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Study Protocol

Combined exercise and meditation as a treatment for patients with chronic back pain

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Protocol Summary Form

Combined exercise and meditation as a treatment for patients with chronic back pain

1. Statement of the research question

Determine the feasibility of a combined exercise and guided meditation practice on reducing pain in individuals with lower back pain.

We will investigate an experimental condition: guided meditation with subsequent treadmill walking, and three control conditions (negative control, meditation only, exercise only) in participants with clinically diagnosed lumbar spinal back pain without neuropathy or radiculopathy. Participants will receive meditation training then complete a guided meditation, using standard pre-recorded guided meditation audio, prior to a 5x per week treadmill walking experience for 4 weeks. Our goals are to:

> We hypothesize that back pain will show greater improvement following completion of a combined treatment protocol of both exercise and meditation.

2. Purpose and significance of the study

Chronic pain is a serious problem in the US that affects 116 million adults[1]. A number of chronic pain conditions can be linked both epidemiologically and biologically with various anxiety disorders[2,3]. It is well known that anxiety can increase pain and that many patients with pain exhibit increased anxiety. Standard treatment options for chronic pain include prescribed pharmaceuticals and physical therapy. Anxiety is most commonly treated with prescribed pharmaceuticals and psychotherapy. A major gap in the development of effective therapies has been the lack of focus on the interaction between pain and anxiety disorders. That is, treatment of pain but not anxiety, or vice versa, is likely not as effective as treatment of both disorders or sets of symptoms at the same time. Fortunately, a number of integrative therapies, such as exercise and meditation, have been shown to be effective in separate studies for both pain and anxiety. Exercise is analgesic, is anxiolytic, low cost, and has many positive side-effects. Similarly, meditation has demonstrated efficacy in the context of chronic pain and anxiety. A therapy regimen consisting of both exercise with mindfulness meditation in these patient populations may produce greater benefits but it is currently unknown whether this combination of treatment is feasible. Issues of interest in developing a combined treatment regimen that is feasible to implement include: patient adherence and acceptance and the use of appropriate measures to assess symptoms following intervention. Before exploring this combined treatment approach in a full clinical trial, we will first determine the feasibility of this intervention in persons with spinal low back pain.

Our *overall objective* is to investigate the feasibility of an intervention that combines exercise and guided meditation in individuals with back pain. We will also investigate the feasibility of using a standard set of non-invasive human pain tests for predicting change in symptoms following intervention. These objectives are necessary in order to achieve our *long-term goal* of determining prescribed exercise/meditation protocols with the best cost-to-risk ratio as a therapy for improving symptoms in patients with chronic pain and comorbid anxiety. Our *central hypothesis is that a combined exercise and meditation protocol will be feasible in this clinical population as indicated by high recruitment rates, subject retention, and treatment acceptance.*

3. Research design and procedures

This study is designed as a randomized single-blinded (for QST testing) trial with repeated measures.

The participants will primarily be recruited through a University of Pittsburgh approved IRB patient registry (Pitt IRB protocol #REN16070141/PRO12030122 “Department of Physical Medicine and Rehabilitation Research Registry (PMR3) see “participant” recruitment below for additional details). Registry use is managed with co-PI Dr. Eric Helm (MD, University of Pittsburgh Department of Physical Medicine and Rehabilitation). Secondarily, we will recruit from the Clinical and Translational Science Institute’s Pitt + Me registry.

The co-primary investigators (co-PIs) will be involved in the procedures listed below. Graduate research students (e.g. Anna Polaski, Biological Sciences) and technicians will assist with recruitment, data collection, and data processing. These additional technicians have yet to be identified but will be added to the protocol with subsequent amendments. The graduate student and technicians will be trained on all procedures involved in this study by the co-PIs. Prior to data collection, the prospective subjects will complete a full screening, using a checklist of the inclusion/exclusion criteria and the AHA health questionnaire (see "Instruments") to determine eligibility. The purpose of the study, the methods of data collection and all potential risks will be verbally communicated to prospective subjects at the initiation of the first data collection session (Day 1) (**Figure 1**). Prospective subjects will be given an approved informed consent form to read and sign. Subjects will then complete additional questionnaires to assess baseline activity level and state anxiety (see "Instruments" below). The researcher will explain the questionnaires to subjects and will be available to answer any questions while the subjects complete these forms. Basic health information obtained from the subject will assess whether the subject has been diagnosed with any cardiac, respiratory, neurological or musculoskeletal disorder, chronic pain or currently has acute pain (AHA health questionnaire). Subjects who report any of the above medical diagnoses or pain (with the exception of chronic low back pain) during screening will be excused from participation in the study. Subjects who cannot walk independently without a device will be excused from participation as well. Any identifying information used to determine eligibility, including the checklist of inclusion/exclusion criteria and the health questionnaires, will be destroyed.

Figure 1 – Time-line of four week trial for participants in combined intervention group.

Day	1	2	3	4	5	6	7	8
Activity	-Consent -Intake surveys -Baseline pain assess (*In clinic*)	-15 min meditation -30 min exercise (*In clinic*)	-15 min meditation -30 min exercise	-15 min meditation -30 min exercise	-15 min meditation -30 min exercise	-15 min meditation -30 min exercise	Rest	Rest
Day		**9**	**10**	**11**	**12**	**13**	**14**	**15**
Activity		-15 min meditation -30 min exercise (*in clinic*)	-15 min meditation -30 min exercise	-15 min meditation -30 min exercise	-15 min meditation -30 min exercise	15 min meditation -30 min exercise	Rest	Rest
Day		**16**	**17**	**18**	**19**	**20**	**21**	**22**
Activity		-15 min meditation -30 min exercise (*in clinic*)	-15 min meditation -30 min exercise	-15 min meditation -30 min exercise	-15 min meditation -30 min exercise	-15 min meditation -30 min exercise	Rest	Rest
Day		**23**	**24**	**25**	**26**	**27**	**28**	**29**
Activity		-15 min meditation -30 min exercise (*in clinic*)	-15 min meditation -30 min exercise	-15 min meditation -30 min exercise	-15 min meditation -30 min exercise	-15 min meditation -30 min exercise	Rest	Pain Assess and Exit Survey (*In clinic*)

Each trial is designed to last 29 days including an intake session and a post-meditation/exercise pain testing session. Pain testing is performed during the intake session (baseline) and on day 29 (48 hours after the last intervention). See **Figure 1** for illustrative time-line of individual trials for individuals assigned to the meditation then exercise group. Analogous time-lines will be used for exercise only subjects (30 minutes of exercise each day and 15 minutes of audiobook), meditation only subjects (15 minutes of meditation each day and 30 minutes of audiobook) or negative control subjects (15 minutes of audio book followed by 30 minutes of rest each day).

During the enrollment period, subjects will also be given a full description of all sensory and pain measures that will be taken. With initial consent, all subjects will be allowed to experience all sensory/pain measures before baseline pain testing is completed. All sensory and pain assays are based on well-established assays used in both healthy human participants and patients with chronic pain[4,5]. All assays involve either innocuous (non-painful stimuli) or acute noxious stimuli (painful stimuli) that do not damage tissue. Sensory testing will be completed on both the non-dominant forearm and low back. For testing completed on the forearm, subjects will be seated in a chair with their arm supported. For testing completed on the low back, subjects will be positioned in prone on a plinth table with a head rest. Time between different tests will be >5 min to allow the subject to rest. Order of the three stimuli (e.g. mechanical, thermal, pressure) will be randomized during each day 1 versus day 29 testing. Training and description of each measure is as follows:

Cutaneous mechanical sensitivity assay[4]: Assay involves determining the sensitivity threshold for innocuous cutaneous stimulation and noxious cutaneous stimulation. Stimulation is provided with standard sensory evaluator filaments. These small nylon filaments each apply a single force (ranging from 0.008g to 4g). Before the start of the first experimental trial (baseline testing), subjects will be allowed to feel and manipulate the filaments. Starting with the smallest filament (0.008g; typically below the sensory threshold for human detection), 5 trials will be directed at the subject's forearm and low back. Experimenter will ask "Can you feel

this" while the experimenter applies the filament to the subject's forearm and lower back. With each filament, the experimenter will apply the filament 3 times in the "positive" trials. For the other 2 trials, the experimenter will not apply the filament but ask the subject, "Can you feel this?" These 2 "negative" trials will be randomly inserted with the 3 "positive" trials and are designed to test for false responses. If a subject detects $\geq$2 of the positive trials and 0 negative trials for a filament, that force will be the subject's "mechanical sensory threshold." For a single filament, if the subject detects <2 of the real trials and/or >0 of the false trials, the experiment will start another round of 5 trials with the next biggest filament until the sensory threshold is reached. Typical testing time is about 5 min per body part. After the sensory threshold is reached, testing will continue until the "pain threshold" is reached. Pain experienced from these filaments is transient and is roughly equivalent to firmly pushing the end of a paper clip into one's skin. As soon as the patient says that an individual filament feels painful, the trials will stop. This is the cutaneous pain threshold. Typical testing time is about 5 min per body part.

Heat sensitivity assay[4]: Assay involves determining the sensitivity threshold for painful thermal stimulation. Stimulation is provided with a small thermal device, which will be strapped to the subject's forearm then lower back at the site of back pain (Medoc Instruments). Before the start of the training/ experimental trials, subjects will be shown the device and allowed to feel the stimulus with their hand. Subjects are told to press the 'stop' button on a remote and/or verbally tell the experimenter to stop testing when they feel the stimulus transition from "innocuous warmth or heat" to "painful heat." Each trial lasts for a maximum of 20 sec. The device is set so that typical withdrawal thresholds occur at approximately 10 seconds into the trial. The temperature on the probe tip at this point is ~47^{o}C (116^{o}F). The maximum temperature of the trial at the 20 second cutoff time point is 50^{o}C (120^{o}F). Temperatures in US desert areas often reach this temperature and research has shown that testing of the skin at this temperature for this length of time does not produce skin damage[6]. Additionally, this testing modality has been safely used a part of a standard pain/sensory testing protocol[5]. Total testing time is <5 min.

A second assay will be used to evaluate the quality and unpleasantness of thermal pain. Each subject will receive a constant 45^{o}C stimulus. 45^{o}C is a standard temperature that is the typical minimal stimulus necessary to feel thermal pain. Stimulus (3cm x5cm heating block) will be applied for 3 seconds. Immediately following stimulus, the subject will be asked to evaluate the quality and unpleasantness of the pain. This is done with a standard 0-10 visual analog scale (VAS). On the "quality scale", "0" is represented as "no pain" and "10" is represented as "the worst pain imaginable." On the "unpleasantness scale", "0" is represented as "not unpleasant" and "10" is represented as "the most unpleasant sensation imaginable."

Example instructions for quality VAS – *"Please use the scale below to tell us how intense your pain is. Place an "X" on the scale that best describes the intensity of your pain."*

Example instructions for unpleasantness VAS – *"Now that you have told us about the physical quality of the pain, we want you to tell us overall how unpleasant your pain is to you. Words used to describe very unpleasant pain include "miserable" and "intolerable." Remember, pain can have a low intensity, but still feel extremely unpleasant, and some kinds of pain can have a high intensity but be very tolerable. With this scale, please tell us how unpleasant your pain feels."*

Mechanical pressure sensitivity assays[7]: Assay involves determining the sensitivity threshold for painful pressure stimulation and then determining the quality and unpleasantness of that same pressure in a separate trial. Stimulation is provided with a standard clinical pressure algometer (see below "instrument" section). This device consists of a probe connected to a pressure meter. The probe is placed on the subject's forearm and low back at the site of back pain and pressure is gradually applied. Before the first training/experimental trial subjects will be allowed to apply the stimulus to themselves. During a trial, pressure will gradually be applied until the stimulus transitions from "innocuous pressure" to "painful pressure." At this point, subject will say "stop" and the stimulus will be removed from the subject's lower back. When algometer is removed from the subject, the greatest pressure applied is automatically recorded in the device. This is the "pressure pain threshold" for the trial. 2 trials will be applied to each the forearm and low back in two distinct sites at least 1 inch from each other to avoid damage or sensitization to a single area. After the pressure threshold has been determined for a subject, 1 additional trial will be applied (in a third testing site). In this trial, the subject will be asked to evaluate the quality and unpleasantness of a pressure stimulus given for 3 seconds. This is done with a standard 0-10 visual analog scale (VAS). On the "quality scale", "0" is represented as "no pain" and "10" is represented as "the worst pain imaginable." On the "unpleasantness scale", "0" is represented as "not unpleasant" and "10" is represented as "the most unpleasant sensation imaginable." During this trial, the experimenter will tell the subject that they are going to apply a painful stimulus to the subject and then ask the subject to evaluate that pain (on the two VASs). The exact stimulus will be matched to the subject's pain threshold determined during the baseline trials

(e.g if baseline trials indicated a pressure threshold of 50 N then subject will be asked to evaluate the pain of that stimulus). During final testing trial (day 29), the pressure pain threshold will be re-measured to determine if there is a change from baseline. For the quality/unpleasantness testing, subjects will be tested on day 29 at their original baseline pressure threshold (from day 1) AND the new threshold determined day 29. This will allow an analysis of change from baseline and pain at threshold across the experiment.

Following baseline pain testing, subjects (in the exercise only and meditation then exercise groups) will be set-up for training on the exercise protocol. Subjects will become familiarized with the exercise protocol, including the physiological measures to be assessed [heart rate (HR)], the Borg Rate of Perceived Exertion (RPE) Scale, and the treadmill speed at which they will be walking. Subjects will be instructed to step up onto the treadmill and stand on the sides not the belt or belt deck. The researcher will slowly raise the speed to 2 mph. The subject will be instructed to step on the treadmill at this time. After 30 seconds, the speed will be ramped up to 2.5 mph and after another 30 seconds, the speed will be ramped up to their prescribed session speed (±3.5 mph). They will also be instructed to walk with a natural gait pattern, allowing bilateral arm swing. To allow a natural arm swing, subjects are unable to hold onto the treadmill arm rails. Subjects will be introduced to the Borg RPE scale and asked to provide subjective feedback on their level of exertion at the initiation of and during the final minute of this 5 minute training period (Borg).

Intervention Sessions

Subjects will be scheduled for 20 intervention sessions during their time in the study – that is five sessions per week over four weeks. Subjects are only required to return to campus for the first session of each week. The remaining four weekly sessions can be completed at home on a personal treadmill or in the community, such as a local gym. Subjects are able to complete all sessions at Duquesne University if that is their preference. Sessions will be scheduled/encouraged to occur at the same approximate time each day to control for factors that may influence exercise performance and assessments.

This clinical trial will test the methodology and trial retention of one version of a combined therapy (along with comparison control groups). The combination of meditation and exercise will be done sequentially. This methodology is termed (1) Meditation first & then Exercise (Med&Exer). All participants in this exploratory trial will receive the therapeutic intervention, or one of three control options (negative control, meditation only, exercise only) (**Table I**). We describe below the details of the interventions.

Table 1 – Experimental Conditions

Experimental Condition	**Description**
Negative control	In clinic or at home, listen to an audiobook for ~15 minutes followed by 30 minutes of rest (including survey assessments)
Meditation only control	In clinic or at home, 15 minutes of meditation and listen to an audiobook for ~30 minutes (including survey assessments)
Exercise only control	In clinic or at home, listen to an audiobook for ~15 minutes (including survey assessments) then exercise (treadmill) for ~30 minutes
Meditation & then exercise (Med&Exer)	In clinic or at home, 15 min of meditation followed by 30 min of exercise (treadmill) plus survey assessments

Exercise in this exploratory study will consist of 30 minutes of moderate-intensity treadmill walking (starting at 3.5 mph and adjusted up or down to reflect moderate intensity for each individual participant) in the Rangos Human Testing Facility (Fisher Hall) on a treadmill with auto-shut off and integrated heart rate monitor (Polar H1 Heart Rate Sensor) on day 2 (first day of intervention), day 9, day 16, and day 23. During the other intervention days (day 3-6, 10-13, 23-27) participants will have the option of completing trials at Duquesne or “at home.” At home is defined as a participant using a personal treadmill or going to a community fitness center (e.g. YMCA). This “at home” component is designed to reduce the extra burden for patients who would otherwise have to travel to Duquesne for 22 total sessions (20 days of intervention plus intake and outtake sessions). Exercise will

be performed 5x per week (1x per day) for a total of four weeks with two days of rest between the four exercise runs. Participants in the exercise-only group and Med&Exer will be encouraged to exercise when the gym is less busy. Any trials done in the Rangos Human Testing Facility will be donewith the researcher in the room, monitoring the participant. . Walking speed has been prescribed based on a standard equation incorporating metabolic equivalent of the task (METs). METs are a measure of an individual's energy exertion during a physical activity. The speed of treadmill walking was set to ensure energy expenditure falls within the moderate-intensity range (3.00-5.99 METs). Heart rate is monitored continuously before, during, and after exercise.

To evaluate the effect of the meditation on the participants, they will complete the Freiburg Mindfulness inventory (FMI) meditation survey immediately prior to their first meditation before exercise. The FMI will be used again on day 27.

All participants will receive a 45 min meditation and stress training session following baseline pain testing (see Assessment section below) on the intake day (Day 1). These training sessions, done by clinical Psychologist Dr. Ian Edwards (Counseling and Wellbeing Center), discuss the potential of and use of mindfulness and meditation (in the meditation groups only) or about stress management for chronic pain (in the exercise only and negative control group). On subsequent "intervention" days, guided meditation recordings will be used for the two relevant meditation participant groups. Participants will listen to a 15 min guided meditation with mindfulness recording. We have 5 recordings, which will be pre-loaded on a MP3 player (see URLs for Recordings at the end of this Protocol). The participants will be allowed to take this MP3 player home with them if they choose to perform "at-home" trials.

Subjects will perform their exercise session with the researcher in the room, monitoring their heart rate and level of exertion. For subjects exercising "at home," we will instruct the subjects on warning signs to indicate that they should stop exercising. Subjects will be advised to place a chair near the treadmill to sit and rest if they become over-exerted.

4. Instruments

Assessments in this exploratory trial are designed to evaluate four elements of the trial: (1) Pain and Disability, (2) Meditation, (3) Anxiety and Stress, and (4) Fitness and General Health and. Although these elements are not mutually exclusive and multiple survey tools overlap, we describe these elements as individual groups of assessments below for ease of interpretation. General assessment includes demographic information (gender, age, race/ethnicity, and education level) and handedness. The primary outcome of this trial is a reduction in disability as measured by the RMDQ (see below). See Appendix 1 – Instruments for all surveys and questionnaires.

Protocol Pain and Disability

There are multiple assessments for experimental measurement of pain. First, we will use the Roland-Morris Disability Questionnaire, which provide a qualitative analysis of the disability that is associated with an individual's chronic low back pain. This is our primary outcome for the trial. We hypothesize that exercise, meditation, and combined exercise/meditation will decrease disability in patients. Second, we will use standard visual analog scoring of instantaneous back pain for participants before and after exercise (or meditation in the "meditation only" control group or audio book in the negative control group) during each day of the trial. These scales will be included in the subject online diary (Qualtrics Survey Platform) for participants completing "at home" trials.

Finally, we employ quantitative sensory testing (QST) to quantitatively measure participants sensory and pain thresholds for mechanical stimulation, thermal stimulation, and pressure stimulation as described in detail above. *All QST will be performed by a clinician/researcher blinded to meditation and exercise intervention.* These well-validated measures provide a quantitative assessment of pain during the meditation and exercise intervention. QST pain assessment will occur at baseline (intake day) and day 29 (48 hours after the last intervention). All QST measures will occur on the forearm and in the lumbosacral area identified by the individual participant as being painful. Briefly, mechanical testing is accomplished using von Frey filaments and assesses general mechanical sensitivity and mechanical allodynia in cases of cutaneous hypersensitivity. Filaments are similar to fishing line thread and stimulus ranges from undetectable to detectable to painful. Any pain is similar to "pin prick" pain. Thermal pain is assessed using a Peltier-type device (Medoc Pathway) to measure thermal pain threshold. Similarly, we assess the qualitative nature of thermal pain by applying a 45^{o}C constant heat stimulus to the participant's back. 45^{o}C is the molecular activation threshold for pain receptors and allows for an analysis

of thermal allodynia using VAS scales for the sensory and emotional component of pain. Finally, we will use a manual pressure algometer (0.2-2cm diameter, Wagner Instruments) to first measure pressure pain thresholds. Threshold detection is then followed by a constant pressure stimulus at an individual participant's pain threshold to determine the sensory and emotional VAS properties of the stimulus. All of these quantitative sensory techniques are safe and carry only minor risk for participants.

Assessment - Meditation and Mindfulness

All participants in the meditation groups will complete the Freiburg Mindfulness Inventory (FMI) at the beginning of their first day of exercise/meditation and on the last day of the trial. The FMI is a 30-item tool that assesses an individual's experience with meditation and mindfulness. For this feasibility study, data from the FMI will be particularly useful in evaluating whether there were any changes in mindfulness that developed during the trial. Failure to increase mindfulness during the trial might be a sign that a patient failed to "buy in" to the meditation intervention. We will also evaluate the likelihood of a patient to continue to meditate (or exercise) using a qualitative exit survey given on day 29. There are no safety concerns associated with the FMI or custom exit survey.

Assessment – Anxiety

To account for changes in anxiety during the current exploratory trial, we will use the State-Trait-Anxiety Inventory (STAI) form Y to evaluate state anxiety and the Fear-Avoidance Beliefs Questionnaire (FABQ) to evaluate fear avoidance behavior. Subjects will report their state anxiety (using a survey) before and after each trial. FABQ will be evaluated on day 1 and day 29. There are no serious safety concerns associated with this survey.

Assessment - Exercise

As described above, we will be using multiple assessment tools to evaluate physical fitness and exercise in this trial. General fitness will be determined by the International Physical Activity Questionnaire – Short Form (IPAQ-short) and a clearance of physical readiness for exercise will be determined by the AHA/ACSM Health/Fitness Facility Pre-participation Screening Questionnaire. Exercise exertion will be measured daily through active heart rate monitoring during exercise and the Borg Rate of Perceived Exertion (Borg RPE)[8]. Finally, throughout the 4 week trial, participants will be asked to wear wrist-based health activity monitors. These watches monitor and record activity and other factors. There are no serious safety concerns associated with these surveys or monitoring methods.

5. Sample selection

Adults with chronic low back pain who are otherwise healthy will be recruited for participation in this study. The AHA screening questionnaire will be administered during the screening process to determine whether potential subjects meet the inclusion/exclusion criteria.

Eligibility Criteria:

Inclusion criteria

1. Presence of clinically diagnosed nonspecific low back pain for at least 6 months (see below for additional detail)
2. Between age 18-60
3. Body mass index within the normal to overweight range (18.5-29.9)
4. Resting heart rate 60 to 100 beats per minute
5. Resting blood pressure less than or equal to 140/90
6. Able to independently ambulate community distances without external support (e.g., walker, cane)

Exclusion criteria

7. Age less than 18 or greater than 60 years
8. BMI ≥ 30 or ≤ 18.4
9. Cardiovascular or respiratory disease
10. Neurological disease, unrelated to low back pain
11. Radicular low back pain

12. Back pain associated with neuropathy
13. Diabetes mellitus, Types 1 and 2
14. Diagnosed with a chronic pain condition, unrelated to low back pain
15. Acute pain
16. Regular participation in high intensity athletic/sporting activities
17. Sedentary lifestyle
18. Currently pregnant
19. Current cigarette smoker
20. On-going litigation associated with back pain
21. Inability to walk independently without external support (e.g. walker).
22. No regular participation in meditation techniques or training in Mindfulness-based stress reduction

None of the above exclusion criteria are based on gender, race, or ethnicity.

Back pain definition for inclusion:

The target population for this exploratory trial and the subsequent full clinical trial are patients with chronic back (>6 months) pain with no evidence of neuropathic pain, radicular (i.e. sciatica) pain, or referred somatic pain. These diagnoses will be made prior to entry in the study. Diagnostic inclusion criteria for patients is back pain identified as either lumbar spinal pain (localized between the last thoracic spinous process and the first sacral spinous process; e.g. lumbar discogenic pain, internal disc disruption, lumbar zygapophysial joint pain, lumbar muscle sprain and muscle spasm, spondylolysis) and/or sacral spinal pain (localized between the first sacral spinous process and the posterior sacrococcygeal joints; e.g. sacroiliac joint pain). These two types of pain will be grouped together as lumbosacral spinal back pain. Laterally, these pain syndromes are localized between the lateral borders of the erector spinae. Patients with chronic back pain fall roughly into five categories: (1) internal disc disruption (39%), (2) zygapophysial joint pain (15%), and (3) sacroiliac joint pain (15%), with the remaining patients falling into either (4) failed back surgery syndrome, or (5) idiopathic pain.

In our three main clinics, about 45% of patients display idiopathic and failed surgery back pain, 25% of patients demonstrating marked pain in their peripheral limbs indicative of radiculopathy or referred somatic pain, and 30% of patients with neck pain. Our exploratory and clinical trial will be marketed towards a strict definition of lumbosacral low back pain without radiculopathy. The majority of these individuals have spontaneous chronic back pain with or without movement-induced low back pain. QST provides for additional measurements in these populations to characterize on-going pain and changes in pain thresholds (with pain condition and with experimental treatment condition).

6. Recruitment of subjects

Participants will be primarily recruited using in-clinic recruitment to the University of Pittsburgh Department of Physical Meditation and Rehabilitation Research Registry (PMR3) (Pitt IRB # PRO12030122; renewed 7/20/2016). All registry participants have provided informed consent to be contacted for future research studies. The IRB approved advertisement for our study (see Appendix 2 – Advertisements) will be provided to the registry investigators to distribute to potential subjects according to the procedures established in the approved registry protocols. In response to the advertisement, potential subjects will directly contact the research team, if they are interested in participating, or Dr. Szucs will contact patients after consent into the PMR3 database. co-PI Dr. Eric Helm and staff Mr. Ian Smith will be our primary liaisons to identify patients in the registry and hand them our research study flyer.

We will also recruit from the University of Pittsburgh Clinical and Translational Science Institute CTSI patient registry (Pitt + Me), which includes over 100,000 persons, and is a free resource for researchers. Finally, we will also utilize the *free* recruitment services offered by the CTSI. These services include help using bus advertising, community advertising, websites, and social media options for recruitment.

The research flyer contains basic details on eligibility for the study along with contact information for Dr. Szucs. When prospective subjects contact Dr. Szucs (or Dr. Szucs contacts patients who have consented for recruitment), a thorough description of the study and its requirements will be provided. The PI will then conduct a brief eligibility screening to determine general health and fitness level before inviting eligible subjects to enroll.

No private identifiable information will be recorded during this screening. Recruitment and enrollment will be conducted without regard for gender, race or ethnic background.

Compensation for participation in this study is based on the number of sessions completed. Compensation for the intake session and each completed intervention session is $4.50 and compensation for the Exit Session is $100. Therefore, if a participant completes this project in its entirety (intake session, 20 intervention sessions, and the Exit session), they will receive $200. Only participants who complete at least 80% of all intervention sessions (greater than 16 of 20 sessions) and the intake session, will be invited to complete the Exit Session. If the subject chooses to withdraw before completing at least 80% of the intervention sessions, they will receive partial compensation for the sessions that they have completed.

As part of this study, we are also interested in identifying barriers to participant interest and persistent. To identify these barriers, we will utilize an anonymous online survey of participants who drop out of the study. If a participant consents to the Duquesne study but later drops out of the study, they will be directly given a URL for a survey.

7. Informed consent procedures for exercise/meditation study

As noted above, initial consent is obtained through the University of Pittsburgh Department of Physical Meditation and Rehabilitation Research Registry (PMR3) (Pitt IRB # PRO12030122). This consent is obtained by UPMC/Pitt Physician Dr. Eric Helm (co-I), and his partners, Drs. Suehun G Ho, MD, Alan Chu, MD, and Gwen Sowa, MD (see *Support Letter*) along with Physical Medicine and Rehabilitation Clinical Research Coordinator Mr. Ian J. Smith, MS. Backup recruitment efforts will occur in collaboration with the CTSI (see *Support Letter*) using the Pitt + Me registry. IRB approved consent is provided when patients are entered into the Pitt + Me registry.

Subsequent consent for the exercise/meditation study here at Duquesne occurs as follows:

At the initiation of the intake day, Dr. Szucs will explain the purpose of the study, the methods of data collection and all potential risks associated with participation to prospective participants. Prospective participants will then be given an approved informed consent form to read, following the guidelines determined by the Duquesne University IRB. If they agree to participate, they will be asked to sign two copies of the form; one copy to be retained by the PI and the second copy for the subject's records. Hard copies retained by the PI will be stored in a locked cabinet in a locked room. Participants will be made aware during the consent process that they may withdraw from participation at any time during their enrollment.

8. Collection of data and method of data analysis

Qualitative analysis of the online questionnaire will identify main reasons why patients may withdraw from the study. Percentages of eligible participants who withdraw will be carefully monitored and reported providing more accurate estimates of recruitment rates and target population numbers. Proportion estimates will be reported to assess percentages who actually complete the intake questionnaires as well as adherence to the four-week intervention and all daily measurements.

To address the evaluation of the four key elements; meditation, anxiety and stress, fitness and general health, and pain, a variety of analyses and descriptive statistics are necessary to calculate key estimates needed to inform the design and power of a large-scale trial given the different variable types and repeated measures embedded in the methodology. The primary assessment for this study will be a reduction in disability. Means and standard deviations will be reported for all quantitative measures for all groups, effect sizes for comparisons of means and repeated measures, and proportion estimates will be reported for qualitative variables. Where appropriate, correlations between various assessments of mindfulness, pain and disability (self-reported and quantitative measures), anxiety/fear, and activity (i.e. IPAQ-short and exercise performance) will be analyzed.

9. Emphasize issues relating to interactions with subjects and subjects' rights

Subjects will be notified of their rights, all risks and benefits of participation in this study during the informed consent procedure. Subjects will be informed that they may withdraw from participation at any time. Data collection sessions will be scheduled at times that are mutually convenient for the subject and the researchers and all efforts will be made to work with the subject's schedule.

Subjects will be instructed that they are able to stop intervention and pain measurements at any time if they experience excessive discomfort/pain. Treadmill exercise occurring at Duquesne will be monitored visually by a researcher in the adjacent room using a wireless camera system. Physiological measures, including heart rate, will also be monitored in real-time to ensure no issues during exercise. Subjects will be encouraged to stop exercise if they experience any discomfort or symptoms of over-exertion (≥ 17 on the Borg RPE scale). These symptoms will be explained during the informed consent process. There is a risk of falling off the treadmill. Subjects will be instructed to hold onto the rails if they feel like they are losing their balance or are going to fall.

The safety key will be on the waist of their pants to turn off the treadmill if they move too far back on the belt. Specific instructions will be given to patients who exercise or participate “at home.”

Though the likelihood is minimal, there is also a risk of a serious cardiac event, including loss of consciousness, chest pain, shortness of breath, and myocardial infarction, associated with performing moderate intensity exercise. To minimize this risk, eligibility criteria have been set to ensure healthy adults with low risk are enrolled in this study.

During exercise at Duquesne, participants will be monitored for signs associated with a cardiac event based on the American College of Sports Medicine (ACSM) *Indications for Terminating Exercise Testing* protocol. These indications include: onset of angina, signs of poor perfusion (dizziness, confusion, light-headedness, ataxia), failure of heart rate to rise with exercise, severe fatigue, or subject request to stop. To determine if any of these indications occur, participants will be visually monitored and heart rate will displayed in real-time at Duquesne trials. All participants will be notified that they may stop exercising if they feel short of breath, chest pain, abnormal back pain, or extremely fatigued. Also, patients are instructed that if they feel that their exertion reaches a 17 on the Borg Scale, they can stop walking. All research staff will be trained on this protocol and medical emergency management associated with a medical event. An emergency action plan will be stored in the laboratory and will be reviewed quarterly. Dr. Helm, MD will serve as our medical PI on this study. Any adverse reaction will be evaluated by Dr. Helm within 1 week of the event. “At home” trials will be additionally monitored through an online diary using Qualtrics Survey Platform, which allows the patient to record adverse events for the PIs. Qualtrics is supported by both Duquesne University and the University of Pittsburgh for research using surveys. Qualtrics servers are protected by high-end firewall systems and use Transport Layer Security encryption for all transmitted data. For ‘at home’ trials, subjects cannot be monitored for signs associated with a cardiac event, however, subjects will be made fully aware of these signs and told to stop exercising if they experience any of these symptoms. Subjects will be instructed to contact Dr. Szucs or Dr. Kostek via a Google Voice number immediately when these symptoms occur. If these symptoms do not resolve within 15 minutes of resting, subjects will be instructed to seek medical help. Any adverse events will be discussed immediately (subjects will have Dr. Helm’s, Dr. Szucs’ and Dr. Kostek’s contact information) and during the single trial that occurs each week at Duquesne. To ensure Dr. Szucs or Dr. Kostek is available to take these phone calls, a Google Voice number will be set up. This is the phone number subjects will be given. Calling this number will route the call to any of Dr. Szucs’ or Dr. Kostek’s existing phone numbers while maintaining privacy of personal contact information.

Risk of injury related to cutaneous mechanical testing is extremely rare and unlikely[4]. Mechanical testing is widely used and safe. Risks to the individual are minimal, because 1) subjects are instructed that they may stop any procedure at any time with no adverse consequences; and 2) the level of sensation experienced by subjects is at or below their tolerance level and threshold for pain.

Risk of injury related to thermal pain testing is minimal[4]. Thermal testing is widely used and safe. While thermal testing does produce pain, risks to the individual are minimal, because 1) the pain is transient in nature and generally subsides immediately after the procedure; 2) subjects are instructed that they may stop any procedure at any time with no adverse consequences; and 3) the level of pain experienced by subjects is below their tolerance level. With thermal stimulation there is a very slight risk of a burn, but this is minimized by the following: 1) positive lockout of stimulus parameters above 50°C; 2) the stimulator has built in a shut-down system to prevent the delivery of prolonged or high intensity stimuli (20 sec); 3) and before each use, temperature at probe will be verified with an electronic thermometer. Trials will proceed only if temperature detected at 20 sec cutoff is $\leq$ 50°C. Colleagues who have used this pain paradigm inform us that they have completed thermal testing with this stimulator on over 1000 subjects without producing a single burn. However, skin will be monitored for changes consistent with burns, such as redness that persists greater than one day and blistering. If a burn occurs, standard medical treatment will be recommended.

Risk of injury related to pressure pain testing is minimal[4,7]. Pressure testing is widely used and safe. While pressure testing does produce pain, risks to the individual are minimal, because 1) the pain is transient in nature and generally subsides immediately after the procedure; 2) subjects are instructed that they may stop any procedure at any time with no adverse consequences; 3) the level of pain experienced by subjects is below their tolerance level; and 4) the pain applied is never more than that subjects pain threshold, which is well below any pressure that could cause damage.

Participants will be made aware during the consent process that they may withdraw from participation at any time during their enrollment.

URLS TO GUIDED MEDITATION RECORDINGS

We have carefully chosen the following guided meditation recordings based on the experience and practice with guided meditation in a counseling setting of our clinical psychologist (Dr. Ian Edwards). All recordings are from the world-renowned meditation teacher and psychologist Dr. Tara Branch (https://www.tarabrach.com). One of the aspects of Dr. Branch's work that resonates and fits well with the current proposal is her interest in multiple types of guided meditation. This diverse approach recognizes that meditation is not a "one size fits all" intervention. Our hope is that by including a selection of five recordings that all have elements of mindfulness that we will help novice patients get used to meditative practice and prevent boredom during the 4-week trial (each recording will be listened to 1x per week).

Recording 1 (16:58): https://www.tarabrach.com/meditation-vipassana-insight/

Recording 2 (15:58): https://www.tarabrach.com/meditation-quieting-mind/

Recording 3 (12:36): https://www.tarabrach.com/meditation-relaxing-back-presence-2/

Recording 4 (17:08): https://www.tarabrach.com/meditation-living-presence-3/

Recording 5 (12:18): https://www.tarabrach.com/meditation-basic-body-scan/

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