OPTIMUM: Optimizing Pain Treatment In Medical settings Using Mindfulness

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Statistical Analysis Plan- pages 28-33

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Tool Revision History

Version Number	Version Date	Summary of Revisions Made	Consent change Yes/No
1	9/17/20	Original NCCIH Approval of UH3 Protocol	Yes
1.1	11/13/20	Updated to reflect virtual delivery of intervention.	Yes
1.2	11/17/21	Updated to reflect new exclusion criteria • First degree relatives (parents, siblings, child) of someone who has participated or is participating in the OPTIMUM study • Members of the same household • Not a patient at a participating clinic or persons not planning to continue as a patient at a participating clinic for 12 or more months	Yes
1.3	3/1/22	1. Added UNC Healthcare to recruitment sites 2. Added a new definition of AEs 3. Added - Refer to the "Adverse Event workflow" sheet for information on how and when to report AEs/SAEs or Unanticipated problems - to section 7.4 "Reporting procedures"	No
1.4	10/06/22	• Dr. Tuhina Neogi has been removed as a co-Investigator. • Subjects in the control group will be offered the OPTIMUM intervention after their participation in the study is complete. • Added the word "approximately" to the following sentence: Group size will be *approximately* 5-12 patients	No

		per session. (page 18: Frequency, setting and providers)	
1.5		Research Activities now includes new measures: trauma scale and global mindfulness, to be collected once at any time point during study participation.	No (a consent addendum was created)

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SYNOPSIS

Study Title

OPTIMUM: Optimizing Pain Treatment In Medical settings Using Mindfulness

Objectives

The aims of the study are the following: 1) to integrate and test an evidence-based mindfulness clinical pain program, OPTIMUM, for patients with cLBP in the primary care setting. 2) To evaluate use of healthcare resources by patients as documented in the electronic health record. 3)

To evaluate PCP and practice site use of, satisfaction with, and integration of OPTIMUM.

Design and Outcomes

This is a Pragmatic Clinical Trial (PCT) with a goal of informing clinicians, patients, administrators and policy makers how mindfulness can work in a real-life clinical setting, impact outcomes, increase access to non-opioid treatments and be reimbursable. It will be conducted with four HCS sites (Boston Medical Center, MA, a safety net health system; UPMC, Pittsburgh, PA, a large academic health system; Piedmont Health Services, NC, a network of federally funded health centers in partnership with the University of North Carolina Chapel Hill (UNC-CH); and UNC HealthCare).

The trial involves an evidence based 8-week medical group mindfulness clinical pain program (OPTIMUM) modeled on Mindfulness Based Stress Reduction (MBSR) and delivered in primary care settings through a telehealth and videoconferencing format at the three different healthcare sites.

A sample of 450 patients with chronic low back pain (cLBP) will be randomized to either OPTIMUM or to primary care provider (PCP) usual care. The PEG will be the primary outcome measure, which is a composite measure of pain and function. Secondary outcomes of psychological function will also be self-report. Health care system utilization will be obtained through the electronic health record (EHR) and includes opioid prescriptions, imaging, ED visits, and hospitalizations. We will also measure patient, clinic staff, and PCP satisfaction with OPTIMUM.

Interventions and Duration

Using Mindfulness to treat chronic low back pain in primary care settings. Patients will meet virtually via ZOOM (a video-conference application) weekly, for 8 weeks for 90 minutes in a group. Prior to the start of the intervention, patients meet one on one (approximately a 5-10 minute telehealth visit) with the clinician who is co-facilitating and may be billing for the medical care provided during the telehealth visit. Currently, only Boston Medical Center is billing. Neither UNC or Pittsburgh sites are billing. Patients will be encouraged to see their PCP at the beginning and end of the program. Measures to determine the impact of OPTIMUM in the real-world setting will be obtained at baseline (T1), program completion (T2) and six and 12 months after program completion (T3 and T4). The main outcome time point will be at six months (T3), which allows time for durability of effects to be determined. Participants will also complete monthly assessments of the pain medications they take and their health care system encounters.

Total length of time each participant will be in study: 12 months.

Sample Size and Population

Our target sample size of 450 patients with cLBP ≥ 18 years of age will be individually randomized either to an 1) 8-week mindfulness clinical pain program (n=225) + PCP Usual Care or 2) PCP Usual Care (n=225).

To ensure balance between groups, we will use permuted block randomization with block size of 4 or 6, in a 1:1 ratio, stratified by clinic and sex.

1. STUDY OBJECTIVES

1.1 Primary Objective

Specific Aims of the study are:
Aim 1: To integrate and test an evidence-based mindfulness clinical pain program, OPTIMUM, for patients with cLBP in the primary care setting.

Primary Hypothesis: Patients in OPTIMUM will have significantly improved pain intensity and interference as measured by the PEG composite score at completion of the program and 6 months (primary end point) and 12-months later, as compared to PCP Usual Care.
Hypothesis 2: Patients in OPTIMUM will have significantly improved psychological function as measured by the PROMIS-29 Mental Health Summary Scale at completion of the program and 6-and 12-months later, as compared to PCP Usual Care.
Hypothesis 3: Patients in OPTIMUM will be less likely to start and more likely to reduce or stop an opioid prescription for cLBP as compared to those in PCP Usual Care.

1.2 Secondary Objectives

Aim 2: To evaluate use of healthcare resources by patients as documented in the EHR.

Hypothesis: Patients in OPTIMUM will have fewer emergency department visits, fewer hospitalizations, fewer imaging procedures (CT/MRI), and fewer procedures (injections, surgery) than PCP usual care.

Aim 3: To evaluate PCP and practice site use of, satisfaction with, and integration of OPTIMUM.

2. BACKGROUND AND RATIONALE

2.1 Background on Condition:

Chronic pain is one of the most common conditions treated in the primary care setting, with cLBP costing over 30 billion dollars a year; yet treatment remains unsatisfactory for many patients.[1] The slippery slope of opioids to treat cLBP has many unintended consequences such as addiction, overdose, and diversion.[2,3] Compounding the problem, Primary Care Providers (PCP) have very little time during the 15-20 minute office visit to address the complex psychosocial and functional needs of the person with cLBP.[4] The opioid crisis has underscored the urgency of alleviating patients' cLBP with effective therapies, including evidence-based non pharmacological approaches that also address biopsychosocial needs. Mindfulness is effective for the treatment of cLBP yet remains underutilized as it has not been regularly woven into the outpatient clinical setting and is not reimbursed by health insurance companies.[5, 6] Mindfulness-based Stress Reduction (MBSR) is now part of the evidence-based guidelines of the American College of Physicians for initial treatment of cLBP.[7] We have shown that an 8-week program modeled on MBSR decreased pain and increased short-term function in older adults with cLBP.[5]

The burden of chronic low back pain: Chronic low back pain (cLBP) affects an estimated 5-10% of U.S. adults.[8] The National Ambulatory Medical Care Survey has found that low back pain symptoms are the 10th most common reason for a patient office visit.[9] The 2011 Institute of Medicine (IOM) report, Relieving Pain in America, highlights that low back pain (LBP) is the most common type of pain and the second most common reason that patients visit their primary care providers (PCP).[10] Patients have high levels of satisfaction with their providers but are less satisfied with the outcomes of cLBP treatment.[11] The PCP may escalate to opiates in the hopes of achieving satisfactory pain control despite the lack of evidence of their long-term benefit in cLBP.[12,13] The opiate crisis has spurred the need for non-pharmacological options for cLBP management. In response to this need the American College of Physicians updated their evidence-based guidelines for the treatment of cLBP in 2017.[7] They recommended that initial treatment be non-pharmacological, including mindfulness-based stress reduction (MBSR). However, many of these therapies are not yet widely available or are underutilized. To address this need, we are proposing an evidence-based, non-pharmacological clinical pain program for patients with cLBP delivered out of the primary care office.

Evidence base for a group mindfulness pain program: Two recent large clinical trials have demonstrated the beneficial effects of mindfulness in improving pain and function in adults with cLBP. Our randomized clinical trial (RCT) of MBSR vs. an education control of 282 older adults with cLBP found clinically and statistically significant improvement in pain and physical function at program completion.[5] Cherkin et al. randomized 342 adults to cognitive behavioral therapy (CBT), an 8-week MBSR program or usual care.[6] CBT and MBSR both showed clinically significant improved function (30% improvement from baseline) 28-weeks after program completion as compared to usual care (57.7% and 60.5% vs. 44.1% respectively, overall P=.04). These studies have withstood the rigorous evaluation of meta-analyses. As a result, in addition to the American College of Physicians' (the main professional organization for internal medicine) recommendation of MBSR as the initial treatment (along with 12 other non-pharmacological therapies) for cLBP, the Agency for Healthcare Research and Quality also recommended MBSR for the treatment of cLBP in their recent comprehensive systematic review.[7,14] While these landmark studies demonstrate the efficacy of the intervention, they were conducted under the controlled environment of a clinical trial. Translating the intervention to the clinical setting is the crucial next step for integrating the program into the "real world".

The value of group delivered self-management support in primary care: Common chronic diseases seen in a PCP's office such as hypertension, diabetes, obesity, and cLBP all require extensive patient education. Yet the time constraint of a typical 15- or 20-minute visit only allows the PCP to provide cursory advice. Medical group visits (MGV) in the primary care setting with patients who have a chronic disease are an efficient and effective way to communicate, provide support, advice and education.[15] For example, Cleveland Clinic offers over 200 types of shared medical appointments, Kaiser and Harvard Vanguard health systems all offer MGVs. Offering a group mindfulness pain program is an ideal opportunity to provide an evidence-based program to patients, which teaches them skills to learn to cope with and improve their pain and function without the use of opioids. Our program, modeled on MBSR, provides ample opportunity for discussion, allowing time to clarify misconceptions around chronic pain. Our proposal is in line with the 2011 Institute of Medicine Report "Relieving Pain in America"

which calls for new models of care for patients with chronic pain as we are embedding the program directly in the clinic.[10]

Medical Group Visits: Current studies suggest MGVs improve health status indicators such as health-related quality of life, patient satisfaction, and patient trust in their physician, as well as improving coordination and culturally competent care.[16, 17] MGVs can also reduce costs through the reduction of preventable emergency department (ED) visits and hospitalizations.[18-21] MGVs are organized in many different ways, and no one best model has been demonstrated in the literature. MGVs include individual medical attention, teaching (didactic and interactive), and patient self-management. Groups range from 4-20 patients with one to two facilitators and meet at regular intervals–anywhere from weekly to monthly and from one to four hours. The clinician's assessment and management can be conducted in an adjacent private examining space, and clinicians charge for the visit using established patient reimbursement codes. Integrative MGVs are also emerging for underserved populations.[22-24]

Interest in mindfulness is widespread and growing in the United States: It is estimated that 18 million Americans use meditation for health.[25] In our experience, patients have been enthusiastic about learning mindfulness meditation and mind-body methods. In Pittsburgh alone, over 800 people have taken the fee-for-service MBSR program offered by the UPMC Center for Integrative Medicine. In Chapel Hill, NC the University of North Carolina (UNC) Program on Integrative Medicine's Mindfulness-based Stress and Pain Management Program has taught year-round community-based fee-for service courses since 2000. For Dr. Morone's mindfulness R01 study for cLBP, over 1,000 people called with interest in participating. We believe the local interest in mind-body methods reflects the national interest in mind-body medicine. By providing a convenient, evidence-based group mindfulness pain program in primary care, we propose to parlay that interest into improved access to the program, and thus, to improved health.

2.2 Rationale

The rationale for a medical group pain program that is mindfulness-based: PCPs are in need of more non-pharmacological treatment options for their cLBP patients instead of falling back on medications (acetaminophen and nonsteroidal anti-inflammatory drugs [NSAIDs]) and referring out for treatment or prescribing opiates. The current model of caring for chronic pain patients does not allow for the time and attention that PCPs need to adequately address the complex needs of their patients. The medical group model increases patient education, social support, access to a clinician, and a sustainable way to bill for the treatment. Our proposed project will address the need for non-pharmacological treatments for cLBP in the following way; a) the mindfulness pain program will be delivered in the primary care setting so that PCPs have another evidence-based therapy to offer patients; b) the mindfulness pain program provides the time and attention that is necessary to adequately educate patients about chronic pain; c) the medical group model provides for a reimbursable model of care.

Impact: By translating an evidence-based group mindfulness pain program to the primary care setting we will 1) inform clinicians, patients, administrators and policy-makers how a medical group-based mindfulness pain program can be embedded into clinical practice; 2) determine the impact of this intervention under usual care circumstances; 3) demonstrate how the mindfulness pain program can be embedded in a variety of Health Care Systems; 4) demonstrate how the

mindfulness pain program can be delivered to an underserved population, which we expect will make up at least 2/3 of our total sample; 5) provide PCPs with more evidence based non-opioid, non-pharmacological therapies to treat their cLBP patients, which is currently limited to writing prescriptions for medications and referring out to other providers; 6) expand the access and availability of evidence-based treatments to patients with cLBP, who otherwise may not be able to participate in an integrative mindfulness pain program; and 7) signal to patients that pain management is important, by delivering services in their local primary care clinic locations.

3. STUDY DESIGN

It is a Pragmatic Clinical Trial (PCT) which will be conducted with four health care system (HCS) sites (Boston Medical Center, MA, a safety net health system; UPMC, Pittsburgh, PA, a large health system; Piedmont Health Services, NC, a network of federally funded health centers and UNC HealthCare, both in partnership with the University of North Carolina (UNC), Chapel Hill). The primary goal is to determine the impact of this intervention under usual care circumstances as defined in the FOA (vs. implementation research). The long-term goal is to increase the accessibility of evidence-based mindfulness programs to primary care patients with chronic pain.

This study involves an evidence-based 8-week medical group mindfulness clinical pain program (OPTIMUM) modeled on MBSR and delivered in primary care settings through a telehealth videoconferencing format. We will randomize 450 patients with cLBP to either OPTIMUM or to PCP usual care. Patients will meet virtually via HIPAA-compliant ZOOM for 8-weeks for 120 minutes in a group. Prior to the start of the intervention, patients virtually meet one on one (approximately 10 minutes) with the clinician who is co-facilitating and billing for the medical care provided (via telehealth). Measures to determine the impact of OPTIMUM in the real-world setting will be obtained at baseline (T1), program completion (T2) and six and 12 months after program completion (T3 and T4). The main outcome time point will be at six months (T3), which allows time for durability of effects to be determined. Participants will also complete monthly assessments of the pain medications they take and their health care system encounters. Pain intensity (PEG composite score) at six months will be the main outcome measure (obtained through online self-report surveys). Secondary outcome of psychological function will also be self-report and obtained online, or if the patient prefers, by telephone. Health care system utilization will be obtained through the EHR and includes opioid prescriptions, imaging, ED visits, outpatient primary care visits, physical therapy visits, injections, and hospitalizations. We will also measure patient, clinic staff, and PCP satisfaction with OPTIMUM. Totally, participants will remain in the trial for 12 months including the follow-up period.

4. SELECTION AND ENROLLMENT OF PARTICIPANTS

Our target sample size of 450 patients with cLBP ≥ 18 years of age will be individually randomized either to a 1) 8-week mindfulness clinical pain program (n=225) + PCP Usual Care or 2) PCP Usual Care (n=225). The selection criteria are kept broad to include most patients referred to the PCT.

4.1 Inclusion Criteria

Participants must meet all of the inclusion criteria to participate in the trial.

- Age ≥ 18
- Chronic low back pain, which is pain that persists for at least 3-months and has resulted in pain on at least half the days in the past 6 months
- A score ≥ 3 on the PEG
- Willing and able to provide online or telephone informed consent
- Speak English as the intervention manual is currently written in English

4.2 Exclusion Criteria

Participants meeting the exclusion criteria at baseline will be excluded from the trial.

- Do not meet the above inclusion criteria
- Red flags- recent (past month) worsening of pain, unexplained fever, unexplained weight loss
- Pregnancy
- Metastatic cancer
- First degree relatives (parents, siblings, child) of someone who has participated or is participating in the OPTIMUM study
- Members of the same household
- Not a patient at a participating clinic or persons not planning to continue as a patient at a participating clinic for 12 or more months

1. Study Enrollment Procedures

The HCS sites that were chosen represent diversity in practice delivery and in-patient population. We expect a full 2/3 of our sample will be underserved and/or an underrepresented group. Multiple approaches will be used at all three HCS sites to recruit participants into the PCT. Detailed recruitment procedures are in the Standard Operating Procedures document. Some of the approaches are described here. The electronic health record will be reviewed each week for patients with a diagnosis of low back pain who have an upcoming appointment, once identified, patients will be approached by the study research assistant, with consent of the provider, for screening for study eligibility. Patients will also be informed of the program by a letter from their PCP or clinic administrator (e.g. Medical Director, healthcare system administrator) which will also invite them to participate. Flyers and rack cards describing the program will be placed throughout the clinics. Referral at the point of care may occur by creating an order in the EHR that will refer patients to OPTIMUM. This workflow is well established at UPMC and BMC and will be integrated into the EHR at PHS.All four HCSs use an EHR. BMC, UPMC, and UNC Healhcare use EpicCare (Epic), one of the most common EHRs, now deployed in an estimated 35% of healthcare systems in the United States. PHS uses Centricity. The different EHRs used are seen as a strength as it will demonstrate integration of OPTIMUM into different EHRs. Each site will have the opportunity to customize recruitment in order to fit the unique needs of each HCS. For example, UPMC may create an electronic alert which would pop-up when clinicians

were seeing a patient with LBP. If the patient is interested, the clinician would click to refer the patient to OPTIMUM.

Randomization procedure: To ensure balance between groups, we will use permuted block randomization with block size of 4 or 6, in a 1:1 ratio, stratified by clinic and sex.

5. STUDY INTERVENTIONS

5.1 Interventions, Administration, and Duration

OPTIMUM: The medical group mindfulness clinical pain program will retain the format, meditation exercises and discussions about the mind-body connection and pain of the original program we studied, which was modeled on the MBSR program that we successfully delivered to older adults with cLBP.[5] The program teaches a variety of mindfulness meditation methods. Mindfulness meditation is simple and safe because it takes ordinary activities like breathing, eating, and walking and turns them into a meditation by creating greater awareness of the moment-to-moment sensations, emotions, thoughts and behaviors that arise during these activities.[52] The program will incorporate several modifications we made during the large clinical trial to tailor it to the patient with cLBP. This included understanding pain from a mind-body perspective, and viewing pain as a stressor on physical sensations, thoughts, emotions, and behavior. It also included discussion on patients' use of mindfulness to work with pain and pain-themed meditations.

Program Protocol: We are following the evidence-based protocol used in our large clinical trial of MBSR for cLBP. Both this trial and our pilot work used similar formats. Both these trials were included in the evidence-base of MBSR for cLBP by the American College of Physicians.[5,7,26]

During the *first week* participants will be introduced to the principles and practice of mindfulness meditation. The homework requirement of daily meditation (six of seven days/week) lasting 5-45 minutes will be reviewed. Support materials of downloadable MP3, MP3 player with uploaded guided meditations, YouTube link to the guided meditations or CD recording and reading materials will be distributed. As a result of the pilot, the YouTube link works best, it is a private link that cannot be found by searching YouTube, participants are emailed the link. The body scan technique will be taught at the first session. If physical discomfort should arise during any meditation, participants will be encouraged to change to a more comfortable position. The first class introduces mindful eating, which is done through a guided exercise of eating a raisin (or other food at meditation instructor's discretion). This exercise begins to introduce the concept of informal meditation, in that mindfulness can be brought to everyday activities like eating.

During the *second* and following weeks the sessions will include a general discussion of the patients' experience with the meditation method, including problem-solving regarding obstacles to the meditation practice. Theoretical material related to meditation, pain and the mind-body connection will be presented. About 30 minutes will be spent at each session in these discussions. Also during the second week, quiet sitting meditation with mindfulness of breathing will be introduced. Gentle chair-based stretching exercises are introduced at the second class (i.e., mindful stretching). The *third* session will introduce pain theory and the multidimensional response to pain. The role of expectation will be reviewed.

The *fourth* session will introduce the flight or fight reaction. This is an interactive session with participants describing their reactivity to stress as well as their response to mindfulness meditation. Stress and the relaxation response will be discussed in relation to worsening or decreasing pain.
At the *fifth* week's session, walking meditation or mindful movement may be introduced. How to use mindfulness meditation methods to work with pain will be discussed. This will occur at this and the sixth session. Participants will also be taught how to work with pain during formal meditation. They will learn this by a guided meditation during this session, as well as a recording of the body scan that is specific for working with pain.
At the *sixth* week's session, mindfulness in interpersonal relationships and everyday life will be discussed. There will be a review of using mindfulness methods to work with pain, as well as interactive discussion of participants' use of mindfulness to work with pain.
At the *seventh* week's session, using mindful attention to perceive the choices that are available at this moment, and that can affect our pain, health, and well-being will be discussed.
The *eight* week's session will include discussion of the application of mindfulness to everyday situations as well as breaking through habitual tendencies of coping with pain. Integrating what has been learned over the course of the program will be reviewed.
All sessions may include yoga.
Mindfulness instructors have flexibility to review content in a different order so that they can customize their instruction to the participants.

The structure of each session will be approximately 45 minutes (total) of meditation and 45 minutes of discussion. This format was applied successfully during our large clinical trial.[5]

PCP Usual Care Control: PCP Usual Care was chosen as the comparator as it is currently the most commonly used treatment option for patients with cLBP. We will verify patients' attendance at a PCP visit during the study through the EHR as well as the meditation instructor taking attendance. Participants in the PCP usual care control group will be given the option to receive the OPTIMUM mindfulness pain management program at the end of their participation in the study.

Frequency, setting and providers: Participants will be seen in a group format virtually via HIPAA compliant ZOOM once a week for 120 minutes for 8-weeks. Group size will be approximately 5-12 patients per session. We found this group size to be optimal in both our pilot work and large clinical trial because the group was small enough to encourage individual participation, but not too large that participants were afraid to speak. This is also consistent with group size for MGVs. The original and proposed group mindfulness pain program is modeled on the MBSR program we successfully delivered to older adults with cLBP[5.] All sessions will be led by a clinic-based provider (MD or DO, nurse practitioner, physician assistant, social work therapist, or psychologist) to whom we provide training in co-leading the program, as well as an experienced MBSR instructor. Training at the three HCS sites will consist of several one-hour sessions facilitated by Dr. Gardiner. We have chosen this model because the clinic-based provider will be able to schedule patients under their name, document in the medical record, provide face-to-face time, and bill for the sessions. The MBSR instructor has the necessary expertise to teach the program. We will use materials that have been previously developed for MGV provider training and adapt them to OPTIMUM. These materials will be used for wider

dissemination. All sessions will occur in a HIPPA compliant version of ZOOM (video-conference application).

Technical Training: All participants will receive technology training on using videoconferencing during a one hour session. The intervention will require technology support. Details of the technical training and technical support during the intervention sessions is detailed in the Technical Training and Support Standard Operating Procedures.

5.2 Handling of Study Interventions

Three methods of mindfulness meditation will be taught, consisting of: 1) the body scan; 2) sitting practice/awareness of breathing; 3) mindful movement/yoga. An instructor manual has been created to guide the providers at all three HCS sites.

5.3 Concomitant Interventions

5.3.1 Allowed Interventions

OPTIMUM medical group mindfulness clinical pain program.

5.3.2 Required Interventions

None.

5.3.3 Prohibited Interventions

None.

5.4 Adherence Assessment

Assessment and monitoring: Attendance at group sessions will be obtained through the EHR (registered appointment) as patients will need to check in as a telehealth visit and that check-in is logged into the EHR. Unblinded study staff will record attendance. Adherence-promoting strategies include providing guided meditation recordings and instructional materials. Group sessions will stress the importance of home practice and group participation, and discussion will include problem-solving around barriers to the meditation practice and coping with pain.

Treatment fidelity and credibility: The mindfulness instructors will meet weekly during the first 6-months of the UH3 phase of the trial along with Dr. Morone, Dr. Gaylord, and Dr. Gardiner to discuss the delivery of the program in primary care through a telehealth video format, review the structure and format of the sessions, and troubleshoot barriers as they arise. After the first 6-months meetings will be biweekly and starting in Year 2 of the UH3 will be monthly. More frequent or less frequent meetings will be at the discretion of the group. It is critical during this demonstration project to meet regularly to address issues of program delivery and integration into clinic. Additionally, Dr. Greco has been trained in the use of the Mindfulness-based Interventions-Teaching Assessment Criteria (MBI-TAC), a standardized system for rating competency of mindfulness instructors and she will be able to provide guidance on evaluating treatment fidelity in a pragmatic setting. Training and monitoring at the three HCS sites will consist of: 1) a combined 3-hour online MGV training led by the respective site PIs and facilitated by Dr. Gardiner; 2) weekly to monthly meetings, as noted above; and 3) facilitator evaluation and group fidelity monitoring, led by Dr. Greco.

6. STUDY PROCEDURES

6.1 Schedule of Evaluations (Table 1)

Assessment	Screening & Consent	Baseline (T1)	OPTIMUM Program 1-8 weeks, End of 8 weeks (T2)	Monthly Pain Medication and Healthcare Encounters	Follow-up after 6 months (T3)	Follow-u mo (T
Informed Consent Form	X					
Demographics		X				
Screening Questionnaire	X					
Inclusion/Exclusion Criteria	X					
Enrollment/Randomization	X					
Adverse Events			X		X	
Study Measures		X	X	X	X	

6.2 Description of Evaluations

6.2.1 Screening Evaluation

Procedures to determine whether a potential participant is eligible to take part in the trial are known as screening procedures.

Consenting Procedure

We have requested and received IRB approval for a waiver of the requirement to obtain a signed, written informed consent for the preliminary screening procedures used to determine the eligibility of potential participants. Screening will occur over the phone and an IRB approved script will be used, followed by the screening questionnaire.

In person screening: After the COVID pandemic, in-person screening procedures may occur since potential participants can be identified before their visit through medical record review. When potentially eligible patients are identified before their upcoming in person office visit

because they have a low back pain diagnosis, they will be approached ONLY if their provider agrees. They will be asked if they would be interested in hearing about the study, some brief eligibility questions and if they are eligible, would they like to hear more about the study. This will count as verbal consent (IRB approved script will be followed) for the preliminary screening procedure Since, the screening procedures consist only of the basic information from interested potential participants, we believe it is conventional to defer obtaining written informed consent.

Informed consent: We have obtained IRB permission to obtain verbal informed consent, obtained through a telephone interview. After the screening procedure, eligible participants will be provided with a copy of informed consent through email. All will be encouraged to review the consent form before undergoing informed consent. A listed investigator or designated study team member trained in informed consent will obtain informed consent from each study participant before the start of any research/intervention procedures. A page-by-page review of the consent form will occur and the potential study subject will be asked for a verbal indication of their understanding of the material contained in the consent form. They will also be asked if they have any questions. Participants will then be asked to verbally consent, if they agree with the material and wish to be enrolled in the study. The potential participants may reschedule their enrollment visit should they feel that they need more time to decide about enrollment.

We will also administer an electronic informed consent for subjects who wish to complete the procedure online and not over the telephone.

Screening

Screening will be established by telephone. Participants will undergo screening if they are identified in EPIC (Electronic Health Record System) or they self-refer as a result of having heard about the trial from the HCS sites research registry, clinician referral or posted flyers or if they receive a letter from their provider to participate in the study. Recruitment will also occur by using the Clinical Data Warehouse at Boston Medical Center that allows for identifying patients with a diagnosis of low back pain. At the University of Pittsburgh a similar process is available through the University of Pittsburgh CTSI. Additionally, all sites may use research registries to identify subjects. Screening includes questions designed to inform potential participants about the study and help the study team in determining whether he/she is initially eligible. This procedure takes approximately 6-10 minutes to complete.

Potential participants will be informed about the eligibility during the screening procedure.

Because the intervention is delivered in cohorts, if there has been more than an 8-week delay between screening and the start of the cohort, then the participant will be rescreened for eligibility with the PEG. If the score is < 3 they will be ineligible.

6.2.2 Enrollment, Baseline, and/or Randomization

Enrollment

Enrollment in the trials refers to the stage when participant is completely eligible, has given informed consent, completed the required screening and demographics and has been randomized. Randomization will occur after the baseline assessment.

Baseline Assessments and Study Measures

Once informed consent has been obtained and eligibility confirmed baseline measures will be completed. The baseline and subsequent assessments (T1-T4 and monthly assessments) will be completed electronically or over the telephone, per patient preference. We will also mail the measures to patients if that is the only way they will complete the measures. A self-addressed, stamped envelope will be included.

Assessing improvement in a patient's chronic pain condition is challenging because unlike diabetes, hypertension, or obesity there is not yet bloodwork or objective measurements that can be easily ordered or obtained. PCPs thus rely on self-report of improvement that may or may not involve a scale. The CDC's guidelines for the prescription of opioids for chronic pain provide recommendations for pain evaluation and treatment that inform our outcomes. The CDC guidelines include evaluating the multidimensional impact of chronic pain with validated scales that measure pain intensity, function (in its broader sense to include physical, emotional and social function or quality of life), mood, sleep, pain catastrophizing, and anxiety.[59] Additionally, they reiterate that a 30% improvement in pain and function is clinically meaningful. A recent comprehensive review of measures to include in chronic pain trials recommended the PEG composite score, PROMIS 4-item function (obtained from the PROMIS 29) and scales for evaluating mood, anxiety, and global impression of change. To avaluate the association between pain and trauma, we have added the Life Events Checklist for DSM-5 (LEC-5). We have followed these recommendations for the patient-reported outcomes (PRO) measures as shown in Table 3. Given these recommendations, as well as the well-established use of the PEG composite score in clinical practice and its low patient burden we will use the PEG composite score as the primary outcome measure. Because administering these measures is not part of usual care, except for the PEG composite score, we will capture PROs directly from patients during four key time points of the PCT.

We will obtain healthcare resource utilization directly from the EHR (Table 3). The EHR will evaluate opioids according to prescriptions written; CT/MRIs performed; invasive procedures such as injections and surgeries; outpatient primary care visits, physical therapy visits, urgent care visits, ED visits, and hospitalizations. Most utilization outcomes will be treated as count data and cumulative opioid exposure as continuous (i.e., cumulative morphine equivalents).

All 450 participants who are included based upon the screening criteria outlined above will receive identical assessments. We will use a paperless data management system that is described below. The measures are quick to administer and complete. In our experience, almost all the individual measures can be done in 5 minutes or less. The total time for assessment is expected to be 20 minutes, with many people completing measures in less time.

We will also conduct an online survey with all PCPs in the participating practice, to learn about their perspectives on how well the study procedures integrated with their work flow, overcame common barriers to chronic pain management, and were consistent with the practice's typical referral and feedback protocols. This survey will also ask PCPs to report if/how many of their patients enrolled raised safety concerns during the study, overall satisfaction with the program, and open-ended questions will solicit feedback for protocol improvements.

Outcome Measures Table (Table 2)

	T1 Baseline	**T2 8-wks**	***T3 6-mo**	**T4 12-mo**	**Number of Questions**
Patient-reported Measures					
**PEG	X	X	X	X	3
PROMIS-29 (Q.1-4 & 17-20 same as PROMIS Physical Function & PROMIS Sleep	X	X	X	X	29
Current Opioid Misuse Measure	X	X	X	X	17
CAMS-R (mindfulness)	X	X	X	X	12
Satisfaction, single item		X	X	X	1
Ethics, single item		X			1
Patient Global Impression of Change PGIC		X	X	X	1
Opioid Use, single item	X	X	X	X	1
Pain Catastrophizing Scale Short Form	X	X	X	X	6
Demographics	X				~23
Tobacco, Alcohol, Prescription medications, and other Substance (TAPS).	X			X	5
Screening questionnaire	X				~10
Pain Medication (s) *This form will be asked monthly*	X	X	X	X	
Charlson Co-Morbidity Index	X				23

Health Care System Utilization (self-report). *This form will be asked monthly*		X	X	X	~20
HEAL-Expectation	X				6
Telehealth Usability Questionnaire	X	X			7
Total Questions OPTIMUM					(baseline) (other time points)
Life Events Checklist for DSM-5 (LEC-5), *This form will be asked once at any upcoming timepoint (including monthly assessments)		*	*	*	17
Global Mindfulness				X	13
EHR Outcomes					
Opioid prescriptions and other prescriptions for pain, CT/MRIs of lumbar-sacral spine, injections of lumbar-sacral spine, ED/urgent care visits for LBP, Surgeries of lumbar spine, hospitalizations for LBP, PCP visits for LBP, physical therapy referrals for LBP	X		X	X	
Core HEAL Pain Data Measures					
PROMIS Physical Function (questions 1-4 same as in PROMIS 29 questions 1-4)	X		X		2 additional questions
PROMIS Sleep (questions 1-4 same as in PROMIS 29 questions 17-20)	X		X		2 additional questions
Sleep Disturbance	X		X		2
Depression PHQ-2	X		X		2
Anxiety GAD-2	X		X		2

*Primary Timepoint **Primary outcome.
Pain impact is defined as Pain intensity, pain interference and functional status calculated from 9 items of the PROMIS-29. PROMIS: patient reported outcomes measurement information system.
Yellow Highlight=Core HEAL Measures incorporating into OPTIMUM outcomes.

Additional Baseline Variables: We will assess age, sex, race, ethnicity, and socioeconomic status, involvement in workers' compensation, work status, previous treatment including nonpharmacological therapies, and marital and educational status. Biomedical factors will include: a) comorbidity: data on comorbidity will be gathered using the Charlson Co-Morbidity Index T1;[60] b) pain medications (regularly scheduled and as-needed) at T1-T4 and will be categorized into sub-classes: i) salicylates (aspirin > 1200 mg/day, salsalate); ii) non-aspirin, non-COX2 selective NSAIDs; ii) COX2 selective NSAIDs; iv) acetaminophen; v) opioids; vi) skeletal muscle relaxants; vii) adjunctive agents (e.g., corticosteroids, capsaicin, Neurontin); and c) antidepressants and antianxiety medications. Regularly scheduled opioid analgesics will be converted to daily oral morphine equivalents.[61]

Randomization

To ensure balance between groups, we will use permuted block randomization with block size of 4 or 6, in a 1:1 ratio, stratified by clinic and sex. Participants will be randomized after completion of baseline measures.

6.2.3 Blinding

This is a double-blinded study as research assistants who assist participants in their assessments and the study statistician will be blinded to treatment assignment. Participants will not be blinded to group assignment. Detailed table below.

Study Staff	**Blinding: Justification**
Principal Investigator (PI)	Unblinded: Any AEs that occur need to be reported and reviewed. Can serve as back-up for mindfulness instructor or provider
Site Co-Principal Investigator Site Co-Principal Investigator	Unblinded: Any AEs that occur need to be reported and reviewed. At UNC one site co-PI is blinded due to involvement with EHR data and programming local REDCap
Co-Investigators (Co-I)	Blinded
Project Manager	Unblinded: Needs to interact with all staff, point of contact for AEs along with PI, randomizes participants

Study Coordinator	Not all sites have separate study coordinators-UNC only. One will be blinded and the other will be unblinded because she is the technology assistant for the intervention
Research Assistants	Blinded
Biostatistician	Blinded
Data Analyst	Blinded
Programmer	Unblinded: will need to respond to requests which may involve randomization status

6.2.4 Follow up Visits

All outcomes will be assessed at program completion and after six and twelve additional months of follow-up (eight weeks (T2), six months (T3), and twelve months (T4) from the start of the program, respectively), except satisfaction with OPTIMUM and Global Impression of Change, which will be assessed at program completion and at the six months and twelve months timepoints (T2, T3 & T4) Moreover, pain medications and healthcare utilization form will be assessed every month. Study participants will each be enrolled for up to twelve months. Follow-up for twelve months was chosen to evaluate duration of program effect on patients' cLBP.

6.2.5 Completion/Final Evaluation

Final Evaluation at twelve months (T4) will have the same assessments as at the end of the program (T2) and at six months (T3).

7. SAFETY ASSESSMENTS

We will monitor patient safety throughout 12 months of duration of the study. Potential risks of mindfulness interventions are minimal and may include the following:

- Emotional discomfort or distress may arise for some participants during exercises or at home practice related to awareness of negative emotions, thoughts, or physical sensations.
- Participants might face discomfort when sitting in a chair.
- Participants might face discomfort when doing gentle chair exercises (chair yoga)

Risks associated with mindfulness interventions are generally minimal and transient and can be managed with instructor guidance and continued experience with the practices. These risks will be explained to participants at study enrollment. An experienced mindfulness instructor will lead the sessions. Participants will be encouraged throughout the sessions to discuss their experiences with the exercises, including any emotional difficulties. Additionally, the beginning of each session will include time to discuss home practices and the participant will problem-solve with the instructor any issues that came up in practice during the week. Participants will be reminded

that the sessions are confidential in order to encourage disclosure of difficulties. For discomfort while sitting in a chair, participants will be instructed on how to be mindfully aware of discomfort and then to gently change position to one that is more comfortable.

7.1 Specification of Safety Parameters

Participants may experience discomfort in answering some of the questionnaire questions or in making disclosures in the sessions. Participants will be told that they may skip questions that they do not wish to answer and that disclosures in the program are also entirely voluntary. All patients are advised to refrain from disclosing anything said during the sessions outside the group.

7.2 Methods and Timing for Assessing, Recording, and Analyzing Safety Parameters

In the two large studies of MBSR for chronic low back pain, no significant adverse events related to the intervention were reported.[5,6] Given that mindfulness methods take ordinary activities like sitting down, eating, lying down and walking and turn them into a meditation through directed breathing, adverse events are rare. Any adverse event reported to the MBSR instructor will be recorded, reviewed by the PIs and reported to the IRB when unexpected and study-related, and all AEs whether expected, unexpected, study related or study unrelated will be reported to the independent monitoring committee. Any adverse event that results in patient injury or requires immediate medical attention will be brought to the attention of the study team and PIs immediately. The MBSR interventionists and study team will have immediate access to the PIs through pager or cell phone number. We will collect health care system encounters every month. Any positive responses will be explored by study personnel to obtain additional information. This will then be reviewed by the PIs.

7.3 Adverse Events and Serious Adverse Events

For determining severity of an adverse event we use the following definitions (below). If a participant has an emergency department visit (but not hospitalized and discharged to home), then they are assigned of moderate intensity and if the participant is hospitalized it is assigned of serious intensity.

Adverse Event: *any untoward medical occurrence (whether physical or psychological) associated with the use of meditation or mind and body methods, or breach of confidentiality and which may have a causal relationship with the study procedures.*

Mild: Awareness of signs or symptoms, but easily tolerated; are of minor irritant type; causing no loss of time from normal activities; symptoms would not require medication or a medical evaluation; signs and symptoms are transient.

Moderate or greater severity. This adverse event requires medical evaluation and/or medical treatment; or is a serious adverse reaction.

Serious. This adverse event is fatal or life-threatening; requires hospitalization; or produces a disability.

Solicited adverse events and serious adverse events: will occur during the monthly assessments when health system utilization will be queried.

7.4 Reporting Procedures

When participants report an AE or SAE a description of the AE will be recorded in REDCap and brought to the attention of the PI who will then determine if it is study related. Clinicians will make a note during the 8-week sessions, if any adverse effect comes up and report it to the study team who will record the event on the Important Medical Event Form and then notify the PI. Any unanticipated problems involving risk to subjects or others and study-related will be reported to IRB as per the University of Pittsburgh sIRB guidelines. (Refer to the "Adverse Event workflow" sheet for information on how and when to report AEs/SAEs or Unanticipated problems)

7.5 Follow up for Adverse Events

We will follow patients until the adverse event is resolved.

7.6 Safety Monitoring

A formal Independent Monitoring Committee will be set up which will follow the procedures of the NCCIH.

8. INTERVENTION DISCONTINUATION

Circumstance for Withdrawal without Consent:

Withdrawal Procedures: Participants are permitted to withdraw from the study at any time during the intervention or follow-up process. To withdraw from the study, participants should contact the PI at the corresponding site. Participant data prior to withdrawal will be retained in the case of withdrawal from the study.

9. STATISTICAL CONSIDERATIONS

9.1 General Design Issues

OPTIMUM is a multi-site Randomized Controlled Trial/ Pragmatic Clinical Trial (PCT) to treat chronic low back pain (cLBP) in primary medical settings using mindfulness through a telehealth HIPAA-compliant videoconferencing format The study participants will be randomized at an individual level.

Specific Aims of the study are
Primary Objective, Aim 1: To integrate and test an evidence-based mindfulness clinical pain program, OPTIMUM, for patients with cLBP in the primary care setting.

Primary Hypothesis: Patients in OPTIMUM will have significantly improved pain intensity and interference as measured by the PEG composite score at completion of the program and 6 months (primary end point) and 12-months later, as compared to PCP Usual Care.
Hypothesis 2: Patients in OPTIMUM will have significantly improved psychological function as measured by the PROMIS-29 Mental Health Summary Scale at completion of the program and 6-and 12-months later, as compared to PCP Usual Care.

Hypothesis 3: Patients in OPTIMUM will be less likely to start and more likely to reduce or stop an opioid prescription for cLBP as compared to those in PCP Usual Care.

Secondary Objective, Aim 2: To evaluate use of healthcare resources by patients as documented in the EHR.
Hypothesis*:* Patients in OPTIMUM will have fewer emergency department visits, fewer hospitalizations, fewer imaging procedures (CT/MRI), and fewer procedures (injections, surgery) than PCP usual care.

Secondary Objective, Aim 3: To evaluate PCP and practice site use of, satisfaction with, and integration of OPTIMUM.

9.2 Sample Size and Randomization

Our target sample size of 450 patients with cLBP ≥ 18 years of age will be individually randomized either to an

1) 8-week mindfulness clinical pain program (n=225) + PCP Usual Care or

2) PCP Usual Care (n=225).

Randomization and Treatment Assignment Procedure
To ensure balance between groups, we will use permuted block randomization with block size of 4 or 6, in a 1:1 ratio, stratified by clinic and sex. Co-I Dr. Weinberg (lead statistician) will generate the randomization sequence using SAS version 9.4, which will be implemented in the database so that the group allocation will be revealed only when each patient consents and is randomized. The randomization schedule will be created prior to enrollment and the study statistician will remain blinded to treatment assignment. We chose to randomize at the patient level rather than at the cluster level (provider or clinic) based on our responses to design choice clarification questions recommended by the NIH Collaboratory: 1) the impact of the pain program in the real-world setting is primarily at the level of the individual patient, as OPTIMUM is delivered to the patient and not the provider, for example, we are not studying implementation of provider treatment guidelines, which could result in contamination if randomized at the patient level 2) randomization at the patient level will not interfere with usual care for the patient with cLBP 3) contamination, if it occurs, will be minor. Contamination cannot be completely eliminated in either cluster or traditional RCT designs and we expect either design has a small risk of staff or patients discussing study details (“comparing notes”) as medical care is delivered in teams and patients go to a variety of clinics depending on appointments with specialists. Additionally, randomization at the patient level allows for efficient use of limited resources (reducing cost and time to completion of the study) while still including a large sample size and maintaining scientific rigor.

9.3 Definition of Populations

All analyses for treatment group comparisons will use the original treatment assignment as randomized for each participant (intention-to-treat). We will also perform a per-protocol analysis for the primary outcome for participants who attended at least 6 out of 8 (75%) of sessions.

9.4 Interim Analyses and Stopping Rules

The interim analyses and stopping rules will be assessed by the independent monitoring committee.

This study will be stopped prior to its completion if (1) the intervention is associated with adverse effects that significantly impact the risk-benefit ratio; (2) study recruitment or retention becomes futile; (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.

9.5 Outcomes

9.5.1 Primary Outcome

The PEG composite score is the primary outcome measure. This will be used to measure the pain intensity, interference, and enjoyment. Six months (T3) will be the primary time point.

9.5.2 Secondary Outcomes

Secondary outcomes are listed in Table 2 above.

9.6 Data Analyses

Data Evaluation:

Prior to conducting the analyses outlined below, we will evaluate the statistical properties of our baseline information and outcome measures. Descriptive statistics, including measures of central tendency (means, medians, other percentiles) and dispersion (standard deviations, ranges) will be computed for continuous data such as the age at enrollment, PEG composite score and other continuous measures. We will also check for potential outliers, normality and missing data. Frequency distributions will be calculated for categorical data such as sex.

We will compare the distributions of baseline characteristics between the two groups to assess the effectiveness of the randomization. All analyses for treatment group comparisons will use the original treatment assignment as randomized for each participant (intent-to-treat). We will adjust for any baseline variable that either statistically (based on a p-value cutoff of $p<0.2$) or clinically differs between the two groups. Data transformations may be applied to outcomes depending on the shape of the distribution to better approximate normality. We will consider ease of interpretation and clinical meaningfulness when choosing transformations.

Aim 1: To integrate and test an evidence-based mindfulness clinical pain program, OPTIMUM, for patients with cLBP in the primary care setting.
Primary Hypothesis: patients in OPTIMUM will have significantly **improved pain intensity and interference as measured by the PEG composite score** at completion of the program and 6 months (primary end point) and 12-months later, as compared to PCP Usual Care.

We will compare the PEG (primary outcome) at T2 (8 weeks from baseline) and T3 and T4 (6 months and 12 months from T2) with PEG at T1 (baseline) included in the vector of repeated measures using a mixed effects model. We will include the intervention group indicator, time

and their interaction as fixed effects, with random effects for repeated measures on individuals over time and random class effects for group in the intervention arm. We are proposing to control for clustering effect within each class using a random effect because the response of participants in the same class might be correlated. In the study by Dr. Lynn DeBar, the intraclass correlation coefficient for the class was 0.053.[5] We have also taken this into account in our sample size consideration. Alternative covariance structures for the repeated measures over time will be compared using Akaike's Information Criteria (AIC). This model will be used to test specific hypotheses using contrast statements and to compare temporal changes over time between the intervention and control groups. Variables with baseline imbalances can be incorporated as additional fixed effects. We will also examine a clinically meaningful 30% improvement in PEG from baseline as a binary outcome (yes or no) at each follow-up time point using a logistic mixed effects model incorporating a random effect for class clustering. All analyses will be conducted in SAS version 9.4 with $p<0.05$ considered statistically significant unless otherwise specified.

Hypothesis 2: patients in OPTIMUM will have significantly improved psychological function at completion of the program and 6- and 12-months later, as compared to PCP Usual Care.
Analyses will mirror those described above using a mixed effects model with random effects for the clustering effect of intervention classes and repeated measures on individuals over time, with fixed effects for group, time and their interaction. Contrast statements will be used to compare changes from baseline to specific time points. All analyzes will be conducted in SAS version 9.4 with $p<0.05$ considered statistically significant unless otherwise specified.

Hypothesis 3: patients in OPTIMUM will be less likely to start and more likely to reduce or stop an opioid prescription for cLBP as compared to those in PCP Usual Care.
We will examine opioid prescription for cLBP in two ways. First, we will examine the dose of opioids as morphine dose equivalent (continuous outcome) for those subjects with an opioid prescription at baseline. The analytic approach will mirror the mixed models described for Hypothesis 1 to compare group doses over time and in relation to baseline. Next we will use a binary outcome which is yes/no for opioid prescription (any) for each patient at each time point. Analytic methods will again mirror methods for Hypothesis 1 now using a logistic mixed effects model.

Aim 2. To evaluate use of healthcare resources by patients.
Hypothesis*:* patients in OPTIMUM will have fewer emergency department visits, fewer hospitalizations, fewer imaging (CT/MRI), and fewer procedures (injections, surgery) than PCP usual care.
Healthcare utilization over 6- and 12-months (prescriptions of opioids, injections, surgery, CT/MRI, ED visits, hospitalizations) are mostly in the form of counts. We will fit a series of GEE models with each outcome as the dependent variable, a negative binomial distribution to account for over dispersion, a log link, exposed time period as an offset, intervention arm (OPTIMUM/Usual Care) as the independent factor of interest, and an exchangeable correlation structure for clustering. Alternative correlation structures will be examined via the QIC statistic. Intervention arm incident rate ratios and their significance will constitute the test of the hypothesis.

Aim 3. To evaluate PCP and practice site use of, satisfaction with, and integration of OPTIMUM.
PCP satisfaction with the pain program will be summarized using descriptive statistics and histograms. We will also investigate if these measures are different depending on the demographic characteristics of the PCPs, such as gender, age, race, ethnicity, clinic location, and years since training, or the outcome of the patients using t-test, chi-square test, Pearson or Spearman correlation tests. Number of 8-week programs delivered at each clinic will also be summarized with descriptive statistics. Adoption of EHR tools and OPTIMUM after study completion will be described.

Planned Analysis & Power Assessment
The table below is of power calculations for the Optimum study using the PEG as the primary outcome. An ICC estimate of 0.053 was used, which came from Dr. Lynn DeBar's pragmatic clinical trial funded by NINDS which used the PEG. The other assumptions are $\alpha = 0.05$, SD of change = 2.5 and 20% attrition. As the table illustrates, with a total sample size of 450, with an average of 10 subjects per cluster, we have close to 90% power to detect a 1-unit difference in the PEG between groups. The table also illustrates calculations for a range of power and effect sizes.

ICC = 0.053

Obs	power	meandiff	SD	clustsize	final_npergroup
1	0.80	1.0	2.5	10	184.625
2	0.85	1.0	2.5	10	210.473
3	0.90	1.0	2.5	10	245.551
4	0.80	1.5	2.5	10	83.081
5	0.85	1.5	2.5	10	94.159
6	0.90	1.5	2.5	10	110.775
7	0.80	2.0	2.5	10	48.003
8	0.85	2.0	2.5	10	55.388
9	0.90	2.0	2.5	10	62.773
10	0.80	2.5	2.5	10	31.386
11	0.85	2.5	2.5	10	35.079
12	0.90	2.5	2.5	10	42.464
13	0.80	3.0	2.5	10	22.155

Obs	power	meandiff	SD	clustsize	final_npergroup
14	0.85	3.0	2.5	10	25.848
15	0.90	3.0	2.5	10	29.540

Missing Data Considerations:

We anticipate 20% attrition at the 8-week time point. We chose a higher attrition rate than in our previous work as we anticipate more attrition in the PCT as patients will not have the "high touch" of participants in the RCTs.[5, 26, 28] Our sample size analyses have accounted for this amount of missing data. We will compare baseline characteristics between patients with the assessment immediately following the 8-week program to those without in order to assess potential bias in study completion. We will also try to obtain reasons for study drop out so that we can assess the missing data mechanism (missing completely at random (MCAR), missing at random (MAR), non-ignorable missingness). At a single time point, we will conduct sensitivity analyses assigning poor scores and good scores for missing values differentially by treatment assignment to evaluate the impact on our study results.

The mixed models proposed for analysis are robust to missing data under MCAR and MAR missing data mechanisms. If the amount missing data differs between treatment groups or appears to be non-ignorably missing, we will conduct sensitivity analyses with imputed data based on varying assumptions (ignorable vs. non-ignorable missingness).

10. DATA COLLECTION AND QUALITY ASSURANCE

10.1 Data Collection

Paperless Data Entry: A paperless data-entry system will be created in REDCap, a secure web application for building and managing online surveys and databases available to the PI (Morone) through the Boston University Clinical and Translational Science Institute. REDCap has proven to be a sophisticated yet easy-to-use data entry system that provides customizable templates for use in clinical trial research. All study participants will be assigned unique study identifiers that will appear on all data collection instruments, documents, and files used in the statistical analysis and manuscript preparation. REDCap allows for specific data quality measures to be implemented. These include data verification and built-in data validation mechanisms such as logic and out of range data checks.

10.2 Data Management

EHR Data: Consenting and eligible participants will provide contact information containing protected health information (PHI) to each HCS's research staff. PHI will be stored separately from clinical data in a password protected electronic file and will be used to link and extract clinical data from each center's EHR on a bi-weekly basis. Limited use datasets will be created

at each HCS and will contain a unique study identifier and clinical data including date of birth and visit dates; name, address, social security number and medical record number information will be removed. Limited use datasets will be transferred to the central data repository housed at Boston University Biostatistics and Epidemiology Data Analytics Center (BEDAC). The BEDAC is supported by the Boston University Medical Campus (BUMC) Information Systems and Technology group (IS&T). Data will reside on virtual machines stored inside the BUMC IS&T premium secure environment. Under IS&T, project database access is configured to require encrypted connections, databases are encrypted at rest (AES-256), and all actions to the database are logged. Database transfer will be electronically encrypted via IPsec tunnel or secure socket layering (SSL) encryption technology so that only the intended recipient can decode the data. Applications and databases will be protected by network firewalls that restrict access to designated users and hosts. Restriction and permissions to update the database and to share the database will be controlled by the BEDAC based on staff user role. The BEDAC data manager will develop data transfer specifications and work with each HCS to obtain data through the secure BEDAC portal. The limited use EHR data will be cleaned, aggregated and merged with study data for subsequent analysis.

Missing data: We do not expect substantial missing data due to it being directly entered into the electronic data collection system, which we have used previously. This system has many safeguards such as prohibiting closure of a page if a question has not been answered or the answer is out of range. For instruments with several questions we will use the approach recommended by their authors for calculating total scores and composites when values for an item are missing.

Compliance: We will estimate compliance by the number of sessions attended and estimate the Proportion of participants with various levels of compliance. We will also calculate the proportion of participants missing each session to describe the pattern of compliance.

Dropout analyses: Participants informing us they no longer want to continue in the study will be considered dropouts, and we will look at when these events occur. Dropout rates will be calculated as proportions of participants randomized, and as a cumulative probability of remaining in the study, using survival analysis techniques such as the product-limit estimator. Unlike proportions, the latter statistics, which can be estimated at various times following randomization, take into account when dropouts occur. The information contained in these descriptive analyses may help us to devise strategies for keeping people in the study.

10.3 Quality Assurance

10.3.1 Training

Protection of Human Subjects Training: All the members of the study team, investigators and staff, will complete the required training on protection of human subjects before engaging in any activities related to human subjects. According to the institution's requirements, they will recertify if and when needed.

Training of Mindfulness Instructors: We will train the Mindfulness instructors before starting the trial. We will explain the treatment protocol, appropriate adaptations for patient's comfort

and emotional stresses and when to discontinue treatment. We will develop procedures for instructors so as to ask questions when issues surface and to communicate that information to instructors at other HCS sites. All sites have back-up instructors if needed.

Training of Informed Consent Takers: Study personnel who will be taking informed consent from the study participants will be trained for the procedure.

10.3.2 Quality Control Committee

Principal Investigator (PI), Site Principal Investigators (s-PI), Co-Investigators (Co-I), Biostatistician and other study members as needed, will have a weekly or monthly (depends on study recruitment) to keep up with the day to day operations at each HCS site and assist if needed. They will discuss the progress of the trial, recruitment status and IRB concerns if applicable.

10.3.3 Metrics

We will develop automated reports that will include the number of participants screened, number enrolled, study assessments completed, participants missing assessments, and those participants with upcoming assessments. We will monitor intervention adherence with bimonthly reports. We will obtain data on age, gender, race and ethnicity to assure balanced randomization. For each timepoint we aim to achieve an 85% or higher follow-up rate. We anticipate other metrics and reports will be developed as we implement the pilot study.

10.3.4 Protocol Deviations

A protocol deviation will be defined as any lack of compliance with the study protocol, manual of operations or any other study related procedures that could increase the risk to the participant or affect the integrity of the trial. These deviations will be tracked down in a scheduled manner and reviewed at study team meetings. Additionally, they will be documented for IRB or NIH.

10.3.5 Monitoring

Study staff will all undergo training to obtain consent and administer measures. Fidelity will be monitored monthly for the MBSR instructors. Recruitment and retention will be monitored and reviewed at weekly meetings across sites. Safety will be monitored at monthly meetings. Additional monitoring procedures will be developed as required during the pilot trial.

11. PARTICIPANT RIGHTS AND CONFIDENTIALITY

11.1 Institutional Review Board (IRB) Review

The OPTIMUM study uses a single IRB (sIRB) which is the University of Pittsburgh. The protocol and the informed consent document (Appendix A) and any subsequent modifications will be reviewed and approved by the sIRB who is responsible for oversight of the study. The consent form and protocol are separate documents.

11.2 Informed Consent Forms

A verbal consent will be obtained from each participant. The consent form will describe the purpose of the study, the procedures to be followed, and the risks and benefits of participation. A copy will be emailed to each participant.

11.3 Participant Confidentiality

All precautions will be taken to ensure that participant's privacy is respected. The collection of sensitive information related to participants is limited to the amount necessary to achieve the aims of the research, so that no unneeded sensitive information is being collected. Any screening that will be done in the clinic or research office will be done in a private room.

All efforts will be taken to keep all the data collection electronic. Documents will be password protected and accessibility will be given only to the approved staff. All computer entry and networking programs will be done using PIDs only. Minimum paper format data collection will be attempted. Any paper format data will be kept in locked file cabinets in locked offices and access to these files will be limited to study personnel.

Identifying information will be coded and a key to decipher the code will exist, enabling linkage of the identifying information to the private information. If the participant withdraws from the study, any identifiable research or medical information recorded for or resulting from participation in the study before the date the participant formally withdraws consent may continue to be used and disclosed by the investigators for the purposes described in the study protocol. Research records including identifiable data will be securely stored indefinitely.

11.4 Study Discontinuation

The study may be discontinued at any time by the IRB, the NCCIH, the OHRP, or other government agencies as part of their duties to ensure that research participants are protected.

12. COMMITTEES

Collaboratory Core Working Group Members:

Ethics/Regulatory:

- Natalia Morone (PI)
- Susan Gaylord (Site-PI)

Biostatistics and Study Design, Health Care Systems Interactions:

- Janice Weinberg (Co-I)

Patient-Centered Outcomes:

- Carol Greco (Site-Co-I)

Electronic Health Records

- Kathleen Mctigue (Site Co-PI)
- Kim Faurot (Site Co-PI)

Health Care Systems

- Natalia Morone (PI)

13. PUBLICATION OF RESEARCH FINDINGS

Publication of the results of this trial will be governed by the policies and procedures developed by the Collaboratory and Core Working Group Members. Any presentations, abstracts, or manuscripts will be made available for review by the NIH and the NCCIH prior to submission.

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15. SUPPLEMENTS/APPENDICES

Appendix A: Informed Consent Form Updated

CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Title: Group-based mindfulness for patients with chronic low back pain in the primary care setting versus usual care

Principal Investigator:
<Insert local Principal Investigator here>

Co-Investigators:
<Insert local Co-Is here>

Source of Support: National Institutes of Health, National Center for Complementary and Integrative Health

CONCISE SUMMARY
The purpose of this research study is to determine whether a group pain management program modeled on Mindfulness-Based Stress Reduction can improve pain and function for persons with chronic low back pain as compared to persons receiving usual care by their primary care providers. All persons who are eligible will complete surveys about pain, function, sleep, pain medicine use, tobacco, alcohol and substance use, mood and anxiety symptoms, experience with telehealth and quality of life. The surveys will take up to an hour to complete. Once the surveys are complete, all persons will be randomized to the group-based pain management program or to

usual care. If you are randomized to the group pain management program you will meet for 8 weekly group sessions via ZOOM. Each session will last for 120 minutes. The first 30 minutes will be a standard of care telehealth video visit with a primary care provider and the last 90 minutes will be the video group pain management program. Regardless of which group you are assigned to, you will be emailed and asked to complete follow-up surveys that will occur at 8 weeks, 6 months and 12 months. You will also be asked to complete a monthly survey about any visits to the hospital or your primary care provider, and you will be called monthly to review your pain medications. If you are randomized to the usual care group you will not participate in the pain management program, but you will receive the surveys to complete and the monthly phone call. The total time for your participation in this study will be 12 months.

The greatest risks of this study if you are randomized to either group is loss of confidentiality. The greatest risks of this study if you are randomized to the 8-week pain management program include the possibility of discomfort when sitting in a chair or doing mindfulness meditation which includes mindful chair exercises, emotional discomfort or distress arising during meditation related to increased awareness of negative emotions, thoughts or physical sensations.

ClinicalTrials.gov
A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

What are some general things you should know about research studies?
You are being asked to take part in a research study. To join the study is voluntary.
You may choose not to participate, or you may withdraw your consent to be in the study, for any reason, without penalty.

Research studies are designed to obtain new knowledge. This new information may help people in the future. You may not receive any direct benefit from being in the research study. There also may be risks to being in research studies. Deciding not to be in the study or leaving the study before it is done will not affect your relationship with the researcher, your health care provider, or the <Insert local language here>. If you are a patient with an illness, you do not have to be in the research study in order to receive health care.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study.

You will be given a copy of this consent form or you will be mailed or emailed a copy of the consent form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

Why is this research being done?
The purpose of conducting this research is to determine if an 8-week mind-body program known as Mindfulness-Based Stress Reduction helps adults with chronic low back pain when offered in their doctor's office in a telehealth video visit as compared to usual primary care.

Who is being asked to take part in this research study?
You are being invited to take part in this research study because you are an English-speaking adult who is at least 18 years old and you have chronic low back pain. People invited into this study can be either male or female. You will be one of approximately 150 people to be asked to participate at this location. At all sites up to 450 volunteers will take part in this study.

What procedures will be performed for research purposes?
If you decide to take part in this research study, you will undergo the following research procedures:

Baseline Testing:
If you decide to join the study, you will undergo the following procedures that are not part of your standard medical care. They will take about 60 minutes of your time and will happen over the phone, mailed to you with a self-addressed return envelope, or can be completed online. If you complete the questionnaires online you will be sent a link that only you can access.
You will be asked a series of questions about your mood, pain levels, sleep, health, activity, tobacco, alcohol, substance use, experience with telehealth and functional abilities. You will also be asked questions about demographic factors like age, gender, and ethnicity, as well as questions about medications that you take and healthcare that you receive.

Experimental Procedures
After you complete the baseline testing, you will undergo the following experimental procedures:

Randomization:
You will be assigned to one of the two options by randomization (like the flip of a coin), and you will have a 50% chance of being randomized to one of these options. One option will be usual care which means you will not participate in the group pain management program.

The other option will be the group pain management program modeled on the Mindfulness-Based Stress Reduction Program. The program meets weekly for 8 weeks via ZOOM for a total of 2 hours each week.

During the first week you will be introduced to the principles and practice of mindfulness meditation. The home practice assignment of daily meditation (six of seven days/week) will be reviewed. Support materials of guided meditation and a group manual will be provided. The sessions will occur in a videoconferencing format using HIPPA-compliant ZOOM.

Follow-up Testing for Everyone:

<u>8 Week Follow-Up</u>:
After about 8-weeks from completing the Baseline surveys you will again be asked to answer the questions described under <u>Baseline Testing</u> above. You will also be asked about your satisfaction with the program if you were randomized to the pain management program. This will take on average 60 minutes, and you will be emailed a unique link to complete the surveys. The surveys

can also be completed over the telephone, over Zoom, or mailed to you with a self-addressed stamped envelope to return the questionnaires.

Monthly Assessments:
You will receive monthly phone calls or meet over Zoom to review your pain medications. You will also be emailed one survey to complete each month about any visits you made to a doctor, ER, hospital, or other healthcare facility related to your low back pain.

6-Month and 12-Months Follow-Up:
You will be asked to answer the questions described under Baseline Testing above after 6 months and 12 months.

Interview:

If you are randomized to the group pain management program and when you complete the 8-week program you will be invited to participate in an interview. The purpose of the interview is to collect personal accounts of the experience of learning mindfulness and how it has affected your life as well as your experience with the videoconferencing format.

In order to ensure that we do not miss any of your comments, we ask permission to audio record your interview using ZOOM. This audio recording will only be listened to by members of the research team and will be securely stored on password protected servers. We will transcribe the recording without your name or any identifiers, but rather with a Study ID. Your identity will never be associated with your comments in any reports about this study. If you do not wish to be recorded, please let us know, and we will take notes only.

What are the possible risks, side effects, and discomforts of this research study?
There is less than minimal risk and discomfort associated with this research.

For all participants there is a risk of breach of confidentiality. The risk will be minimized by the use of study IDs in place of participant names on all study related materials.

If you are randomized to the 8-week group pain management program you may also have the following possible risks:

- You may experience increased discomfort in your back from sitting on a chair during sitting meditation. However, you will be taught how to mindfully change your posture if worsened back pain should occur.

- You may experience increased discomfort in your back from doing any of the mindfulness meditations like the mindfulness chair exercises. You will also be taught how to mindfully change your posture if worsened back pain should occur.

- Emotional discomfort or distress may arise during meditation related to increased awareness of negative emotions, thoughts, or physical sensations. These symptoms are usually transient. You can avoid any practices that lead to more than transient discomfort.

- For the group pain management program we will use Zoom, a videoconferencing program that uses end-to-end encryption. Although every reasonable effort has been taken, confidentiality during Internet communication activities cannot be guaranteed and it is possible that additional information beyond that collected for research purposes may be captured and used by others not associated with this study. Moreover, the use of video allows other participants to see and hear anything that occurs in your background surroundings while the camera and microphone are on during the sessions. We will provide a headset to you so that others who are in the room with you cannot hear what is being said by others on Zoom.

What are the possible benefits from taking part in this research study?
The potential benefit of your participation in the study is that you will learn techniques and information that may reduce your pain. There is no guarantee that you will receive such a benefit, but knowledge will be gained that may help others.

If you agree to take part in this research study, will you be told of any new risks that may be found during the course of the study?
You will be promptly notified if any new information develops during the conduct of this research study which may cause you to change your mind about continuing to participate.

Will it cost you anything to be in this study?
Neither you, nor your insurance provider will be charged for the costs of conducting procedures specifically being performed for research purposes. The procedures being performed specifically for research are the completion of surveys, the MSBR sessions, the interview when the program is finished and a medical record review.

<INCLUDE BELOW LANGUAGE ONLY IF IT APPLIES TO YOUR SITE>However, you or your insurance provider will be charged for any procedures performed as part of your standard medical care (care you would receive even if you were not participating in this research study), in the usual manner. For this research study, the telehealth video group-based medical visits that will occur with a physician or primary care provider, prior to the MSBR sessions, are being completed for standard of care purposes. You may also need to pay for parking or public transportation. You may also need to pay a co-pay for your standard of care medical visit. You will not be charged for any other study procedures.

Will you be paid if you take part in this research study?
<INCLUDE BELOW LANGUAGE FOR WHAT APPLIES TO YOUR SITE>
You will be paid <INSERT LOCAL AMOUNT TO BE PAID FOR EACH SURVEY> after the completion of surveys at baseline, 8 weeks, 6 months, 12 months, and monthly surveys. This means if you complete all the surveys you will receive a total of <INSERT LOCAL AMOUNT TO BE PAID FOR COMPLETING all the SURVEYS>. You will also be paid <INSERT LOCAL AMOUNT TO BE PAID FOR THE INTERVIEW> if you complete the interview. If you are randomized to the pain management program and you do not have a computer, laptop, smart phone, or tablet then one will be provided for you. This device may be returned at the end of your participation.

<INSERT LOCAL LANGUAGE - If your institution has any additional local language that is needed regarding how payments are provided (cash, debit card) or if personal identifiers such as SSN need to be collected to process payments at your institution, insert it here>

Who will pay if you are injured as a result of taking part in this research study?

<Insert local compensation for injury language here>

What if you are a <Insert local language here> student*? <If your institution does not have an academic center attached to it, this entire section can be deleted>*
You may choose not to be in the study or to stop being in the study before it is over at any time. This will not affect your class standing or grades at the <Insert local language here>. You will not be offered or receive any special consideration if you take part in this research.

What if you are a <Insert local language here> employee?
Taking part in this research is not a part of your University duties, and refusing will not affect your job. You will not be offered or receive any special job-related consideration if you take part in this research.

How will information collected about me be kept confidential?
We must use information that shows your identity to do this research. Information already collected about you will remain in the study record even if you later withdraw.

We will store your information in ways we think are secure. We will store paper files in locked filing cabinets. We will store electronic files in computer systems with password protection and encryption. However, we cannot guarantee complete confidentiality.

With your permission, we will use texts to send you information like appointment reminders or requests to complete study activities. Texting is unencrypted and therefore there is a chance this information can be intercepted. However, we will only text information that is not sensitive. If you do not wish to be texted, please let us know.

As the Funder of this project, the National Institutes of Health requires that the researchers share all of the data we collect in this research study into a National Institutes of Health data repository called HEAL (Helping to End Addiction Long-term). The purpose of this data repository is for people who do research in the future to use the data to answer more research questions. All of your personal identifiers will be removed from the data before being placed in the repository.

This study is covered by a Certificate of Confidentiality (CoC) from the National Institutes of Health. All studies funded by the National Institutes of Health that involve identifiable information are covered by a CoC**.** The CoC provides how we can share research information. Because we have a CoC, we cannot give out research information that may identify you to anyone that is not involved in the research except as we describe below. Even if someone tries to

get your information in connection with a legal proceeding, we cannot give it to them. The CoC does not prevent you from sharing your own research information.

Will this research study involve the use of your medical record information?
Yes, the Researchers involved in this study are requesting your authorization or permission to review your medical records.

Who is requesting the Protected Health Information (PHI) for research?
The researchers involved in this study are also requesting your authorization or permission to review your medical records.

Why is this information needed?
To determine whether you meet the conditions for participation in this study, to compare your earlier test results to the findings from this study, and if possible, to use your previous exam results in place of, or in addition to, some of the exams needed for this study.

What will be disclosed?
We will obtain the following information: your diagnoses, age, past medical history, medications, past surgeries, social history, diagnostic procedures including CT scans and MRIs, emergency department visits, surgeries, hospitalizations, urgent care visits, visits to your primary care clinic, physical therapy visits, injections for your back, and results of any blood tests.

Will research data be placed in the medical record?
No research data will be placed in the medical record.

How long will this information be made available to the researchers?
This identifiable medical record information will be made available to members of the research team for an indefinite period of time.

Who (other than the investigators) will receive the PHI, and how will they use it?
Your medical information, as well as information obtained during this research study, may be shared with other groups, possibly including authorized officials from the Food and Drug Administration, the National Center for Complementary and Integrative Health, the National Institutes of Health and the <INSERT name of local office that handles post-approval monitoring at your institution>, for the purpose of monitoring this study. Authorized representatives of <INSERT LOCAL LANGUAGE HERE> or affiliated health care providers may also have access to this information to provide service and addressing billing and operational issues.

Your research data may also be shared with other research investigators who are not involved in this particular research study. These secondary research investigators will use the data to conduct future research studies. However, all identifiers will be stripped from your data before it's provided to other researchers. So, your identity will not be shared with these secondary investigators.

What is the potential risk that PHI will be re-disclosed by a recipient?

We will protect your privacy and the confidentiality of your records, as described in this document, but cannot guarantee the confidentiality of your research records, including information obtained from your medical records, once your personal information is disclosed to others outside <INSERT LOCAL LANGUAGE HERE> or the University.

How long will this authorization be valid?
This authorization is valid for an indefinite period of time.

Do I have the right to revoke authorization, and how do I revoke it?
You can always withdraw your authorization to allow the research team to review your medical records by contacting the investigator listed on the first page and making the request in writing.

What are the implications of revocation of authorization?
If you do so, you will no longer be permitted to participate in this study. Any information obtained from you up to that point will continue to be used by the research team.

What are the implications of not providing consent to participate in the study?
If you do not provide consent you cannot participate in the study.

If you agree to take part in this research study, can you be removed from the study without your consent?
The investigators have the right to stop your participation at any time. This could be because you have had an unexpected reaction, or have failed to follow instructions, or because the entire study has been stopped.

VOLUNTARY CONSENT:
All of the above has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions about any aspect of this research study during the course of this study, and that such future questions will be answered by the researchers listed on the first page of this form.

If you have any questions about your rights as a research subject or wish to talk to someone other than the research team, please call the <Insert local language here> Human Subjects Protection Advocate toll-free at <Insert local language here>.

Participant's Agreement:
I have read the information provided above. I have asked all the questions I have at this time. I provide my voluntary consent to participate in this research study and authorization for my medical records to be accessed and recorded for research purposes.

CERTIFICATION OF INFORMED CONSENT

I certify that I have explained the nature and purpose of this research study to the above-named individual(s), and I have discussed the potential benefits and possible risks of study participation. Any questions the individual(s) have about this study have been answered, and we will always be available to address future questions, concerns or complaints as they arise. I further certify that no research component of this protocol was begun until after informed consent was provided.

Appendix B: Important Medical Event Form

Participant ID _____ Form Completion Date _____

Form Completed by _____ Group: _____ Arm: O1 O2 O3

DO NOT ask the questions below directly (except for #5). Allow the participant to describe the event and then ask for clarification, if needed. Fill out a separate form for each event.

1. Important medical event occurred [ ] Yes [ ] No Date of the event _____

2. Nature of the event:
   [ ] Hospitalization
   [ ] Emergency Room visit
   [ ] Acute Care Visit
   [ ] Pregnancy
   [ ] Outpatient Procedure

[ ] Other, Specify _____

3. Description of the event and its follow up (include details in the space below):
   [ ] Injury [ ] Illness [ ] Surgery [ ] New Medication [ ] Other (specify)

4. Ask the participant: "Was this event related to your participation in the OPTIMUM study?"
   [ ] Yes [ ] No

5. Severity of the event
   [ ] Mild: required no or minimal treatment; able to carry out normal activities
   [ ] Moderate: resolved with treatment; normal activities conducted with some limitations
   [ ] Severe: required extensive medical attention; unable to carry out normal activities
   [ ] Very severe: life-threatening, disabling, fatal

6. Action taken by study staff:
   [ ] Instructed participant to contact PCP [ ] Study contacted PCP
   [ ] Instructed participant to follow MD orders [ ] Study contacted IRB and DSMB

NOTE: This form should be immediately shared with the study Project Coordinator or PI.

Appendix C: Screening Questions

Obtain verbal consent to continue with these questions before proceeding.

_____ Check here when you have obtained that consent. **DO NOT continue without verbal consent.**

Today's Date: Time:

Date of Birth: Age: **Participants MUST be at least 18 years old. If not STOP AND EXCLUDE**

Gender: ○ MALE ○ FEMALE ○ Unknown ○ Other, Specify _____

1a. Do you have low back pain or discomfort right now? ○ Yes ○ No **If yes go to # 2. If no go to # 1b.**

1b. Have you ever had low back pain or discomfort? ○ Yes ○ No **If yes go to # 2. If no STOP AND EXCLUDE**

2. How long has low back pain been an ongoing problem for you?

○ Less than one month ○ 1-3 Months ○ 3-6 months **If 1-3 months or less STOP AND EXCLUDE**
○ 6 months-1 year ○ 1-5 years ○ More than 5 years

3. How often has low back pain been an ongoing problem for you over the past 6 months?

○ Every day or nearly every day in the past 6 months

○ At least half the days in the last 6 months

○ Less than half the days in the past 6 months

If less than half the days in the past 6 months STOP AND EXCLUDE

4. a) What number best describes your pain on average in the past week?
__0 __1 __2 __3 __4 __5 __6 __7 __8 __9 __10
No Pain Pain as bad as you can imagine

b) What number best describes how, during the past week, pain has interfered with your enjoyment of life?
__0 __1 __2 __3 __4 __5 __6 __7 __8 __9 __10
Does not Interfere Completely Interferes

c) What number best describes how, during the past week, pain has interfered with your general activity?
__0 __1 __2 __3 __4 __5 __6 __7 __8 __9 __10
Does not Interfere Completely Interferes

If the average of the three questions is < 3 STOP AND EXCLUDE

5. Do you practice mindfulness meditation at least once a week? ○ Yes ○ No
If Yes, **STOP AND EXCLUDE**

6. Have you had any unintentional weight loss? ○ Yes ○ No
How much weight loss? ____ **If ≥ 10 lbs STOP and EXCLUDE**

7. Do you currently have an unexplained fever? ○ Yes ○ No
If Yes, **STOP AND EXCLUDE**

8. Do you have cancer? If Yes, go to 8a ○ Yes ○ No

8a. Are you currently being treated for cancer? ○ Yes ○ No
If Yes, **STOP AND EXCLUDE**

9. Has there been a recent unexplained worsening of your pain? ○ Yes ○ No
If Yes, **STOP AND EXCLUDE**

10. Is your back pain caused by an injury that occurred within the last 3 months? ○ Yes ○ No
If Yes, **STOP AND EXCLUDE**

11. Are you pregnant or have plans to become pregnant in the next 3 months? ○ Yes ○ No

If Yes, **STOP AND EXCLUDE**

Eligible for study? ○ Yes ○ No

If eligible, interested in participating? ○ Yes ○ No ○ Uncertain/undecided ○ Declined

If declined, why did he/she decline?
_____

COMMENTS (please print, enter only essential information):

Contact Information:

Name: _____

Address: _____

Phone Number: _____

E-mail Address: _____

Appendix D: Timeline of the study updated.

OPTIMUM – PCT Schedule

UH3 Phase: Total 450 study participants

Short Summary:

TIMUM + PCP Usual Care (n=225)			PCP Usual Care (n=225)			8 Week Mindfulness Program	6 months Assessment Date	12 mon Assessme
	Pittsburgh	North Carolina	Boston	Pittsburgh	North Carolina			
1	Cohort 1	Cohort 1	Cohort 1	Cohort 1	Cohort 1	Mar 2021 to Apr 2021	August 2021	February
2	Cohort 2	Cohort 2	Cohort 2	Cohort 2	Cohort 2	Jun 2021 to Jul 2021	November 2021	May 2(
3	Cohort 3	Cohort 3	Cohort 3	Cohort 3	Cohort 3	Late Aug 2021 to Sep 2021	February 2022	August
4	Cohort 4	Cohort 4	Cohort 4	Cohort 4	Cohort 4	Nov 2021 to early Jan 2022	April 2022	October
5	Cohort 5	Cohort 5	Cohort 5	Cohort 5	Cohort 5	Feb 2022 to Mar 2022	July 2022	January
6	Cohort 6	Cohort 6	Cohort 6	Cohort 6	Cohort 6	Late Apr 2022 to Early Jun 2022	September 2022	March 2
7	Cohort 7	Cohort 7	Cohort 7	Cohort 7	Cohort 7	Jul 2022 to Aug 2022	December 2022	June 2(
8	Cohort 8	Cohort 8	Cohort 8	Cohort 8	Cohort 8	Late Sep 2022 to Early Nov 2022	February 2023	August
9	Cohort 9	Cohort 9	Cohort 9	Cohort 9	Cohort 9	Dec 2022 to Jan 2023	May 2023	Novembe
10	Cohort 10	Cohort 10	Cohort 10	Cohort 10	Cohort 10	Mar 2022 to Apr 2023	August 2023	February

Enrollment Status	Dates	Cohorts
25% Enrollment Complete	May 2021	Cohort 1 – Cohort 3
50% Enrollment Complete	February 2022	Cohort 4 – Cohort 5

75% Enrollment Complete	August 2022	Cohort 6 – Cohort 8
100% Enrollment Complete	February 2023	Cohort 9 – Cohort 10

Detailed Schedule:

aseline ssessmen T1)	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	**8 Weeks Post Program Assessment (T2)**	**Assessment at 6 months (T3)**
icipants (3 = OPTIMUM + PCP Usual Care, 2 = PCP Usual Care)										
ecember 020- ebruary 021	First week of March 2021	Second week of March 2021	Third week of March 2021	Fourth week of March 2021	Fifth week of March 2021	First week of April 2021	Second week of April 2021	Third week of April 2021	Fourth week of April 2021	August 2021
icipants (24 = OPTIMUM + PCP Usual Care, 24 = PCP Usual Care)										
pril-May 021	First week of June 2021	Second week of June 2021	Third week of June 2021	Fourth week of June 2021	Fifth week of June 2021	First week of July 2021	Second week of July 2021	Third week of July 2021	Fourth week of July 2021	November 2021
icipants (24 = OPTIMUM + PCP Usual Care, 24 = PCP Usual Care) Complete										

uly-August 021	Third week of August 2021	Fourth week of August 2021	First week of September 2021	Second week of September 2021	Third week of September 2021	Second week of October 2021	Fourth week of September 2021	Fifth week of September 2021	First week of October 2021	February 2022

ticipants (24 = OPTIMUM + PCP Usual Care, 24 = PCP Usual Care)

eptember-October 021	First week of November 2021	Second week of November 2021	Third week of November 2021	Fourth week of November 2021	First week of December 2021	Second week of December 2021	Third week of December 2021	Fourth week of December 2021	First week of January 2023	April 2022

ticipants (24 = OPTIMUM + PCP Usual Care, 24 = PCP Usual Care)
Complete

anuary-ebruary 022	First week of February 2022	Second week of February 2022	Third week of February2022	Fourth week of February 2022	First week of March 2022	Second week of March 2022	Third week of March 2022	Fourth week of March 2022	Fifth week of March 2022	July 2022

ticipants (24 = OPTIMUM + PCP Usual Care, 24 = PCP Usual Care)

March-April 2022	Fourth week of April 2022	First week of May 2022	Second week of May 2022	Third week of May 2022	Fourth week of May 2022	Fifth week of May 2022	First week of June 2022	Second week of June 2022	Third week of June 2022	September 2022

ticipants (24 = OPTIMUM + PCP Usual Care, 24 = PCP Usual Care)

May-June 022	First week of July 2022	Second week of July 2022	Third week of July 2022	Fourth week of July 2022	First week of August 2022	Second week of August 2022	Third week of August 2022	Fourth week of August 2022	Fifth week of August 2022	December 2022

ticipants (24 = OPTIMUM + PCP Usual Care, 24 = PCP Usual Care)
Complete

uly-August 022	Second week of Septembe r 2022	Third week of Septembe r 2022	Fourth week of Septembe r 2022	First week of October 2022	Second week of October 2022	Third week of October 2022	Fourth week of October 2022	First week of Novembe r 2022	Second week of November 2022	February 2023

ticipants (24 = OPTIMUM + PCP Usual Care, 24 = PCP Usual Care)

October- November 022	First week of December 2022	Second week of December 2022	Third week of December 2022	First week of January 2023	Second week of January 2023	Third week of January 2023	Fourth week of January 2023	Fifth week of January 2023	First week of February 2023	May 2023

rticipants (26 = OPTIMUM + PCP Usual Care, 25 = PCP Usual Care)
t Complete

anuary- ebruary 023	First week of March 2023	Second week of March 2023	Third week of March 2023	Fourth week of March 2023	First week of April 2023	Second week of April 2023	Third week of April 2023	Fourth week of April 2023	First week of May 2023	August 2023