978-0-9873426-6-9

6. Farb NA, Daubenmier J, Price CJ, et al. Interoception, contemplative practice, and health. *Frontiers in psychology*. 2015;6:763. doi:10.3389/fpsyg.2015.00763

7. Vachon-Presseau E, Berger SE, Abdullah TB, Griffith JW, Schnitzer TJ, Apkarian AV. Identification of traits and functional connectivity-based neuropsychotypes of chronic pain. *bioRxiv preprint doi* ***http://dxdoiorg/101101/421438***. 2018

## 8.0 Drugs and Devices

**8.1 * DRUGS AND/OR BIOLOGICS: Are you STUDYING any drugs and/or biologics that are either approved or unapproved: (REQUIRED)**

○ Yes ◉ No

**If you have questions about FDA requirements for drug or device research, you can send an email to request a consult.**

**Note: This question is frequently answered incorrectly. If any drugs or biologics, approved or unapproved, are being administered under this protocol, you should check 'Yes' unless you are *absolutely* sure that NONE of the drugs are part of the research protocol. Tip: Ask the PI or the sponsor if you are not sure how to answer this question.**

**8.3 * MEDICAL DEVICES: Are you STUDYING any medical devices, in vitro diagnostics, or assays that are either approved or unapproved:(REQUIRED)**

○ Yes ◉ No

**If you have questions about FDA requirements for drug or device research, you can send an email to request a consult.**

## 9.0 Sample Size and Eligibility Criteria

**9.1 ENROLLMENT TARGET: How many people will you enroll:**

50

If there are multiple participant groups, indicate how many people will be in each group:

A total of 50 participants will be enrolled into this study. 40 participants with cLBP will be enrolled into 4 consecutive MBPR classes (*n* = 10 for each course). 10 participants with cLBP will be in the MBSR as the control group.

Specifically, the first 30 participants of the total 50 enrolled in the study will be assigned to MBPR classes and the final 20 participants will be randomly assigned to MBSR (*n* 10) or to MBPR (*n* 10) to test recruitment and randomization approaches.

**9.3 SAMPLE SIZE JUSTIFICATION: Explain how and why the number of people was chosen. For multi-site studies, this is referring to the number that will be enrolled across all sites:**

The primary goal of this study is to prepare for a rigorous RCT comparing efficacy of the MBPR intervention to alternatives. We are not aiming to test efficacy in the current study and do not have adequate sample size for this assessment. The proposed sample sizes were selected based on the numbers we estimate will be needed to adequately refine the intervention and assess its acceptability and feasibility, and to obtain variance estimates to inform future work. However, we will conduct **exploratory analyses** to obtain estimates of ICCs of the repeated measures from linear mixed models, and run linear mixed models with pain as outcome, and an interaction between study period and psychological variables (e.g. PCS-SF, FABQ-PA, and MAIA-2) as predictors, with nested random effects of person nested within class group. Although using all participants across all iterations of MBPR is limited by variations in the intervention, with a total MBPR sample size of 40 (out of 50 total enrolled, with a control/MBSR group of *n* 10), we will have 80% power (two-tailed alpha = 0.05) to detect a statistically significant correlation if the expected coefficient of determination is 0.43 or greater.

**9.4 * PARTICIPANT AGE RANGE: Eligible age ranges: (REQUIRED)**

- [ ] 0-6 years
- [ ] 7-12 years
- [ ] 13-17 years
- [x] 18-64 years
- [x] 65+

**9.5 * STUDY POPULATIONS: Data will be collected from or about the following types of people (check all that apply): (REQUIRED)**

- [ ] Inpatients
- [x] Outpatients
- [ ] Family members or caregivers
- [ ] Providers
- [ ] People who have a condition but who are not being seen as patients
- [ ] Healthy volunteers
- [ ] Students
- [ ] Staff of UCSF or affiliated institutions
- [ ] None of the above

**9.6 * SPECIAL SUBJECT GROUPS: Check the populations that may be enrolled: (REQUIRED)**

- [ ] Children / Minors
- [ ] Adult subjects unable to consent for themselves
- [ ] Adult subjects unable to consent for themselves (emergency setting)
- [ ] Subjects with diminished capacity to consent
- [ ] Subjects unable to read, speak or understand English
- [ ] Pregnant women
- [ ] Fetuses
- [ ] Neonates
- [ ] Prisoners
- [ ] Economically or educationally disadvantaged persons
- [x] None of the above

**9.7 INCLUSION CRITERIA: Briefly describe the population(s) that will be involved in this study. Include anyone that data will be collected from or about (e.g. patients, healthy controls, caregivers, providers, administrators, students, parents, family members, etc.):**

Inclusion criteria:

1. Chronic low back pain (cLBP) defined according to the NIH Research Task Force recommendation on Research Standards for cLBP: pain at least half the days in the past 6 months, by using 2 questions and a human figure drawing illustrating the region as the space between the lower posterior margin of the rib cage and the horizontal gluteal fold.

2. Average pain in the last month at least 3 out of 10 on Numeric Rating Scale [range 0 – 10, for 0 signifying no pain and 10 signifying worst pain imaginable]. This level of pain allows comparability of the study results with the majority of cLBP studies. Pain rated less than 3 is too mild to detect improvement.

3. Men and women aged 18 years old and older. We are not enrolling younger children as they are not part of the Intensive Pain Rehabilitation Therapy program.

4. Eligibility will be assessed using the following questions: "(1) How long has back pain been an ongoing problem for you? and (2) How often has low-back pain been an ongoing problem for you over the past 6 months?" A response of greater than three months to question 1, and a response of "at least half the days in the past 6 months" to question 2 would meet the cLBP eligibility criterion.

5. Ability to speak English. We do not have the capacity, given the resources available in this proposal, to translate all course material and conduct groups into another language. We have previously enrolled Hispanic participants into other studies who were fluent in English, and expect to do this in the proposed study.

6. Owning a smart phone (for EMA) and a computer (or tablet for Zoom participation in group)

7. Veteran subjects may be incidentally enrolled.

**INCLUSION OF CHILDREN**

Under NIH definition, all individuals under the age of 21 are considered children. Eligible participants who are 18 years of age or older will be recruited for this study. Younger children will not be included in this study because a pediatric sample may require different intervention approaches.

**9.8 EXCLUSION CRITERIA: List any exclusion criteria (e.g. reasons why someone would not be included in the study):**

Exclusion criteria:

1. Unable to provide informed consent.

2. A substance abuse, mental health, or medical condition that, in the opinion of investigators, will make it difficult for the potential participant to participate or that may need immediate changes in medical management that will affect study outcome measures. Such conditions may include cancer, diabetes, liver failure, renal failure, pain conditions from inflammatory diseases (e.g. rheumatoid arthritis, ankylosing spondylitis, lupus), malignancies or abdominal aortic aneurysm, muscle weakness from radiculopathy. Radiculopathy or sciatic pain is NOT excluded as long as the condition is stable and does not lead to significant movement restrictions or <4/5 muscle weakness. Persons with significant substance abuse or mental health conditions that interfere with social functioning may be disruptive. Oher medical or mental health conditions that need immediate changes in management need to be addressed before starting the study so that more reliable baseline measurements can be made. Patients who may need assessment for potentially necessary surgical interventions may not be able to complete the study. Regular opioid prescription is not an exclusion if stabile over the past 3 months.

3. Spine related current or history of spine fusion surgery, spine infection, spine tumor, vertebral fracture, cauda equina syndrome. Condition would increase heterogeneity of the sample.

4. Blindness, severe vision problems, deafness, severe hearing problems, bipolar or manic depression and not taking medication, major depression, psychoses (major), a substance abuse condition, dementia, unable to get up and down from the floor. Condition might make it difficult to participate.

5. Some other serious medical conditions that may alter key study outcomes, including untreated hypothyroidism, renal failure, and cirrhosis. Conditions that may alter key study outcomes.

6. Involvement in a lawsuit related to their back. Complicated medico-legal issues that could lead to individuals having a financial incentive to not report improvement.

7. Involved in Worker's Compensation claim.

8. Pregnant, breast-feeding, or planning to get pregnant in the next 12 months or less than 3 months post-partum. Particular back problems than may be associated with pregnancy and delivery may confound study outcomes.

9. Lack of stable housing or plan to move out of the area within the next 6 months.

10. MRI-related exclusion criteria: Cardiac pacemaker, metal fragments in eyes/skin/body (shrapnel), subjects who have ever been a metal worker/welder; history of eye surgery/eyes washed out because of metal, aortic aneurysm clips, prosthesis, by-pass surgery/coronary artery clips, hearing aid, heart valve replacement, subjects with an I.U.D, a shunt (ventricular or spinal), electrodes, metal plates/ pins/screws/wires, or neuro/bio-stimulators (TENS unit), vision problems uncorrectable with lenses, claustrophobia; inability to lie still on one’s back for approximately 60 minutes; prior neurosurgery; older tattoos with metal dyes; unwillingness to remove nose, ear or face jewelry, braces or permanent dental retainers. Iron-containing metal parts in the body can potentially be dislocated by strong magnetic fields and preclude assessment with MRI. As aging changes the brain, and in order to decrease variance in brain structure for the small study sample, MRI will only be done in participants not older than 65 years of age. If potential participants are excluded from the MRI due only to MRI exclusion criteria but pass study eligibility otherwise, they still are eligible for participation in the MBSR-MBPR study at UCSF but will not take part in the MRI assessment at the SFVA.

11. Received a steroid or botox injection in or near the spine in the last 3 months. This may alter key study outcomes.

12. Color-blindedness

13. Left-handedness

14. Enrollment in MBSR program within the last year

15. Current regular meditation practice consiting of 20 minutes of meditation or more.

**9.9 * RESEARCH CONDUCTED ON PATIENT CARE WARDS: Do any study activities take place on any patient care units including inpatient wards, peri- or post-operative care units, operating rooms, or in the Emergency Department at UCSF Health medical facilities: (REQUIRED)**

○ Yes ◉ No

**9.11 * EMERGENCY DEPARTMENT: Does your protocol or study involve any of the following patient related activities in the emergency department (e.g. subject identification, recruitment, consent, blood draws, specimen retrieval, involvement of ED staff (nursing, tech, and/or physician), or any other ED based procedures): (REQUIRED)**

○ Yes ◉ No

## 10.0 Recruitment and Consent

**10.1 * COMPETITIVE ENROLLMENT: Is this a competitive enrollment clinical trial? By competitive enrollment, we mean that sites who do not enroll participants early may not get to participate at all: (REQUIRED)**

○ Yes ◉ No

**10.2 * SUBJECT IDENTIFICATION METHODS: What kinds of methods will be used to identify potential participants for recruitment (check all that apply): (REQUIRED)**

- ☑ Review of patients' conditions, history, test results, etc. (includes patients seen in clinic, scheduled for surgery, a procedure, imaging, or tests, or seen in the Emergency Department as well as searching through medical record data for possible cohort identification)
- ☐ Already approved recruitment registry
- ☑ Re-contact of participants from the investigators' previous studies
- ☑ Referrals from colleagues (attach the 'Dear Colleague' letter or other recruitment materials you will provide to colleagues)
- ☑ Referrals from the community / word of mouth
- ☑ Advertisements (flyers, brochures, radio or t.v. ads, posting on clinical research sites or social media, presentation of the study at community events/media, etc.)
- ☑ Online recruiting tool (describe below)
- ☑ CTSI Recruitment Services unit
- ☑ Posting on UCSF Clinical Trials, ClinicalTrials.gov or other publicly available clinical trial website
- ☐ Other method (describe below)

**Attach your recruitment materials (e.g., flyers, ads, recruitment letter templates, email text, etc.) in the Other Study Documents section of the Initial Review Submission Packet Form.**

* Provide details about the subject identification methods: **(REQUIRED)**

Participants will be recruited through advertisement in newspapers, social media and flyers, and from the current UCSF Spine Center cLBP
cohort. In addition, we will identify potentially eligible participants through review of our Medical Center's electronic medical records and send letters inviting study participation
using a service available through the UCSF CTSI. The CTSI will be given ICD-10 codes applied to the APEX electronic medical records at UCSF of the the past 12 months: codes are M54.06, M54.07, M54.16, M54.17, M54.30, M54.31, M54.32, M54.50, M54.51 and send out MyChart notices to invite these patients to go to the study website to check for eligibility.

We plan to recruit both males and females. We anticipate that male/female ratio will match the gender, racial and ethnic composition of San Francisco county population.

At the UCSF Osher Center: We will hang out flyers in its clinic space and may contact participants in prior studies who have consented to be contacted for further studies.

ResearchMatch.org will be utilized as a recruitment tool for this protocol. ResearchMatch.org is a national electronic, web-based recruitment tool that was created through the Clinical &

Translational Science Awards Consortium in 2009 and is maintained at Vanderbilt University as an IRB-approved data repository.

* Did all the participants of previous studies provide permission to be contacted for future studies: **(REQUIRED)**

(•) Yes ( ) No

**10.3 * SEARCHING OF MEDICAL RECORDS: (REQUIRED)**

Whose patients are they:

- [ ] Investigators' own patients or patients seen within the same practice
- [x] Patients not under the care of the investigators

How and by whom will records be accessed and searched (check all that apply):

- [x] Self-search in APeX or other medical records source
- [x] Self-search using UCSF's Research Cohort Selection Tool
- [x] CTSI Consultation Service Recruitment Services
- [ ] UCSF Academic Research Services (ARS)
- [ ] University of California Research Exchange (UC ReX)
- [ ] Other method (describe below)

**10.4 DETERMINATION OF ELIGIBILITY: How, when, and by whom will eligibility for recruitment be determined:**

After making initial contact with the subject and prior to enrollment, eligibility screening will be conducted by trained research staff. Due to the extentive nature of the eligibility screening, participants will be asked to give verbal consent (see section 10.7) before the screen is conducted. If a potential subject is interested in participating and provides verbal consent, he or she will be asked a series of eligibility questions. If he/she meets initial requirements for preliminary eligibility and is interested in participating, the potential participant will be invited and potentially scheduled for a zoom-based appointment with the study team at the UCSF Osher Center.

Potential participants enrolled in REACH have passed the same eligibility criteria.

**10.5 * INITIATION OF CONTACT: Who initiates contact (check all that apply): (REQUIRED)**

- [x] Investigators/study team
- [x] UCSF recruitment unit (e.g. CTSI Consultation Services)
- [x] Potential participant
- [x] Other (explain below)

Provide details about how contact is initiated:

Investigator's colleagues in clinics (i.e. pain clinic; Osher Center clinic, Family Medicine Clinic, etc) may introduce study to potential participants and provide them with the study team's recruitment material(s) and/or contact information.

**Click here to review the process and rules for use of CTSI's Consultation Services for recruitment.**

**10.6 * HOW IS CONTACT INITIATED: (check all that apply): (REQUIRED)**

- [x] In person
- [x] Phone
- [x] Letter / email
- [x] Website or app
- [x] Other (explain below)

**Attach the telephone recruitment script in the Other Study Documents section of the Initial Review Submission Packet Form. If potential participants will initiate contact, attach the telephone screening script that will be used to provide more information about the study and determine if callers are eligible to participate.**

**Attach the recruitment letter or email template in the Other Study Documents section of the Initial Review Submission Packet Form.**

**Provide the URL for any website in Recruitment Plan section, or attach a mock-up of the website or the app screens in the Other Study Documents section of the Initial Review Submission Packet Form.**

**10.7 RECRUITMENT PLAN: Based on the checkboxes you chose above, please provide a narrative describing your recruitment plan. We want to know:**

- **Who is conducting the search for potential participants, and how?**
- **How are potential subjects being approached for recruitment? By whom, and when?**

**If there will be more than one participant group (e.g. patients, healthy controls, caregivers, family members, providers, etc.), provide details about the recruitment plans for each group. (Recommended length - 100-250 words)**

All recruitment is done by trained research staff who are assigned to this study, using aforementioned recruitment methods as well as methods listed below. Subjects can either contact the study staff, or study staff may contact the subject. The study team will not initiate contact with subjects by telephone unless they have received permission from the potential subject to be contacted by telephone. Permission is provided verbally (in the case of provider referrals), implied or written (in the case of VA approved research mailings), or explicitly by the potential subject. Initial contact by the study team must be in-person (including by phone and/or zoom) or by mail, unless the subjects initiates contact. Upon contact, subject will be given information about the study. They will then be asked if they are interested in participating and will be screened for eligibility.

In addition, we will identify potentially eligible participants through review of our Medical Center's electronic medical records and send *letters inviting study participation using* the UCSF CTSI.

Interested candidates who either 1) respond to recruitment solicitation and initiate contact with the study team via e-mail or phone or 2) who are approached by the study team directly will be given an overview of the study and its enrollment requirements, and will be initially screened by an online screener and telephone. If a potential participant is interested and meets initial requirements for participation, he/she will be invited for a zoom appointment with a trained staff member (CRC) at the UCSF Osher Center or the PI. This appointment, which will take place via zoom, will entail meeting with trained research personnel (CRC) who will describe the study in detail, address any questions/concerns, and obtain informed consent for study participation.

Recruitment strategies: Recruitment methods and media may include fliers; in-person presentations; a study specific webpage; informational letters; print newsletters; press releases or advertisements in print, internet, television, and radio, public service announcements; public

notice-board postings; contact with and referral from relevant clinicians; social media, pamphlets; informational sessions about the research. In clinical settings, care providers will also be given informational materials to distribute to potential candidates.

The above mentioned recruitment strategies will also take place at social service agencies, community mental health clinics, community organizations/events, including local professional organizations, consenting support and recovery centers, local hospitals and healthcare systems, regional employee assistance programs, religious organizations, cultural centers, public transportation vehicles and stations, social clubs, and universities.

Any recruitment materials (fliers, brochures, etc.) that will be used will be submitted to IRB for approval prior to use.

**10.8 * CONSENT METHODS: How will permission to participate (i.e., informed consent) be obtained from each potential participant. If there will be multiple groups and different plans for consenting each, check all that apply. See the orange Help bubble to the right for more detailed guidance. Participants will (check all that apply): (REQUIRED)**

- [x] Sign a paper consent form at the end of the consent discussion (signed consent)
- [x] Sign an electronic consent form using DocuSign (signed consent)
- [ ] Provide online consent through an app, a website, or a survey tool such as Qualtrics or REDCap (waiver of signed consent)
- [x] Be told about the study and be given a handout/information sheet and be asked if they agree to participate (verbal consent - waiver of signed consent)
- [ ] Complete the study activities and turn in materials, as in the case of a completed survey that is placed in a drop box or mailed to the study team (implied consent - waiver of signed consent)
- [ ] Not be able to provide consent and will have a family member consent for them, as in the case of a critically ill or unconscious patient (surrogate consent)
- [ ] Not able to provide consent (emergency medicine, greater than minimal risk waiver/alteration of consent - requires an approved community consultation plan)
- [ ] Not able to provide consent (emergency medicine, minimal risk waiver/alteration of consent)
- [ ] Not know about the study, as in the case of chart reviews or observations of public behavior (waiver of consent)
- [ ] Other method (describe below)

**Attach your consent form, information sheet, or electronic consent text in the Informed Consent Documents section of the Initial Review Submission Packet Form.**

**10.9 * CONSENT PROCESS: Describe the process for obtaining informed consent, including details such as who will have the consent discussion and when participants will be asked to sign the consent form in relation to finding out about the study: (REQUIRED) We encourage researchers to review our guidance on obtaining and documenting informed consent.**

- **If there are multiple groups being consented differently, provide details about the consent process for each group.**
- **If you are relying on verbal or implied consent, provide details about how that will happen.**
- **For studies using online recruitment and consent or consent via mail, provide details here.**

**Prior to eligibility determination (phone screening):**

In order to determine a subject's eligibility, a phone screening will be conducted. We will obtain verbal consent, as in-person consenting is not an option. Verbal consent is obtained by trained phone screeners. Verbal consent for phone screen is part of the phone screen itself.

**Prior to enrollment:**

After determining the subject is preliminarily eligible and prior to enrolling them in the study, the subject will receive consent documents by mail (with post-marked return envelop) or/and e-

mail. In a separate phone call or zoom meeting, trained research staff will obtain consent and go over the various sections of the consent documents, ensuring that the subject has comprehended the consent documents and does not have any questions. Participants will sign consent via docusign or mailed forms. We will send the consent forms by mail to those potential participants who are VA subjects. The UCSF DocuSign option will only be used for non-VA potential participants.

A total of 50 participants will be enrolled into this study. The first 30 subjects will be participate in the single arm MBPR study. The final 20 participants will be randomly assigned to MBSR (*n* 10) and to MBPR (*n* 10).

Randomization will be done by a computer-generated randomization program. Blinding is not necessary, as this is for assessing willingness to be randomized rather than an efficacy study comparing two interventions.

The VA research team will provide a copy of the HIPAA form to all participants to be signed in person by hand on paper before any SFVA study procedures (fMRI). This occurs at the SFVA when participants arrive for the MRI. The SFVA research team is fully trained in obtaining HIPAA signatures and signing consents.

UCSF-DocuSigned consent forms will be stored on secure UCSF Box. Veterans that sign consent on paper will send the signed consent form back to the UCSF team, which will scan the form and store it in the secure UCSF Box folder. The VA research team will have access to this secure UCSF Box folder and will be able to transfer the consent forms to store behind VA firewall on the secure R-drive. Any paper forms will be stored in secured, locked file cabinets at the SFVA Building 203 in room 1C12.

* It is important that the people obtaining consent are qualified to do so. Briefly describe the training and experience these individuals have in obtaining informed consent: **(REQUIRED)**

Only trained study staff will be obtaining consent from participants. These study staff will have gone through training with either the PI or the study coordinator. Training includes but is not limited to becoming familiar with consenting guidelines, mock consent practice, etc.

**10.10 * CONSENT COMPREHENSION: Indicate how the study team will assess and enhance the subjects' understanding of study procedures, risks, and benefits prior to signing the consent form (check all that apply): (REQUIRED) Tip: Review the Consent Comprehension - Learning Notes in the Help bubble at the right for specific questions that can be asked to assess comprehension, consider using the UCSF Decision-Making Capacity Assesment Tool, and review our guidance on obtaining written or verbal informed consent for more detail on how to conduct the assessment.**

- [x] The study team will engage the potential participant in a dialogue, using open-ended questions about the nature of the study or the experimental treatment, the risks and benefits of participating, and the voluntary nature of participation
- [x] Potential participants will be asked or shown a series of questions to assess their understanding of the study purpose, procedures, risks and benefits, as well as the voluntary nature of participation (especially appropriate when the consent process happens online or through a mobile health app)
- [ ] Other method (describe below):

Provide details of the other approaches that will be used, if using another method to assess comprehension:

N/A

**10.11 * DECEPTION: Does this study rely on some deception or misinformation about what the researchers are observing to get valid data? (REQUIRED)**

- ○ Yes
- ◉ No

**10.13 * WAIVER OF DOCUMENTATION OF SIGNED CONSENT: Select the regulatory category under which the IRB may waive the requirement to obtain *signed* consent for this study:**

○ The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether they want documentation linking them with the research. 46.117(c) (1)

◉ The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context. 46.117(c) (2)

**10.14 TIME: What is the estimated time commitment for participants (per visit and in total):**

First round of questionnaires (at home): **~60 minutes**

Informed Consent Discussion (via phone): **~30 minutes**

The study will include up to 2 in-person visits at the San Francisco VA Medical Center for fMRI; all other visits are vie zoom:

Visit 1 (fMRI) (at SFVAMC): **1 to 2 hours**

Initial check-in phone calls (phone or zoom) **~5-30 minutes eac**h depending on participant needs.

Visit 2 (MBPR Orientation Session; via zoom): **~2 hour**

Visit 3-10 (8 Classes MBPR Intervention; via zoom): **2 1/2 hours x 8**

Visit 11 (MBSR retreat day; via zoom): **6 hours**

Visit 12 (fMRI): **1 to 2 hours**

Second round of questionnaires (at home): **~60 minutes**

Potential Visit 5: qualitative interview: **~2 hours** (24 of the 50 participants)

Follow-up questionnaires at 6-months: **~60 minutes**

Total time involved with the study: **~ 33.6 to 38 hours over 9 - 10 weeks.**

The range is so wide, as it depends on the 2-hour exit interview (with 24 of the 50 participants).

**IMPORTANT TIP: Ensure this information is consistent with the information provided in the consent form.**

**10.15 ALTERNATIVES: Is there a standard of care (SOC) or usual care that would be offered to prospective participants at UCSF (or the study site) if they did not participate in this research study:**

○ Yes ◉ No

**10.16 OFF-STUDY TREATMENT: Is the study drug or treatment available off-study:**

- ○ Yes
- ◉ No
- ○ Not applicable

**10.17 OTHER ALTERNATIVES: Describe other alternatives to study participation, if any, that are available to prospective subjects:**

Participation is completely voluntary. Potential study participants may chose to not participate in the study and ask their primary care providers for pain management.

## 11.0 Waiver of Consent/Authorization for Recruitment Purposes

**This section is required when medical records may be reviewed to determine eligibility for recruitment.**

**11.1 * PRACTICABILITY OF OBTAINING CONSENT PRIOR TO ACCESS: Study personnel need to access protected health information (PHI) during the recruitment process and it is not practicable to obtain informed consent until potential subjects have been identified: (REQUIRED)**

- ◉ Yes

If **no**, a waiver of consent/authorization is NOT needed.

**11.2 * RISK TO PRIVACY: A waiver for screening of health records to identify potential subjects poses no more than minimal risk to privacy for participants:**

- ◉ Yes

If **no**, a waiver of authorization can NOT be granted.

**11.3 * RIGHTS/WELFARE: Screening health records prior to obtaining consent will not adversely affect subjects' rights and welfare:**

- ◉ Yes

If **no**, a waiver of authorization can NOT be granted.

**11.4 * IDENTIFIERS: Check all the identifiers that will be collected prior to obtaining informed consent:**

- ☑ Names
- ☑ Dates
- ☑ Postal addresses
- ☑ Phone numbers
- ☐ Fax numbers
- ☑ Email addresses
- ☐ Social Security Numbers*
- ☑ Medical record numbers
- ☐ Health plan numbers

- [ ] Account numbers
- [ ] License or certificate numbers
- [ ] Vehicle ID numbers
- [ ] Device identifiers or serial numbers
- [ ] Web URLs
- [ ] IP address numbers
- [ ] Biometric identifiers
- [ ] Facial photos or other identifiable images
- [ ] Any other unique identifier
- [ ] None

Note: HIPAA rules require that you collect the minimum necessary.

**11.5 * HEALTH INFORMATION: Describe any health information that will be collected prior to obtaining informed consent:**

No information will be collected prior to any form of consent.

To determine eligibility over the phone, information on MRI contraindications, general mental health, and physical health will be obtained to assess whether someone can complete the study. All information obtained before informed consent can be seen in the Eligibility Phone Screen, attached in Other Study Documents. All of the health information collected is necessary to determine eligibility. Because this information is collected prior to an in-person consent for eligibility purposes, a verbal consent will be obtained.

Note: HIPAA requires that you collect the minimum necessary.

**11.6 * DATA RETENTION/DESTRUCTION PLAN: Describe your plan to destroy any identifiable data collected to determine eligibility for recruitment. This should be done at the earliest opportunity. If you plan to retain identifiable recruitment data, provide the justification for doing so:**

All data collected for eligibility purposes is collected via RedCap or Qualtrics and will remain electronic throughout the course of the study. While this data will not be used for analysis, it will be preserved as it is used to contact potential future participants (upon their consent to do so). All retained data collected is behind the secure UCSF firewall.

Subject identifiers will be kept separately from the research data in locked cabinets and locked office at the UCSF Osher Center.
Participant data will also be stored on VA servers at the Center for Imaging of Neurodegenerative Diseases at the San Francisco VA.

## 12.0 Risks and Benefits

**12.1 RESEARCH-RELATED RISKS: Check if your study involves any of these specific research-related risks to participants that may need to be disclosed in the consent form:**

- [x] Physical discomforts or pain
- [ ] Risks to employment, or social or legal standing
- [x] Risk that the study team may observe possible evidence of child abuse, elder abuse, or a threat to self or others that they are required to report

For reportable information, include details of the reporting plan below. (See

the Help link for Mandated Reporter child and elder abuse resources.)

* For any boxes checked above, describe how you will minimize these risks and discomforts, e.g., adding or increasing the frequency of monitoring, additional screening to identify and exclude people with diminished kidney or liver function, or modification of procedures such as changing imaging studies to avoid giving contrast agent to people who are more likely to suffer side effects from it, etc.: **(REQUIRED)**

Data are password-protected and stored on secured UCSF PHI drive, only accessible on UCSF server. The computers will be checked regularly for proper and safe operation. Identifiable information is also stored as a hard copy in a locked office and locked file cabinet. Subjects will be carefully screened and subsequentially informed about the fact that the principal investigator will be available at all times during the experiment. Subjects are informed that they may end the test session at any time and that participation in this research is voluntary.

Subjects are told that all information obtained is completely confidential and that their medical treatment at UCSF or the VA will not be affected, whether or not they choose to participate in this study. Coded numbers are assigned to each file in the data base to ensure patient privacy. To minimize the risk that sensitive subject information may be disclosed, all subject information will be kept in locked cabinets or in databases with secured passwords.

Records and data will be rigorously protected. Examiners will be clinically trained and sensitive to signs of stress, anxiety, or fatigue so that testing will be immediately terminated should any subject experience signs of discomfort. Any incidental findings regarding subjects' health will be submitted to his/her physician at subjects' request.

**Reportable information:** Evidence of elder or child abuse, as well as threat to self or others, will be reported. Participants are notified of this in the verbal and in-person consents. If it is suspected that the subject is in danger of harming him/herself or someone else, or if child abuse or neglect or elder abuse has occurred, appropriate authorities will be notified as required by law.

**Self-report measures:** The main risks associated with these procedures are fatigue and irritability with the testing procedure. The investigator and research assistants are trained to frequently check the subjects about their willingness and ability to continue with the testing. If the subjects express concerns about continuing with the testing, the investigator has instructed the research assistants to stop testing, offer a break, or, in case the subject is not willing to continue, to terminate the testing session. Overall, however, previous comparable studies have not resulted in any significant discomfort or anxiety expressed by the participating subjects.

**Risks associated with functional magnetic resonance imaging:** According to the FDA, there is currently no evidence that MRI with approved scanners of up to 7 Tesla signal strength are associated with adverse effects. moreover, other fMRI centers across the country are regularly using up to 7T MRI scanners for research purposes. However, there are two major sources of risk. First, the subject may experience discomfort being in the confined and sometimes noisy environment of the scanner. Second, the strong magnetic field will affect electronic, magnetic, and metal devices that subjects carry with them or that have been implanted in the subject's body. Additionally, female subjects capable of child-bearing, will be asked a number of questions regarding their use of reliable contraceptive methods in order to be as sure as possible that they are not pregnant. Even though there are no known risks to an unborn child associated with fMRI, women of child-bearing potential who are not using reliable contraceptive methods will be excluded from this study.

**Data collection:** The risks involve some degree of loss of privacy. This will be minimized as much as possible, as described elsewhere in this application.

**Yoga:** it is possible that yoga exercises can cause discomfort or pain. To minimize potential side effects exercises instructed over the internet (interactive Zoom), a second yoga instructor (CRC Kirsten Rogers) will observe the participants and correct as needed. Furthermore: a questionnaire for medical spine conditions that would require more individual attention and exercise modification will be used before the first yoga session. Thereby exercises, although taught in a group, can be partially individualized, and the risk of injury can be reduced.

**12.2 * RISKS: Describe any anticipated risks and discomforts not listed above: (REQUIRED)**

See section 12.1.

**12.3** **MINIMIZING RISKS: Describe the steps you have taken to minimize the risks/discomforts to subjects. Examples include:**

- **designing the study to make use of procedures involving less risk when appropriate**
- **minimizing study procedures by taking advantage of clinical procedures conducted on the study participants**
- **mitigating risks by planning special monitoring or conducting supportive interventions for the study**
- **having a plan for evaluation and possible referral of subjects who report suicidal ideation**

All risks and steps to minimize those risks are described in section 12.1 above.

**12.5 * BENEFITS: (REQUIRED) Note: These are the benefits that the IRB will consider during their review. They are not necessarily appropriate to include in the consent form.**

Possible immediate and/or direct benefits to participants and society at large (check all that apply):

- [x] Positive health outcome (e.g. improvement of condition, relief of pain, increased mobility, etc.)
- [ ] Closer follow-up than standard care may lead to improved outcomes or patient engagement
- [x] Health and lifestyle changes may occur as a result of participation
- [x] Knowledge may be gained about their health and health conditions
- [x] Feeling of contribution to knowledge in the health or social sciences field
- [ ] The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children
- [ ] Other benefit (describe below)
- [ ] None

**12.6 RISK TO BENEFIT RATIO: Explain why the risks to subjects are reasonable in relation to anticipated benefits, if any, to the participant or society:**

Chronic Pain is a serious problem, as discussed in section 7.0. Since the risks are relatively small, we believe the potential benefits to society outweigh the risks to the subjects.

**12.7 * DATA AND SAFETY MONITORING: Do you have a Data and Safety Monitoring Plan (DSMP) for this study (A DSMP is required for Greater than Minimal Risk research): (Click the Help link for guidance on risk determination) (REQUIRED)**

(•) Yes ( ) No

**This is not required for minimal risk research but the UCSF IRB strongly recommends one to ensure the data collected are adequate to meet the research aims:**

## 13.0 Data and Safety Monitoring Plan

**13.1 * DATA AND SAFETY MONITORING PLAN (DSMP): (REQUIRED) Provide a summary of the DSMP:**

**All greater than minimal risk studies are required to provide a plan. Lack of an adequate plan is one of the most common reasons why IRB approval is delayed.**

## Instructions:

Describe the plan for monitoring data quality and participant safety. Key areas that should be included in the plan are:

- An explanation of the plan to monitor data collection, study progress, and safety
- A description of who will perform the monitoring and at what frequency (e.g., the PI only, a contract research organization, a Data and Safety Monitoring Board or Data Monitoring Committee, etc.)
- The type of data and events that will be reviewed (e.g., adverse events, breaches of confidentiality, unanticipated problems involving risk to participants or others, unblinded efficacy data, etc.)
- Procedures and timeline for communicating monitoring results to the UCSF IRB, the study sponsor, and other appropriate entities

As appropriate:

- A plan for conducting and reporting interim analysis
- Clearly defined stopping rules
- Clearly defined rules for withdrawing participants from study interventions

Data and Safety Monitoring Plan (DSMP)

This DSMP was reviewed and accepted by NIH-NCCIH

Independent Monitoring Committee

**Feasibility Clinical Trial of Integrated Mind-Body Therapy for Chronic Low Back Pain (**MBPR Study)

| | |
|---|---|
| **NIH Institute or Center:** | National Center for Complementary and Integrative Health |
| **Grant Number:** | R34AT010921-01A1 |
| **Version Date:** | 10/02/2020 |
| **Version Number:** | 1 |

# 1 STUDY OVERVIEW

1. Purpose of Study

The overall goal of this project is to developing a modified version of Mindfulness-Based Stress Reduction (MBSR) that we believe will prove to be more effective for chronic low back pain. Following the initial protocol development informed by a panel of international experts, 4 x 10 = 40 participants will undergo 8-week Mindfulness-Based Pain Reduction (MBPR) classes that are iteratively improved through participant feedback. This study will enroll a total of 50 individuals with chronic low back pain, which includes a control group of 10 participants that will receive MBSR.

2. Adherence Statement

The Data Safety Monitoring Plan (DSMP) outlined below will adhere to the protocol approved by the UCSF IRB**.**

All protocol amendments, other than minor administrative changes as defined by the NCCIH Guidance on Changes in Clinical Studies in Active Awards will be submitted in a prospective manner to NCCIH except when necessary to protect the safety, rights, or welfare of subjects. IRB-approval will not be sought until after NCCIH approval of the protocol amendment has been obtained.

# 3 CONFIDENTIALITY

## 3.1 Protection of Subject Privacy

Subject confidentiality is strictly held in trust by the investigators, study staff, and the sponsor(s) and their agents. This study does not include testing of biological samples and genetic tests in addition to any study information relating to subjects.

The study monitor or other authorized representatives of the sponsor may inspect all study documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) for the study subjects. The clinical study site will permit access to such records.

## 3.2 Confidentiality During Adverse Event (AE) Reporting

AE reports and annual summaries will not include subject or group-identifiable material. Each report will only include the identification code.

# 4 EXPECTED RISKS

**4.1 Behavioral / Psychological Questionnaires:** These carry a minimal risk for emotional discomfort and stress.

**4.2 Post-Intervention Interviews**: These carry a minimal risk for emotional discomfort and stress.

**4.3 Privacy:** Participating in the study may result in a loss of privacy because the intervention is administered in a group setting. Participants will be asked not to share information related to other individuals when they are outside of class, but this cannot be guaranteed. Questionnaires will include background medical information and psychological scales and all research data will be stored on the secured web-based Research Electronic Data Capture (REDCap) and Qualtrics systems. Subjects are informed that they are free to refuse to participate in any stage of the work and can refuse to answer specific questions or questionnaire items if they wish.

**4.4 Unexpected Events**: A physician is present or on call during all study procedures, and will be available if a participant experiences suicidal ideation or other mental health problem. All subjects will be provided with contact numbers in case distress arises following the experiment or intervention.

**4.5 Yoga-type movements and postures as a component of MBPR/MBSR:** Yoga has been found to be relatively safe in a number of large-scale randomized trials however any exercise program may result in muscle soreness or strains. Adverse events do occasionally occur and it is important that participants report any injuries to study staff. To improve safety, all participants will complete a pre-intervention assessment.

Prior to the start of MBPR/MBSR classes participants will be evaluated to determine if their pain worsens with flexion or extension. We will monitor pain levels during physical exercises. Classes are much smaller than common MBSR classes (10 participants instead of 15-25) and instructors are better able to help participants with individual adjustments and advice.

Finally, for those doing yoga-type exercises and postures, several minor adverse effects may occur and include increased low back pain intensity, muscle strain or sprain, or dizziness and are generally of short duration and alleviated by local physical measures (such as ice) and physical rest. They will be thoroughly addressed in the intervention.

**4.6 Fluctuations in Pain Levels:** Study physician Dr. Mehling will weekly review the class reports and videos. He will be available by cell phone for more urgent problems between in-person consultations. Primary care physicians for each participant will receive information about the study before the participant begins the study. Study physician will help to make sure that primary care physicians are informed of any medical changes, and will consult with primary care physicians where indicated.

**4.7 MBPR and MBSR:** Similar interventions have been used with thousands of persons, including many with serious illness and pain conditions, and there have not been important adverse events reported to our knowledge. Participants can experience restlessness during the meditation practices or become aware of distressing emotions and traumatic memories. Our instructors are highly trained and experienced and will immediately inform the study physician, who will determine whether referral to behavioral medical care is warranted.

**4.8 Home Exercise Components:** Participants will be requested to do yoga-style exercises at home. Some people may experience initial discomfort when increasing their level of physical activity. There may also be a slight increase for physical risks when partaking in exercise activities. There are minor risks of injury during exercise, but these risks are minor and far out-weighed by the potential benefits of exercise.

4.9 Audio/Video-Taping Instructors During Classes: classes will be audio-videotaped to ensure intervention fidelity and provide feedback and troubleshooting for instructors. Some participants may experience a level of discomfort while being recorded during class. Although the recorders will be placed in front of the class to record the instructors' voice, there is a strong likelihood that some of the participants' movements and voices will be recorded. They may also feel that they are being monitored. Participants will be informed of the recording, and can sit farther from the microphone if they desire. Recordings will be kept on a HIPAA-compliant research network drive with password-restricted access limited to study staff. Recordings will be destroyed once the study is complete. Adverse event/ unanticipated problems

# 5 ADVERSE EVENT/ UNANTICIPATED PROBLEMS

## 5.1 Definitions

### 5.1.1 *Adverse Event (AE)*

An adverse event (AE) is any untoward medical occurrence in a subject during participation in the clinical study or with use of the experimental agent being studied. An adverse finding can include a sign or symptom, or any combination of these regardless of relationship to participation in the study.

### 5.1.2 *Unanticipated Problems (UP)*

The Office for Human Research Protections (OHRP) considers unanticipated problems involving risks to subjects or others to include, in general, any incident, experience, or outcome that meets **all** of the following criteria:

- Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
- Related or possibly related to participation in the research ("possibly related" means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

### 5.1.3 *Serious Adverse Event (SAE)*

Serious adverse events (SAEs) are a subset of all Adverse Events (AEs). A serious adverse event (SAE) is one that meets one or more of the following criteria:

- Results in death
- Is life-threatening (places the subject at immediate risk of death from the event as it occurred)
- Results in inpatient hospitalization or prolongation of existing hospitalization
- Results in a persistent or significant disability or incapacity
- Results in a congenital anomaly or birth defect

An important medical event that may not result in death, be life threatening, or require hospitalization may be considered an SAE when, based upon appropriate medical judgment, the event may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

## 5.2 Time Period and Frequency for Event Assessment and Follow-Up

Unanticipated problems will be recorded in the data collection system throughout the study.

The PI will record all reportable events with start dates occurring any time after informed consent is obtained until 7 (for non-serious AEs) or 30 days (for SAEs) after the last day of study participation. At each study visit, the investigator will inquire about the occurrence of AE/SAEs since the last visit. Events will be followed for outcome information until resolution or stabilization.

## 5.3 Characteristics of an Adverse Event

### 5.3.1 *Relationship to Study Intervention*

To assess relationship of an event to study intervention, the following guidelines are used:

1. Related (Possible, Probable, Definite)
    a. The event is known to occur with the study intervention.
    b. There is a temporal relationship between the intervention and event onset.
    c. The event abates when the intervention is discontinued.
    d. The event reappears upon a re-challenge with the intervention.

2. Not Related (Unlikely, Not Related)
    a. There is no temporal relationship between the intervention and event onset.
    b. An alternate etiology has been established.

### 5.3.2 *Expectedness of SAEs*

The Study PIs and Independent Monitoring Committee will be responsible for determining whether an SAE is expected or unexpected. An adverse event will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information

previously described for the intervention.

### 5.3.3 *Severity of Event*

The following scale will be used to grade adverse events:

1. Mild: no intervention required; no impact on activities of daily living (ADL)
2. Moderate: minimal, local, or non-invasive intervention indicated; moderate impact on ADL
3. Severe: significant symptoms requiring invasive intervention; subject seeks medical attention, needs major assistance with ADL

## 5.4 Reporting Procedures

Serious Adverse Event reporting will be in accordance with the UCSF- Committee on Human Research Regulations and Code of Federal Regulation Title 21 Volume 5 Part 312.32.

We will also follow the UCSF IRB website for guidance in reporting serious adverse events ***https://irb.ucsf.edu/adverse-event***.

### 5.4.1 *Unanticipated Problem Reporting*

Incidents or events that meet the OHRP criteria for unanticipated problems require the creation and completion of an unanticipated problem report form. OHRP recommends that investigators include the following information when reporting an adverse event, or any other incident, experience, or outcome as an unanticipated problem to the IRB:

- Appropriate identifying information for the research protocol, such as the title, investigator's name, and the IRB project number;
- A detailed description of the adverse event, incident, experience, or outcome;
- An explanation of the basis for determining that the adverse event, incident, experience, or outcome represents an unanticipated problem;
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the unanticipated problem.

To satisfy the requirement for prompt reporting, unanticipated problems will be reported using the following timeline:

- Unanticipated problems that are serious adverse events will be reported to the IRB, Independent Safety Monitor(s), and NCCIH within 5 working days of the investigator becoming aware of the event.
- Any other unanticipated problem will be reported to the IRB, Independent Safety Monitor(s), and NCCIH within 10 working days of the investigator becoming aware of the problem.

All unanticipated problems should be reported to appropriate institutional officials (as required by an institution's written reporting procedures), the supporting agency head (or designee), and OHRP within one month of the IRB's receipt of the report of the problem from the investigator.

### 5.4.2 *Adverse Event Reporting of Non-IND Studies*

SAEs that are unanticipated, serious, and possibly related to the study intervention will be reported to the Independent Safety Monitor(s), IRB, and NCCIH in accordance with requirements.

- Unexpected fatal or life-threatening AEs related to the intervention will be reported to the NCCIH Program Officer, and Independent Safety Monitor(s) within 3 days of the investigator becoming aware of the event. Other serious and unexpected AEs related to the intervention will be reported within 5 working days.
- Anticipated or unrelated SAEs will be handled in a less urgent manner but will be reported to the Independent Safety Monitor(s), IRB, and other oversight organizations in accordance with their requirements. and will be reported to NCCIH on an annual basis.
- All other AEs documented during the course of the trial will be reported to NCCIH on an annual basis by way of inclusion in the annual report and in the annual AE summary which will be provided to NCCIH and to the Independent Monitors. The Independent Safety Monitor(s) Report will state that all AEs have been reviewed.

5.5 HALTING RULES

Review of any serious, unexpected, and related AEs by the Medical Monitor, DSMB/ Independent Safety Monitors, IRB, the sponsor, or relevant local regulatory authorities may result in suspension of further study interventions/administration of study product at a site. The study sponsor retains the authority to suspend additional enrollment and study interventions/administration of study product for the entire study, as applicable.

6 QUALITY CONTROL AND QUALITY ASSURANCE

We will develop standard operating procedures (SOPs) that will describe:

- Staff training methods and how such training will be tracked: All key study personnel and those involved in obtaining consent will maintain updated CITI human subjects training. This will be tracked and reviewed by the Project Director yearly or more frequently, with submission of each IRB modification or renewal (i.e. at least yearly).
- How data will be evaluated for compliance with the protocol and for accuracy in relation to source documents.
- The documents to be reviewed (e.g., CRFs, attendance lists, questionnaires, audio or video recordings), who is responsible, and the frequency for reviews.
- Who will be responsible for addressing quality assurance issues (correcting procedures that are not in compliance with protocol) and quality control issues (correcting errors in data entry). It is anticipated that QA review and data verification will be performed by someone other than the individual originally collecting the data, or by double-data entry. The frequency of internal QA review and measures to be taken for corrective action, e.g., for trends in errors, should be included. A statement reflecting the results of the ongoing data review will be incorporated into the Annual Report for the Independent Safety Monitor(s).

## 6.1 Subject Accrual and Compliance

### 6.1.1 *Measurement and Reporting of Subject Accrual*

Review of the rate of subject accrual and compliance with inclusion/exclusion criteria will occur monthly during the recruitment phase to ensure that a sufficient number of participants are being enrolled, in keeping with proposed recruitment projections, and that they meet eligibility criteria and fulfill the targeted ethnic diversity goals outlined in the grant proposal (Targeted/Planned Enrollment Table).

### 6.1.2 *Measurement and Reporting of Participant Adherence to Treatment Protocol*

Data on adherence to the treatment protocol will be collected weekly by research staff and reviewed monthly by the PI (Dr. Mehling). Adherence of participants will be evaluated by attendance list. Available data on adherence to all three indices using an earlier version of the study intervention suggests that 20% or fewer participants had poor adherence. If adherence falls below the suggested rate, which might inhibit the ability of the study to test its primary hypotheses, the PI will suggest a conference call for study investigators to discuss methods for improving adherence.

## 6.2 Justification of Sample Size

The primary goal of this study is to prepare for a rigorous RCT comparing efficacy of the MBPR intervention to alternatives. We are not aiming to test efficacy in the current study and do not have adequate sample size for this assessment. The proposed sample sizes were selected based on the numbers we estimate will be needed to adequately refine the intervention and assess its acceptability and feasibility, and to obtain variance estimates to inform future work. However, we will conduct **exploratory analyses** to obtain estimates of ICCs of the repeated measures from linear mixed models, and preliminary estimates looking at Pearson correlations between changes in pain outcomes and changes in psychometric scale measures that we understand to be potential mediators of change in pain intensity following mindfulness interventions, e.g. PCS-SF, FABQ-PA, and MAIA-2. Although using all participants across all iterations of MBPR is limited by variations in

the intervention, with an exploratory total MBPR sample size of 40, we will have 80% power (two-tailed alpha = 0.05) to detect a statistically significant correlation if the expected Pearson correlation coefficient comparing change scores for pain outcomes with change scores for psychometric scale measures is 0.43 or greater. If we experience a loss to follow-up rate of 10% in our classes, the sample size per subsequent class will be increased to 11 subjects.

## 6.3 Stopping Rules

This study will be stopped prior to its completion if: (1) the intervention is associated with adverse effects that call into question the safety of the intervention; (2) difficulty in study recruitment or retention will significantly impact the ability to evaluate the study endpoints; (3) any new information becomes available during the trial that necessitates stopping the trial; or (4) other situations occur that might warrant stopping the trial.

## 6.4 Designation of a Monitoring Committee

The Independent Monitoring Committee for this study is comprised of Drs. Zeidan (UCSD), Saper (Boston University), and Lazar (Harvard University). Drs. Zeidan, Saper, and Lazar are not associated with this research project and work independently of the PIs, Dr. Mehling and Dr. Hecht. They are not part of the key personnel involved in this grant. No member of the Committee has collaborated or co-published with the PI within the past three years. They are qualified to review the patient safety data generated by this study because of their unique expertise.

## 6.5 Safety Review Plan

Study progress and safety will be reviewed monthly (and more frequently if needed). Progress reports, including patient recruitment, retention/attrition, and AEs will be provided to the Independent Monitors semi-annually. An Annual Report will be compiled and will include a list and summary of AEs. In addition, the Annual Report will address (1) whether AE rates are consistent with pre-study assumptions; (2) reason for dropouts from the study; (3) whether all participants met entry criteria; (4) whether continuation of the study is justified on the basis that additional data are needed to accomplish the stated aims of the study; and (5) conditions whereby the study might be terminated prematurely. The Annual Report will be sent to the Independent Monitors and will be forwarded to the IRB and NCCIH. The IRB and other applicable recipients will review progress of this study on an annual basis

## 6.6 Study Report Outline for the Independent Monitors(s) (Interim or Annual Reports)_

The study team will generate Study Reports for the Independent Monitors and will provide information on the following study parameters: Accrual, demographics, study subject status, error rate pertaining to adherence to inclusion/exclusion criteria and the study protocol, number and type of serious adverse events. Study Report tables will be generated only from aggregate (not by group assignment) baseline and aggregate safety data for the study population.

## 6.7 Submission of On-Site Monitoring/Audit and Inspection Reports

The IRB, IMC, and NCCIH Program Officials will receive copies of all study monitoring/audit or inspection reports within 14 day of PI receipt.

### 6.8 Table A

| Data type | Frequency of review | Reviewer |
|---|---|---|
| Subject accrual (including compliance with protocol enrollment criteria) | Monthly | PI, Internal QA Reviewer |
| | Annually | Independent Monitors |
| Status of all enrolled subjects, as | Monthly | PI, Internal QA Reviewer |

| | | |
|---|---|---|
| of date of reporting | | |
| | Annually | Independent Monitors |
| Adherence data regarding study visits and intervention | Monthly | PI, Internal QA Reviewer |
| | Annually | Independent Monitors |
| AEs and rates (including out-of-range lab values) | Monthly | PI, Internal QA Reviewer |
| | Annually | Independent Monitors |
| | Annually | NCCIH, FDA |
| SAEs (unexpected and related) | Per occurrence | PI, Independent Monitors |
| | | NIH/NCCIH |
| SAEs (expected or unrelated) | Per Occurrence | PI, Internal QA Reviewer |
| | Annually | Independent Monitors, NIH/NCCIH |
| Unanticipated Problems | Monthly | PI, Internal QA Reviewer |
| | Per Policy | IR |

7 DATA HANDLING AND RECORD KEEPING

The investigators are responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported. All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data. The investigators will maintain adequate case histories of study subjects, including accurate case report forms (CRFs), and source documentation.

Participants will be assigned unique, coded, confidential identifiers (code numbers), which will be used to label all data forms, data entries and biological specimens. Identifiable information, such as name, will not appear on these materials. The key linking the subject's identity to their unique coded identifier will be kept in a confidential manner in a database on a secure UCSF server, with access only by the principal investigator and the research staff. No names or individual identities will be used in publications resulting from the study. Physical records will be kept in an area accessible only to research staff. Research data will be stored on a secure, HIPAA-compliant server and drive with monitored and controlled access for study staff and investigators. The web-based survey will be hosted on secure servers. In addition, participants will enter only a study ID number, thus no identifying information will be associated with their questionnaire data.

7.1 Data Management Resposibilities

Data collection and accurate documentation are the responsibility of the study staff under the supervision of the investigators. All source documents and laboratory reports must be reviewed by the study team and data entry staff, who will ensure that they are accurate and complete. Unanticipated problems and adverse events must be reviewed by the investigators or designee.

## 7.2 Database Protection

This study will use a REDCap database. The database will be secured with password protection. The informatics manager will receive only coded information that is entered into the database under those identification numbers. Electronic communication with outside collaborators will involve only unidentifiable information. The database incorporates an electronic audit trail to show change(s) to data after original entry including the date/time and user making the change.

## 7.3 Source Document Protection

Source documents, including all paper records for all subjects, e.g. consent forms, data collection forms, laboratory reports, will be kept in a locked filing cabinet in a room requiring badge access for entry and within a locked suite, accessible only to research staff. Electronic records will be stored on a secure, HIPAA-compliant server and drive with monitored and controlled access for study staff and investigators. The web-based survey will be hosted on secure servers. In addition, participants will enter only a study ID number, thus no identifying information will be associated with their questionnaire data.

7.4 Schedule and Content of Reports

The PI (Dr. Mehling) will ensure continuous and close monitoring of participant safety and will report to the DSMB. Study progress and safety will be reviewed weekly by the PI and core study team. A report that will be submitted to the outside reviewer will be compiled annually and will include a list and summarization of adverse events. In addition, the report will address (1)

whether adverse event rates are consistent with pre-study assumptions; (2) reason for dropouts from the study; (3) whether all participants met entry criteria; and (4) whether continuation of the study is justified on the basis that additional data are needed to accomplish the stated aims of the study. If the DSMB requires an interim analyses based on the occurrence of severe adverse events, we will develop plans for conducting these in consultation with the statistician on this RCT.

The outside monitoring reports will be increased in frequency if two or more Serious Adverse Event's (SAE's) with attribution to study related procedures as possibly, probably or definitely related occur in a 6-month period of time. In this situation, SAE's will be reported monthly, and study procedures will be reviewed to determine if changes are needed to reduce the risk of SAEs.

## 8 INFORMED CONSENT

Informed consent is a process that is initiated prior to the individual agreeing to participate in the study and continues throughout study participation. Extensive discussion of risks and possible benefits of study participation will be provided to subjects and their families, if applicable. A consent form describing in detail the study procedures and risks will be given to the subject. Consent forms will be IRB-approved, and the subject is required to read and review the document or have the document read to him or her. The investigator or designee will explain the research study to the subject and answer any questions that may arise. The subject will sign the informed consent document prior to any study-related assessments or procedures. Subjects will be given the opportunity to discuss the study with their surrogates or think about it prior to agreeing to participate. They may withdraw consent at any time throughout the course of the study. A copy of the signed informed consent document will be given to subjects for their records. The rights and welfare of the subjects will be protected by emphasizing to them that the quality of their clinical care will not be adversely affected if they decline to participate in this study.

The consent process will be documented in the clinical or research record.

To complete the informed consent process at the end of study participation, study staff will inform the subject when his/her participation has come to an end and will document the discussion in the study record.

## 9 REPORTING CHANGES IN STUDY STATUS

During the funding of this study, any action by an IRB, the Independent Monitoring Committee, or one of the study investigators that results in a temporary or permanent suspension of the study will be reported to the NCCIH Program Official within 3 business days of notification.

**13.2 * DATA AND SAFETY MONITORING BOARD (DSMB): (REQUIRED) Will a Data and Safety Monitoring Board (DSMB) be established:**

- (●) Yes
- ( ) No

**13.3 DSMB DETAILS: Provide details about the DSMB, including meeting frequency, and the affiliations and qualifications of members: Attach the DSMB charter to the Other Study Documents section. If the DSMB has not yet been established, submit details and the charter to us as soon as they become available.**

see details above in 13.1
DSMP and DSMB were approved by NIH-NCCIH:

Fadel Zeidan, PhD: faculty at UCSD, renown pain and neuroscience researcher on mindfulness for pain using MRI
Robert Saper, MD, faculty at Boston University, renown clinical researcher on yoga for chronic low back pain and on psychosocial factors in chronic low back pain

Sarah Lazar, PhD, faculty at Harvard University, renown neuroscience researcher on meditation, mindfulness and neuroplasticity using MRI and EEG

## 14.0 Confidentiality, Privacy, and Data Security

**14.1 PROTECTING PRIVACY: Indicate how subject privacy will be protected:**

- [x] Conduct conversations about the research in a private room
- [x] Ask the subject how they wish to be communicated with – what phone numbers can be called, can messages be left, can they receive mail about the study at home, etc.
- [x] Take special measures to ensure that data collected about sensitive issues do not get added to their medical records or shared with others without the subject's permission
- [ ] Other methods (describe below)

**14.2 SENSITIVE DATA: Do any of the instruments ask about illegal or stigmatized behavior:**

(•) Yes ( ) No

**IMPORTANT NOTE: Indicate in the consent form what kinds of sensitive information will be collected.**

**14.3 SIGNIFICANT CONSEQUENCES OF A LOSS OF PRIVACY OR CONFIDENTIALITY: Could a breach of privacy or confidentiality result in any significant consequences to participants, such as criminal or civil liability, loss of state or federal benefits, or be damaging to the participant's financial standing, employability, or reputation:**

(•) Yes ( ) No

Check all that apply:

- [x] Embarrassment
- [x] Criminal or civil liability
- [ ] Loss of state or federal benefits
- [ ] Damaging to the participant's financial standing, employability, or reputation
- [ ] Potential risks to insurability (health, disability, or life insurance)

Describe the potential consequences:

Information regarding drug/alcohol will be obtained via the attached eligibility phone interview, and may be considered embarrassing or may be illegal/stigmatized. Subjects are reminded that they are free to decline any questions that they are not comfortable providing a response for.

Reports of elder or child abuse, or indications of harm to self or others, will be reported and may result in criminal or civil liability.

Only designated study personnel included explicitly on the current IRB application will have access to any study records (both paper and electronic). No research results will be added to the patient's medical record unless medically necessary. Data will only be shared with those parties specified on the HIPAA form, which includes UCSF, UCSF IRB personnel, VA regulatory personnel, and the subject's primary care physician in the event of a medical complication.

Additionally, U.S.C 7332-protected sensitive information will be protected by the same rigorous standard as all other data. identifying information associated with this data will never be shared in reports or at conference proceedings, as with all other data.

If MRI findings appear abnormal during the MRI procedure or analysis process these will be shown to a SFVA radiologist and may be shared with the participants' primary care physician in the event of abnormal MRI. Such results may be relevant to the patient's health.

**14.4 EXTRA CONFIDENTIALITY MEASURES: Explain any extra steps that will be taken to assure confidentiality and protect identifiable information from improper use and disclosure, if any:**

Only designated study personnel included explicitly on the current IRB application will have access to any study records (both paper and electronic). No research results will be added to the patient's medical record unless medically necessary. Data will only be shared with those parties specified on the HIPAA form, which includes UCSF, UCSF IRB personnel, VA regulatory personnel, and the subject's primary care physician in the event of a medical complication.

Additionally, U.S.C. 7332-protected sensitive information will be protected by the same rigorous standard as all other data. Identifying information associated with this data will never be shared in reports or at conference proceedings, as with all other data.

VA research records will be retained within the VA-protected environment (e.g., VA server – please include the R Drive folder location/name, VA lab location, etc.), only accessible by authorized VA personnel, and disposed in accordance with the VHA Records Control Schedule (RCS 10-1). Any VA data shared with an external entity will be transmitted via FIPS 140-2-compliant encrypted methods as required per VA policy.

When using the external Insight Timer meditaton apps, the study coordinator wll create log ins for each participant connected to the participants study ID, to ensure that no identifiable information will be made public via the app. The key/speadsheet connecting study participants with their study ID will be stored in a secure UCSF server.

However, we are unable to protect participants' privacy against spyware such as Pegasus .

**14.5 * REPORTABILITY: Do you anticipate that this study may collect information that State or Federal law requires to be reported to other officials, such as elder abuse, child abuse, or threat to self or others: (REQUIRED)**

(•) Yes ( ) No

**The confidentiality and privacy section of the consent form should include this as a possible risk of participation.**

* Describe the types of reportable information the research team may encounter and provide the details of the reporting plan: **(REQUIRED)**

If it is suspected that the subject is in danger of harming him/herself or someone else, or if child abuse or neglect or elder abuse has occurred, appropriate authorities will be notified as required by law.

**14.6 CERTIFICATE OF CONFIDENTIALITY: Will this study obtain a Certificate of Confidentiality:**

(•) Yes ( ) No

**Please include the recommended Certificate of Confidentiality language in the consent form.**

**14.7 SHARING OF RESEARCH RESULTS: Will there be any sharing of EXPERIMENTAL research test results with subjects or their care providers:**

(●) Yes ( ) No

**Note: This is unusual and not recommended, particularly in cases where the tests are carried out in a non-CLIA certified laboratory, the results are of unproven clinical significance, or where there are not known preventative strategies and/or treatments. If these are the most likely scenarios for your study, you should check 'No.'**

**If you have an incidental finding of clear clinical significance, call the HRPP QIU at 415-476-1814 for a consult.**

Explain under what circumstances research results may be shared:

Abnormal MRI findings identified by the reserach team and confirmed by a radiologist witll be shared with the participant's care provider.

**14.9 * HIPAA APPLICABILITY: Study data will be: (REQUIRED)**

- [ ] Derived from a medical record (e.g. APeX, OnCore, etc. Identify source below)
- [ ] Added to the hospital or clinical medical record
- [ ] Created or collected as part of health care
- [ ] Used to make health care decisions
- [x] Obtained from the subject, including interviews, questionnaires
- [ ] Obtained ONLY from a foreign country or countries
- [ ] Obtained ONLY from records open to the public
- [ ] Obtained from existing research records
- [ ] None of the above
- [ ] Derived from the Integrated Data Repository (IDR) or The Health Record Data Service (THREDS) at SFGH

**14.10 * IDENTIFIERS: Check all identifiers that will be collected and included in the research records, even temporarily: (REQUIRED)**

- [x] Names
- [x] Dates
- [x] Postal addresses (if only requesting/receiving zip codes check Yes to the Zip Code question below instead of checking this box)
- [x] Phone numbers
- [ ] Fax numbers
- [x] Email addresses
- [ ] Social Security Numbers*
- [x] Medical record numbers
- [ ] Health plan numbers
- [ ] Account numbers
- [ ] License or certificate numbers
- [ ] Vehicle ID numbers
- [ ] Device identifiers or serial numbers
- [ ] Web URLs
- [ ] IP address numbers
- [ ] Biometric identifiers

- [x] Facial photos or other identifiable images
- [ ] Any other unique identifier
- [ ] None

*** Required for studies conducted at the VAMC**

* Could study records include *ANY* photos or images (even 'unidentifiable' ones): **(REQUIRED)**

(•) Yes ( ) No

**14.12 * PATIENT MEDICAL RECORDS: Will health information or other clinical data be accessed from UCSF Health, Benioff Children's Hospital Oakland, or Zuckerberg San Francisco General (ZSFG): (REQUIRED)**

(•) Yes ( ) No

**You indicated this research qualifies for Expedited Review but did not check Expedited Review Category 5. Please go back to Section 4: Initial Screening Questions and check Category 5 in question 4.7.**

**14.19 * DATA COLLECTION AND STORAGE: (check all that apply): (REQUIRED)**

Collection methods:

- [ ] Electronic case report form systems (eCRFs), such as OnCore or sponsor-provided clinical trial management portal
- [x] UCSF ITS approved Web-based online survey tools: Qualtrics or RedCap
- [x] Other web-based online surveys or computer-assisted interview tool
- [x] Mobile applications (mobile or tablet-based)
- [x] Text Messaging
- [ ] Wearable devices
- [x] Audio/video recordings
- [ ] Photographs
- [x] Paper-based (surveys, logs, diaries, etc.)
- [ ] Other:

* What online survey or computer assisted interview tool will you use: **(REQUIRED)**

- [x] Qualtrics (Recommended)
- [x] RedCAP (Recommended)
- [ ] Survey Monkey (NOT recommended and may require UCSF ITS Security review)
- [ ] Other

* For each app and device, please provide: **(REQUIRED)**

- the name of the mobile application or wearable device
- name  of the manufacturer / application owner
- the FDA status (required for mobile health applications and mobile health devices)

Qualtrics, RedCap, Insight Timer

* Data will be collected/stored in systems owned by (check all that apply): **(REQUIRED)**

- [ ] Study sponsor
- [x] UCSF data center (including OnCore, RedCap, Qualtrics, and MyResearch)
- [x] UCSF encrypted server, workstation, or laptop residing outside of UCSF data center
- [ ] Personal devices, such as laptops or tablets that are not owned or managed by UCSF
- [x] SF VAMC
- [ ] Zuckerberg San Francisco General Hospital
- [ ] Benioff Children's Hospital Oakland
- [ ] Langley Porter Psychiatric Institution
- [ ] Other UCSF affiliate clinic or location (specify below)
- [ ] Cloud vendor such as Amazon Web Services (AWS), Salesforce, etc. (specify below)
- [ ] Other academic institution
- [ ] 3rd party vendor (business entity)
- [ ] Other (explain below)

**Please consult with the VA's Clinical Research Office at 415-221-4810 x 2-6425 about the VA's requirements for data storage and security.**

**14.20 * ADDITION OF RECORDS TO A REGISTRY: Will patient records reviewed under this approval be added to a research database, repository, or registry (either already existing or established under this protocol): (REQUIRED)**

- ○ Yes
- ◉ No

**14.21 * DATA SHARING: During the lifecycle of data collection, transmission, and storage, will identifiable information be shared with or be accessible to anyone outside of UCSF: (REQUIRED)**

- ○ Yes
- ◉ No

## 15.0 Financial Considerations

**15.1 * PAYMENT: Will subjects be paid for participation, reimbursed for time or expenses, or receive any other kind of compensation: (REQUIRED)**

- ◉ Yes
- ○ No

**15.2 PAYMENT METHODS: Subjects payment or compensation method (check all that apply):**

Payments will be (check all that apply):

- [ ] Cash
- [x] Check
- [x] Gift card
- [ ] Debit card

☐ UCSF Research Subject Payment Card
☑ Reimbursement for parking and other expenses
☐ Other:

**15.3 PAYMENT SCHEDULE: Describe the schedule and amounts of payments, including the total subjects can receive for completing the study:**

- **If there are multiple visits over time, explain how payments will be prorated for partial completion**
- **If deviating from recommendations in Subject Payment Guidelines, include specific justification below**

In return for their time, effort, and travel expenses, participants will be paid $100 per visit at the San Francisco VA Medical Center, plus $15 travel reimbursement, in the form of a check or a gift card. Participants will receive $1.00 for each smart phone response during weeks 1 and 8 of the classes (up to $40). They will receive $50 each time after completing the questionnaires at 8 weeks and 6 months (up to $100). If participants take part in the exit interview they will be paid $100. The total payment amount will be up to $440 plus up to $30 for travel expenses. This is the total amount and includes the amount for the study activities at the VA. Participants will be reimbursed for time when undergoing fMRI for each of two visits ($100 per visit) and up to $15 for travel and parking expenses for each visit.

Timing of payment: VA visits at the end of the visit; smart phone responses and 8 week questionnaire after responding to questionnaire; 6-month questionnaire after responding to the questionnaire.

**15.4 COSTS TO SUBJECTS: Will subjects or their insurance be charged for any study activities:**

○ Yes ◉ No

## 16.0 Other Approvals and Registrations

**16.4 OTHER APPROVALS: Indicate if this study involves other regulated materials and requires approval and/or authorization from the following regulatory committees:**

☐ Institutional Biological Safety Committee (IBC)

Specify BUA #:

☐ Institutional Animal Care and Use Committee (IACUC)

Specify IACUC #:

☐ Controlled Substances

## 17.0 Qualifications of Key Study Personnel and Affiliated Personnel

**NEW: January 2019 - Affiliated personnel who do not need access to iRIS no longer need to get a UCSF ID. Instead, add them below in the Affiliated Personnel table below.**

## 17.1 Qualifications of Key Study Personnel:

# Instructions:

For UCSF Key Study Personnel (KSP)* listed in **Section 3.0,** select the KSP from the drop down list and add a description of their study responsibilities, qualifications and training. In study responsibilities, identify every individual who will be involved in the consent process. Under qualifications, please include:

- Academic Title
- Institutional Affiliation (UCSF, SFGH, VAMC, etc.)
- Department
- Certifications

**NOTE: This information is required and your application will be considered incomplete without it. If this study involves invasive or risky procedures, or procedures requiring special training or certification, please identify who will be conducting these procedures and provide details about their qualifications and training. Click the orange question mark for more information and examples.**

**Training Requirements:**
The IRB requires that all Key Study Personnel complete Human Subjects Protection Training through **CITI** prior to approval of a new study, or a modification in which KSP are being added. More information on the CITI training requirement can be found on our **website.**

* **Definition of Key Study Personnel and CITI Training Requirements (Nov, 2015):** UCSF Key Study Personnel include the Principal Investigator, other investigators and research personnel who are directly involved in conducting research with study participants or who are directly involved in using study participants' identifiable private information during the course of the research. Key Personnel also include faculty mentors/advisors who provide direct oversight to Postdoctoral Fellows, Residents and Clinical Fellows serving as PI on the IRB application.

| KSP Name | Description of Study Responsibilities - Briefly describe what will each person be doing on the study. If there are procedures requiring special expertise or certification, identify who will be carrying these out. Also identify who will be obtaining informed consent. | Qualifications, Licensure, and Training |
|---|---|---|
| Dr. Mehling, Wolf MD, MD | Principal Investigator at UCSF Osher Center: Oversee the overall study, oversee recruitment, obtain informed consent, oversee subjects testing, oversee data collected and management, analyze data and report | UCSF/VA personnel. Dr. Mehling is a Prof. of Clinical Family and Community Medicine and on faculty at the Osher Center for Integrative Medicine. His research focuses on body-oriented complementary therapies and mind-body |

| | | |
|---|---|---|
| | results. | interactions. |
| Dr. Strigo, Irina PhD, PhD | Other Principal Investigator at SFVAMC: Oversee the overall study, oversee recruitment, oversee subjects testing, oversee data collected and management, analyze data and report results | UCSF/VA personnel. Research Physiologist at the SFVAMC and Associate Professor of Psychiatry at UCSF, is an expert in conduction human pain research in veteran and non-veteran populations |
| Dr. Hecht, Frederick MD, MD | Co-Investigator: Advises in questions of mindfulness and task design, is included in data analysis and reporting of results | UCSF personnel. Dr. Hecht is a Prof. of Medicine and the director of research at the Osher Center for Integrative Medicine. His research focuses on mind-body interventions. |
| Rogers, Kirsten, BA | Study coordinator will be responsible for coordination with study staff and scheduling. | UCSF personnel. Clinical Research Coordinator at the Osher Center for Integrative Medicine |
| Goldman, Veronica M | Study coordinator will be responsible for coordination with study staff and scheduling. | UCSF personnel. Clinical Research Coordinator at the Osher Center for Integrative Medicine |
| Dr. Hartogensis, Wendy E PhD | Statistician will be responsible for data analyses | UCSF personnel. Statistician at the Osher Center for Integrative Medicine |
| Murphy, Emily | Study coordinator will be responsible for coordination with study staff and scheduling. | UCSF and VA personnel. Clinical Research Coordinator at the VA Medical Center |
| Menon Vinodkumar, Anitha | Study coordinator will be responsible for coordination with study staff, scheduling, reviewing and analyzing data . | UCSF Personnel. Medical Resident. |

## 17.2 Affiliated Personnel:

### Instructions:

This section is for personnel who are not listed in **Section 3.0: Grant Key Personnel Access to the Study** because their names were not found in

the User Directory when both the iRIS Database and MyAccess directories were searched. Add any study personnel who fit ALL of the following criteria in the table below:

- They meet the definition of Key Study Personnel (see above), **and**
- They are associated with a UCSF-affiliated institution (e.g., VAMC, Gladstone, Institute on Aging, Vitalant, NCIRE, SFDPH, or ZSFG), **and**
- They do not have a UCSF ID, **and**
- They do not need access to the study application and other study materials in iRIS.

**Note:** Attach a **CITI Certificate** for all persons listed below in the **Other Study Documents** section of the **Initial Review Submission Packet Form** after completing the **Study Application**.

Click the orange question mark icon to the right for more information on who to include and who not to include in this section.

Do not list personnel from outside sites/non-UCSF-affiliated institutions. Contacts for those sites (i.e. other institution, community-based site, foreign country, or Sovereign Native American nation) should be listed in the **Outside Sites** section of the application.

**If there are no personnel on your study that meet the above criteria, leave this section blank.**

| Name | Institution | Telephone | E-mail | Role |
|---|---|---|---|---|
| No External Personnel has been added to this IRB Study | | | | |

Please describe the study responsibilities and qualifications of each affiliated person listed above:

## 18.0 End of Study Application

# End of Study Application Form

**To continue working on the Study Application**:
Click on the section you need to edit in the left-hand menu. Remember to save through the entire Study Application after making changes.

**If you are done working on the Study Application**:
**Important:** Before proceeding, please go back to Section 4.0 Initial Screening Questions and **Save and Continue** through the form to make sure all the relevant sections and questions have been included. If you've changed any answers since you started, the branching may have changed. Your application will be incomplete and it will have to be returned for corrections.

Once you are sure the form is complete, click **Save and Continue**. If this is a new study, you will automatically enter the **Initial Review Submission Packet Form**, where you can attach **consent forms** or other **study documents**. Review the **Initial Review Submission Checklist** for a list of required attachments.

**Answer all questions and attach all required documents to speed up your approval.**

The UCSF IRB welcomes feedback about the IRB Study Application Form. Please click the link to answer a **survey** about the application form.