STUDY PROTOCOL

Integrating Mindfulness into the Patient-Centered Medical Home (MINDFUL-PC)

NCT03265600

and

Mindfulness Influences on Self-Regulation: Mental and Physical Health Implications (Mindful Self-Regulation fMRI pilot study)

NCT02972853

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NCCIH protocol template
Version 1.3 (Submitted 7/21/16)

Revisions made:

Version Number: 1.1
Version Date: 1/08/2016

1. Clarified language about group termination and assessment completion (section C.3.h.) (1/8/2016).

Version 1.2:
Version Date: 05/11/2016

2. Changed order of DSMP sections, to create more logical flow (sections D, and separate DSMP document.) (05/11/2016).
3. Changed goals related to recruitment numbers for patients and PCP (A.2.b., C.2., D.3.b.) (05/11/2016).
4. Adjusted Patient screening, inclusion/exclusion, and scheduling procedures for MINDFUL-PC participants (C.3.b.) (05/11/2016).
5. Adjusted dates in Implementation Staging Map (C.4.b., and Table 4. MTPC Implementation Schedule) (05/11/2016).
6. Adjusted Study flow schema for Patient participants (Figure 1b.) (05/11/2016).
7. Removed plans for Haitian-Creole MINDFUL-PC groups (C.3.d.2.) (05/11/2016).
8. Added licensed clinician to conduct screening evaluations for the MTPC groups (C.3.d.2.) (05/11/2016).
9. Added questionnaires (Mindfulness Resources Use Survey, Emotion regulation (DERS) and interoception awareness (MAIA) in section C.3.f.10.) and removed questionnaires (PROMIS-SDSF, PROMIS-PISF, PROMIS-GHSF) (05/11/2016).
10. Added electronic informed consent possibility (C.3.d.1. Informed Consent Visit) and possibility to fill in questionnaires electronically through REDCap (Pre-treatment Assessment Visit, Mid-Training Assessment Session, Post-Treatment Survey Session).
11. Added: food can be provided during the informed consent session (C.3.d.2.) (05/11/2016).
12. Clarified language about Follow-up Survey Sessions (C.3.d.2.) (05/11/2016).
13. Changed participant remuneration related to main MINDFUL-PC study (C.3.d.2., D.7.) (05/11/2016).
14. Added waitlist Biweekly Engagement Phone Call (PT Study Week 1-8) (05/11/2016).
15. Added section on Data Monitoring and Quality Assurance (D.2.c.6.) (05/11/2016).
16. Added description of Session Quality and Protocol Adherence (D.8.) (05/11/2016).
17. Added procedures for Unanticipated Problems that are not Adverse Events: Possible Risk of Suicide (D.2.c.7.) (05/11/2016).
18. Added Description of Sources of Research Materials for all study arms and the fMRI study and describe Data Linkage to subjects and access to data (D.10.) (05/11/2016).

19. Added paragraph on present study personnel, responsibilities and inclusion (D.11.), and added personnel for fMRI study (postdoctoral fellow) (05/11/2016).
20. Added paragraph on Human Subjects and Confidentiality and Recruitment procedures (D.3.) (05/11/2016).
21. Added a fourth task during fMRI scanning (emotion regulation task using pain stimuli) (A.2.a.), including respective additional hypotheses (A.2.b.), and analyses (C.5.b.), and risk assessment (D.2.d.2.), adjusted the timing of the 4 tasks and added a structural (DTI) scan (C.3.a.) (05/11/2016).
22. Changed task choice and reference for the specific inhibitory control task (C.5.b.) (05/11/2016).
23. Adjusted recruitment and informed consent procedure for fMRI participants (C.2.c, C.3.d.3., D.5.c.) (05/11/2016).
24. Adapted and added to fMRI participant inclusion/exclusion criteria (C.1.c.) (05/11/2016).
25. Added a phone-protocol for screening and scheduling participants to the fMRI study, to the group-scheduling phone-call (C.3.d.3.) (05/11/2016).
26. Added details about toxicology and pregnancy screenings of fMRI participants (C.3.d.3.) (05/11/2016).
27. Changed subject remuneration and reimbursement of travel expenses for fMRI participants (D.7.b.) (05/11/2016).
28. Adjusted Study Visit and Assessment Schedule for fMRI Pilot Study Participants (Table 4) (05/11/2016).

Version 1.3:
Version Date: 8/16/2016

29. Corrected typos in protocol and flyer and clarified language around identification code (07/21/2016).
30. Added additional detail about fMRI contraindications and screening process to the ICF and protocol (C.1.c.1./2., C.3.d.3. Group Scheduling Phone Call, and C.3.d.3. fMRI Session Visit) (07/21/2016).
31. Clarified number of subjects in fMRI pilot study in Figure 1b Study flow schema for Patient participants, and consistently added the maximal recruitment number of n=30 for the fMRI pilot study in the text (07/21/2016).
32. Clarified timing and content of pre-fMRI phone calls (C.3.d.3.) (07/21/2016).
33. Specified information on screened drugs (C.3.d.3. Pre-treatment fMRI Session Visit)(07/21/2016).
34. Clarified language around the total payment for the fMRI pilot in the protocol and ICF (protocol section D.7.b, and Table 4. Study Visit and Assessment Schedule for fMRI Pilot Study Participants) and clarified that drug screening completion is necessary for reimbursement (07/21/2016).
35. Removed F. Markovski as Research Assistant, added Angela Lozada and Andrea Chen as Research Assistants (D.11.) (07/21/2016).
36. Added sensors as possible sources of incidental findings (07/21/2016).

37. Added risk of noise during scanning (07/21/2016).
38. Included NIH version dates and numbers on all documents (07/21/2016).
39. Clarified processes after incidental findings (D.2.d.2.3.) (07/21/2016).
40. Clarified that result of drug screenings will not be added to participants' medical records and will only be kept in their research records, and added language about Certificate of Confidentiality application (D.1.a.) (07/21/2016).
41. Clarified how MRI data will be kept at imaging site (Martinos Center) and how it will be incorporated with other CHA study data (D.1.a.) (07/21/2016).
42. Changed nature of response inhibition task to an emotional response inhibition task, using standardized and validated emotional pictures (A.2.b.6, C.5.b.) (07/21/2016).
43. Deleted redundancy in Confidentiality section (07/21/2016).
44. Updated Randomization Schema (C.3.c. Table 1) (07/21/2016).
45. Standardized font type, consolidated text and formatting, and improved readability of protocol organization (7/21/2016).
46. Deleted D.1.c. Sending Data to Research Collaborators Outside CHA, as it is not longer relevant (8/16/2016).
47. Added information about the emotional pictures, used in the emotional Go/NoGo task (C.5.b.6., D.2.d.1.3) in line with the new ICF information (8/16/2016).
48. Added information about storing fMRI data under unique numeric identifier and acrostic, but adding year of birth, in case a radiologist has to assess the brain scan (D.1.a.) (8/16/2016).
49. Added links to Martinos security and imaging manuals for reference (D.1., D.2.d.2) (8/16/2016).

Version 1.4:
Version Date: (February 8th, 2017)

1. Added post-treatment study visits 2 (12 weeks after baseline) and 3 (16 weeks after baseline). For each of these additional visits, patient participants will fill out the Action Plan Initiation Survey (APIS-5). Compensation is $5 for each of these study visits, which will be dispersed at the final 6-month follow-up visit for a total of $30 as the final payment (C.3.d.3.) (10/31/16).
2. Modified APIS-5 and APA-10 instruments to include 6 categories of action plan goals for patient participants to choose from (activity level/exercise, diet/eating/drinking, sleep, self-care practice, medication, and reducing substance use) (C.3.f.6.) (10/31/16).
3. Adapted orientation and informed consent procedure, so that information sheet instead of informed consent are distributed at the orientation session (C.2.c, C.3.d.3, D.2.d.2.3, D.5.c) (11/7/16).
4. Elimination of two survey sessions (10-12 week and 56-week) survey sessions for PCPs who enroll in the study from this point onwards. We are naming this PCP group "Group 3" to distinguish from existing PCP Groups 1 and 2 (11/7/16).

5. Addition of 2 questions regarding actual pain level during the scan and 18 questions, immediately after scanning, regarding the subjective experience with the tasks during the scans (fmri questions) (C.3.f.14.) (11/7/16).
6. Changed instance of first contact about the optional fMRI pilot study from the MINDFUL-PC orientation session to a phone call prior to the MINDFUL-PC orientation session, with the option of sending the fMRI pilot study flyer and information sheet about the optional fMRI pilot study via email prior to the MINDFUL-PC orientation session.

Version 1.5:
Version Date: (April 6, 2017)

1. PCP Enrollment has been completed as of February 10th, 2017
2. Remove PCP Visit Study Session for Patient Participants
3. Expand referral requirements: patients can be referred to MINDFUL-PC by either a licensed CHA primary care provider, or a licensed CHA mental health clinician.
4. Add Action Plan Study Session for Patients during Study Weeks 6-7
5. Add Action Plan Worksheet as a study material to be completed by patients during Action Plan Study Session
6. Modify APIS-5 Survey to reflect changes in Action Plan Worksheet
7. Change APIS-5 study sessions to Weeks 9,10, and 16 ($5 compensation each)
8. Add Study Completion Bonus of $30 to be disbursed at end of study if all study participation items have been completed (Total compensation is now $140).
9. Study payments occur three times: at baseline (up to $20), at 8 weeks (up to $40), and at 24 weeks (up to $80).
10. Clarified which/how many surveys waitlist participants need to complete in order to be eligible for a spot in the next MTPC group once their 6-month study participation is over
11. Clarified how surveys completed on paper will be handled
12. Add two research assistants: Alissa Yap and Yuki Ebihara

Version 1.6:
Version Date: (April 25, 2017)

1. Add one research assistant: Alexandra Brunel

Version 1.7: Version Date: (May 24, 2017)

1. Add one research assistant (Ekaterina Protsenko)

Version 1.8: Version Date: (Add date of approval of Amendment 23)
1. Add one research coordinator (My Ngoc To)

Version 1.9: Version Date: (June 13, 2017)
1. Add one research assistant (Thomas Fatkin)
Version 1.10: Version Date: (July 25, 2017)

1. Add two research assistants (Nermin Hasanovic and Liza Hoffman)

2. Add patient participant adverse events self-report form to be completed at the 8-week and 6-month study sessions
3. Add "STOP ACHE GO" to the patient participant mindfulness practice diary. STOP ACHE GO stands for:
   Stop or Slow down
   Turn towards experience or Take notice of breathing
   Observe with Openness
   Pleasantness/UnPleasantness
   Allow it to be as it is/Accept the ACHE is here/Anchoring to present with breathing
   Compassion/Curiosity
   Holding the experience with warmth
   Expand awareness from ACHE to breathing, then to body, then to all the senses
   Gratitude/Grounding in values
   Open to life, its challenges and beauty/Orient towards experience with kindness

Version 1.11: Version Date: (Retracted on September 26, 2017)

1. Add one research assistant (Sumayyah S. Ahmed)

Version 1.12: Version Date: (October 2, 2017)

1. Add Health, Eating, Activity, and Rest Tracking (HEART) pilot study informed consent and procedures for alumni cohort and concurrent cohort
2. Remove scales HCCQ, VAS, PDRQ, and action plan interview
3. Add compensation related to HEART pilot study
4. Revise analytic methods to include the more robust and flexible mixed methods analysis

Version 1.13: Version Date: (September 29, 2017)

1. Add one research assistant (Tenzin Desel)

Version 1.14: Version Date: (October 19, 2017)

1. Add two research assistants (Alyssa Craparotta and Michael Berry)

Version 1.15: Version Date: (November 17th, 2017)

1. Add research Assistant (Feyisayo Falayi)
2. Add engagement calls for alumni cohort of HEART study protocol
3. Add engagement calls for alumni cohort of HEART study informed consent form

Version 1.16: Version Date: (December 18th, 2017)

1. Add action plan interview for MINDFUL-PC completers
2. Add action plan interview to MINDFUL-PC patient informed consent form
3. Add payment of $15 for action plan interview.

Version 1.17: Version Date: (January 11th, 2018)

1. Remove daily diet picture tracking with a mobile app from the HEART study measures.
2. Remove daily sleep tracking with a mobile app from the HEART study measures
3. Remove ASA24 from HEART study measures

4. Add "Food, Activity, and Sleep Tracking (FAST) Questionnaire" to HEART study measure.
5. Adjust HEART pilot study payment structure to match modifications to health behavior tracking activities
6. Add 3-Factor Eating Questionnaire-R18 as a study measure to MINDFUL-PC patient participant battery

Version 1.18: Version Date: (March 6, 2018)

1. Add Bridget Kiley to protocol

Version 1.19: Version Date: (April 12, 2018)

1. Add Behavioral Measures study visit to HEART Study, and modify HEART Study Informed Consent Form and payment structure accordingly. Behavioral Measures consists of 3 tasks: (Sustained Attention Response Task (SART), Heartbeat Detection Task (HBDT), and 5-Trial Adjusting Delay Hypothetical Discounting Task (HDT).
2. Remove alumni cohort from HEART Study informed consent form and alter the definition of concurrent cohort to include MINDFUL-PC participants who are joining an MTPC group after being in the LDC.
3. Modify Weekly Mindfulness Practice Diary to indicate how blanks will be treated by adding one line that states, "If you leave any field blank we will treat this as a "0" or "No"
4. Add to MINDFUL-PC patient demographics survey optional sections that ask about gender and sexual identity in order to ensure adequate access and representation among underrepresented populations.

Version 1.20: Version Date (May 18, 2018)

1. Add permission for SPEXT.com transcription service to be used on Action Plan interview recordings.

Version 1.21: Version Date: (June 8, 2018)

1. Add Wallis Slater to protocol

Version 1.21: Version Date: (June 27, 2018)

1. Add Annamarie Vu to protocol

Outline:

A. **Introduction, Specific Aims and Hypotheses**
B. **Background and Significance**
C. **Clinical Research Plan: Design and Methods**
D. **Human Subjects Procedures and Confidentiality**

A. Introduction, Specific Aims and Hypotheses:

A.1. Introduction:

This project aims to integrate mindfulness training into the heart of the standard healthcare delivery system. Since Patient-Centered Medical Homes (PCMHs) are recommended by the Affordable Care Act as a model for the current wave of health care reform, this project focuses on harnessing the momentum for change by creating a replicable and sustainable implementation model for mindfulness in the PCMH. This project will train primary care providers (PA, APRN, DO, MD) in Mindfulness-based Stress Reduction (MBSR) and Mindful Communication. In addition, we have developed a modified version of MBSR for primary care called Mindfulness Training for Primary Care (MTPC), which will be implemented directly into the PCMHs throughout a culturally and socio-economically diverse community health system. This project will investigate the effects of MTPC for patients, the effects of MBSR and Mindful Communication for providers, and the effects of the combination of both trainings on patients' experiences of care and providers' experiences of caring. This project will also evaluate the effects of MTPC, Mindful Communication, and the combination of both on patient health outcomes, health maintenance behaviors, and rates of medications prescribed for symptom-relief. This innovative project was developed by a multidisciplinary team with strong support from CHA executive leadership and will become the core project of our new academic Center for Mindfulness and Compassion at CHA.

In addition, the project has been funded as a core clinical trial for the NCCIH Science of Behavior Change UH2 project "Mindfulness Influences on Self-Regulation: Mental and Physical Health Implications." For this project our research team has integrated a PCP-patient visit into this mindfulness-based intervention, while also adding a self-management assessment battery and an evaluative process for measuring rates of initiation and maintenance of jointly-selected health action plans.

In addition, we will conduct an experimental pilot fMRI study to evaluate several mechanistic self-regulation targets and their potential impact on medical regimen adherence as measured by initiation and maintenance of health action plan goals.

A.2. Aims and Hypotheses:

A.2.a. Specific Aims:

1. We aim to train primary care providers in Mindful Communication and implement MTPC directly into PCMHs throughout a culturally and socio-economically diverse community health system (*Implementation Aim*).

2. We aim to investigate the effects of MTPC for patients, MBSR and Mindful Communication for providers, and the combination of the trainings on patients' experiences of care and providers' experiences of caring (*PCP-Patient Relationship Aim*).

3. We aim to evaluate the effects of MTPC for patients, MBSR and Mindful Communication for providers, and the combination of the trainings on patient health outcomes, capacity for self-management of chronic illness, health maintenance behaviors, and rates of medication prescribed for symptom-relief (*Behavioral Health Outcomes Aim*).
4. We aim to investigate the main effects of MBSR and Mindful Communication for providers on provider wellbeing, resilience, and work-place satisfaction (*Provider Resilience Aim*).

5. We aim to investigate the effects of MTPC for patients, MBSR and Mindful Communication for providers, and the combination of the trainings on medical regimen adherence (*Medical Regimen Adherence Aim*).

6. We aim to assess the effect of patient mindfulness training on chronic disease self-efficacy and neuroimaging targets of inhibitory control, self-compassion, interoceptive attention and emotion/pain regulation. This study also aims to evaluate the effects size of the influence of these mechanistic targets on medical regimen adherence outcomes (Self-Regulation Mechanisms Aim).

7. HEART Study: We aim 1) to demonstrate feasibility of using commercially available activity/sleep/diet trackers and online daily surveys for ecological behavior tracking in a MBI RCT and 2) to use the daily behavior tracking to validate the action plan goal setting process and the self-report action plan initiation measure.

A.2.b. Specific Goals and Hypotheses:

1. *Implementation Goal*: Our implementation goals are a) to implement at least two MTPC groups in at least 8 CHA primary care sites within two years, b) to train at least 25-40 primary care providers in Mindful Communication, c) to enroll a socioeconomically-diverse population of patients, and d) to enroll a culturally-diverse population of patients with at least 30% of patients completing the program being non-Caucasian or having a primary language other than English.

2. *PCP-Patient Relationship Hypothesis*: We hypothesize greater satisfaction with the PCP-patient relationship among patients with the combination of provider and patient mindfulness training compared with only one or neither training types.

3. *Health Outcomes Hypotheses*: We hypothesize reductions in depression, anxiety and stress as a main effect of MTPC. We hypothesize reductions in use of medications prescribed for symptom reduction (benzodiazepines, opioids, etc.), and overall improvement in markers of health maintenance and chronic illness management (i.e. PQRS data). We hypothesize the highest levels of initiation and maintenance of self-management action plans will be demonstrated among the MTPC group with Mindfulness-trained providers.

4. *Provider Resilience Hypothesis*: We hypothesize greater workplace well-being, reduced experience of burnout, and increased resiliency among providers as a main effect of provider MBSR + Mindful Communication training.

5. *Medical Regimen Adherence Hypotheses:* We hypothesize a main effect of MTPC group status on levels of initiation and maintenance of medical regimen health behavior change. The highest levels will be demonstrated among the MTPC group with Mindfulness-trained providers. We hypothesize that total formal mindfulness practice, post-study total mindfulness score, baseline mindful non-judgment score, and self-compassion will be associated with successful initiation and maintenance of action plans.

6. *Self-Regulation Mechanisms Hypotheses:* In 4 different fMRI tasks, we hypothesize (a) greater activation of anterior cingulate cortex (ACC) and medial orbitofrontal cortex (OFC) and decreased activation in amygdala/hippocampus after MTPC intervention compared to before intervention (i.e, a pre-post increase) in an emotional Go/NoGo inhibitory control task; (b) greater activation of insula after (compared to before) MTPC in a self-compassion task (that contrasts self-reassurance conditions with a self-criticism condition); (c) greater insula activation during an interoceptive attention task (that contrasts an interoceptive attention condition with an exteroceptive attention condition); and (d) greater rostral ACC (rACC) and ventromedial prefrontal cortex (vmPFC) activation during the anticipation of pain and greater activation in the lateral prefrontal cortex (LPFC) and somatosensory areas during pain in an emotion/pain regulation task, after compared to before the MTPC intervention.
   We hypothesize that all inhibitory control and interoceptive targets will be associated with higher levels of initiation of regimen adherence, while self-compassion, interoceptive targets and emotion/pain regulation will be associated with higher levels of regimen maintenance.

HEART Pilot Study Hypotheses

7. ***HEART pilot study validation goal:*** Our goal is to implement activity and heart-rate tracking, nutrition, sleep, and mindfulness practice tracking in a cohort of MINDFUL-PC alumni to determine whether this suite of behavioral monitoring tasks can behaviorally validate the signal from the self-reported action plan initiation protocol.

   We hypothesize that self-reported action plan initiation with activity, diet, sleep or mindfulness practice will be associated with a behavioral change as assessed with the daily tracking devices.

8. ***HEART pilot study concurrent cohort:*** We hypothesize that participants who are in an 8-week MTPC group will demonstrate higher levels of action plan initiation, with an associated change in behavioral monitoring, than participants who are randomized to the waitlist condition. We also hypothesize that participants who chose to increase activity will have a greater increase in daily activity than those who chose a diet-, mindfulness- or sleep-related action plan goal.

B. Background and Rationale:

The Affordable Care Act (ACA) promotes the Patient-Centered Medical Home (PCMH) delivery model as a tool to reshape the healthcare delivery system [1]. The PCMH model encourages a whole-person orientation, self-management skills for patients with chronic diseases (NCQA, element 4B [2]), and enhanced collaboration for these patients by requiring interdisciplinary integration of clinical, community prevention, and health promotion services (Section 3502, ACA p.1050). In the ACA, both the PCMH and Accountable Care Organization (ACO) models have incentive systems that support initiatives to encourage patient-centered care (PCMH: ACA Section 3502, p.1050; ACO: ACA Section 3022, p.731). If a healthcare delivery system transformation project could demonstrate enhanced levels of patient-centeredness in primary care while also enriching patient self-management skills to cope with chronic illnesses, this project would be innovative and ripe for dissemination within the national PCMH movement.

Mindfulness training is an evidence-based approach to patient-centered caring [3] and whole-person self-management [4]. Mindfulness is "the awareness that emerges through purposely, and non-judgmentally, paying attention to the unfolding of experience moment-by-moment" [5]. Mindfulness-based Stress Reduction (MBSR) is an 8-week program that serves as the basis for multiple different condition-specific mindfulness-based interventions (MBI) provided in medical settings [6]. In 2013, National Institutes of Health invested 44.3 million U.S. dollars into direct funding for MBI research (NIH Reporter 2014), and publications related to mindfulness-related research have exponentially increased over the past 30 years, with more than 500 publications in 2013 alone [7]. Several studies have demonstrated that Mindful Communication training for healthcare providers, which involves training in MBSR followed by 10 months of communication training [3], can reduce provider burnout and increase resiliency, while also increasing patient-centered communication, improving provider empathy and enhancing patient satisfaction [3,8, 9, 10]. Multiple clinical trials have demonstrated that MBIs improved self-management in major areas of community health and chronic illness management [11, 12]. One recent meta-analysis demonstrated that MBIs are broadly effective for anxiety, depression, and pain [13]. MBIs are associated with tobacco smoking reduction [14, 15], reduction in alcohol consumption [16,17,18], reduction in prescription opioid misuse among patients with chronic pain [19], and reduced HIV-risk behaviors [20]. MBIs demonstrate increased asthma-related quality of life with reductions in stress and anxiety [21]. MBIs produce a reduction in systolic and diastolic blood pressure in patients with pre-hypertension [22], and particularly large reductions in hypertension have been seen within studies of African-American patients [23, 24]. Among patients with non-insulin dependent diabetes, one small MBI study demonstrated improved glycemic control [25], while large studies with active controls have demonstrated effective integration of diabetes self-management skills [26], decreased stress and improved

quality of life [27]. MBIs can reduce the stress associated with chronic illness [11, 12], and they are particularly effective in reducing depressive relapse in Major Depressive Disorder [28].

We have been developing a modified version of MBSR called Mindfulness Training for Primary Care (MTPC), which is a MBI adapted specifically for the primary care environment. MTPC combines MBSR skills with additional attention to patient/provider relationships, cultural and socio-economic diversity, coping with chronic illness, reducing unnecessary medical care, and encouraging self-management skills acquisition. In this project, we plan to bring mindfulness directly into the heart of our healthcare delivery system, by offering high-quality training for our primary care providers in MBSR and Mindful Communication [3] while also integrating the innovative MTPC program directly into the PCMH.

Despite all the evidence supporting MBIs, several gaps in the current research and care delivery models may be acting as barriers to rapid dissemination and integration of mindfulness into the healthcare delivery system. First, while there are several provider studies showing increased levels of patient-centered care and provider resiliency, no studies examine the effects of provider mindfulness training on patient health outcomes. Second, while a multitude of patient studies showing reductions in stress, pain, anxiety, and depression exist, no previous studies have been designed to identify whether the combination of training both patients and providers offers a synergistic effect on overall health outcomes as well as the quality of the provider/patient relationship, the level of motivation for health maintenance, and the ability to self-manage and cope with chronic illness. Third, the overwhelming majority of MBSR courses have been conducted in educated, Caucasian, English-speaking populations, leading some to criticize mindfulness as unready for the cultural and socio-economic diversity in the standard healthcare delivery system. Finally, most MBIs are offered through behavioral health or as a complementary private-pay service delivered outside the standard health care system without coverage by insurance payers. This project will address these important gaps in the current research and delivery system, by evaluating the integration of the novel MTPC model into a system of urban, community, multi-cultural, safety-net PCMHs, while also assessing the influence of provider training on outcomes.

In addition, this study offers an opportunity to identify and test mechanistic self-regulation targets (physiologic, psychological, neuropsychological, etc.) that are influenced by mindfulness and potentially account for its effect on medical regimen adherence. Since the majority of medical regimen adherence and health behavior change occurs within primary care, the development of a paradigm for measuring action plan initiation and maintenance among patients within the patient-centered medical home is needed.

Feasibility and Facilities:

The Cambridge Health Alliance (CHA) employs about 160 primary care providers at 15 primary care practices in the Boston Metro-North cities of Cambridge, Somerville, Everett, Malden and Revere. CHA currently has approximately 140,000 primary care patients. Language interpreters are available at every primary care site. The study will be conducted at several CHA primary care health centers, including Cambridge Primary Care Center, Cambridge Family Health, Cambridge Family Health North, East Cambridge Health Center, Windsor Street Health Center, Everett Family Health Center, Revere Family Health Center, Malden Family Health Center, Broadway Health Center, Union Square Family Health, and Somerville Primary Care. Currently,

CHA is undergoing a delivery system transformation initiative integrating mental health into primary care sites, creating patient-centered medical homes across the entire healthcare system over the next 2-3 years.

In addition, the Cambridge Health Alliance has awarded a yearlong grant to the CHA Center for Mindfulness and Compassion (CMC), and CMC faculty and staff eagerly offer support for the MINDFUL-PC project.

The MGH/HST Martinos Center for Biomedical Imaging is a leader in translational research with and development of a host of state-of-the-art imaging technologies. Martinos faculty include world-class experts in disciplines spanning the basic biosciences and clinical investigation. The backbone of the Martinos Center is the Imaging and Computational Core Resources. The Imaging Cores include the MRI, MEG and Optical Imaging Cores, with an extensive and expanding inventory of state-of-the-art imaging facilities and equipment, including related laboratories and testing rooms. The Computational Core oversees data processing, computational infrastructure, software and hardware issues. Together, the Imaging and Computational Cores develop and provide state-of-the art biomedical imaging and image processing technology and techniques to the Center's research faculty and user community.

C. Clinical Research Plan: Study Design and Methods:

C.1. Study population:

This study will have two types of participants: CHA primary care providers (PCP) and CHA patients. In addition, patient participants will be screened for eligibility to participate in an optional fMRI neuroimaging experimental pilot study (fMRI participants).

C.1.a. PCP Participants:

C.1.a.1. PCP Participant Inclusion Criteria:
All of the following are required criterion for inclusion in the study:

1. Current primary care provider at a CHA PCMH
2. Completion of health care training degree, including MD, DO, APRN, and PA
3. Willing to participate in interviews and engage in all procedure.

C.1.a.2. PCP Participant Exclusion Criteria:
Any of the following is regarded as a criterion for exclusion from the study:

1. Previous enrollment or randomization of treatment in the present study
2. .

C.1.b. Patient Participants:

C.1.b.1. Patient Participant Inclusion Criteria:
All of the following are required criterion for inclusion in the study:

1. Current CHA patient with an enrolled CHA primary care doctor.
2. CHA patients 18 years of age and older.
3. Able to tolerate and participate in interviews and engage in all procedures.

4. Able to give written consent in English OR willing and able to provide consent and complete assessments through a professional language translator when necessary.
5. Diagnosis eligible to be covered by insurance for group visits (e.g., anxiety disorder, depression, insomnia, pain syndrome, or adjustment disorder related to chronic illness, etc.).

C.1.b.2. Patient Participant Exclusion Criteria:

Any of the following is regarded as a criterion for exclusion from the study:

1. Any cognitive impairment that precludes informed consent.
2. Patients who, in the opinion of the Principal Investigator, pose an imminent risk of suicide or danger to self or others.
3. Likelihood of potential incarceration such as a conviction or pending charges that may potentially result in imprisonment.
4. Previous enrollment or randomization of treatment in the present study within the 12 months.
5. Behaviors that may cause disruption to a mindfulness group.
6. Patients with symptoms of psychosis, thought disorder, and/or severe mental illness, including schizophrenia, schizoaffective, bipolar disorder, or a current severe episode of major depressive disorder.
7. Refusal of insurance to cover group psychotherapy treatment may lead to exclusion from participation in groups.
8. Patients in their third trimester of pregnancy who foresee conflicts that preclude their commitment to completing all activities.
9. Patients with highly unstable medical problems that put them at a high risk of hospitalization.
10. Temporal Exclusion: Patients with limited English Proficiency as defined by less than 4 out of 7 correct on REALM-SF health literacy screening assessment (equivalent to 7th grade reading level or above) [Note: Patient with limited English Proficiency will be placed on a wait list for specific clinical pilot groups designed for this population, which will be developed for 2016].

C.1.c. Patient Participant fMRI Pilot:

All of the above criteria for patient participants apply to the subset who will take part in the fMRI experiment. In addition, the following criteria will apply:

C.1.c.1. Patient Participant fMRI Pilot additional Inclusion Criteria:

1. Adults 21-60 years old enrolled for participation in the MINDFUL-PC study. (Assessed before the phone-screening using the main study database.)
2. During baseline visit, patient has a history of either major depressive disorder, dysthymia, or generalized anxiety disorder, OR has current mild to moderate symptoms of depression (score range of 10-20 on DASS-21 Depression subscale) or anxiety (score >7 on DASS-21 anxiety subscale). (Assessed before the phone-screening using the main study data from the baseline visit.)
3. Participant does not have a substance use disorder nor intoxication at the time of scanning. Participants must report no more than infrequent recreational cannabis use (i.e.,

no more than two times a month) and must report capacity for abstinence from both cannabis and ethyl alcohol for the 72 hours prior to the scan. (Assessed during the phone-screening.)

4. Normal or corrected-to-normal vision, and correction must be with contact lenses. (The fMRI tasks require ability to read on a screen and there is not enough space for glasses/goggles in the scanner). (Assessed during the phone-screening.)
5. Right-handed as defined by Edinburgh Handedness Inventory [29]. (Assessed during the phone-screening.)

C.1.c.2. Patient Participant fMRI Pilot additional Exclusion criteria:

1. Current severe panic disorder, active severe PTSD symptoms, or psychosis.
2. Current suicidality OR severe depression as evidenced by a score of 20 or higher on the DASS-21 Depression subscale.
3. Standard direct exclusion criteria for undergoing magnetic resonance imaging (MRI) procedures for research purposes (safety standards), i.e., Meniere's disease, epilepsy, strong claustrophobia, currently pregnant or breastfeeding or planning to conceive or breastfeed during the study, cardiac pacemaker, prosthetic heart valve, neurostimulator, implanted pumps, non-MR-compatible implants or devices. (Assessed during the phone-screening.)
4. A history of neurological disease or injury, including a history of seizures or significant head trauma (i.e., extended loss of consciousness, neurological sequelae, or known structural brain lesion), or previous brain surgery. These participants are excluded because they may confound the results of the study due to potential abnormalities in their nervous system. (Assessed during the phone-screening.)
5. Severe skin disease, skin allergies, or multiple reactions to topical preparations, dressings or tapes (because we will be placing sensors on the skin to record cardiac activity and skin conductance). (Assessed during the phone-screening.)
6. Age greater than 60 years old because age effects may confound the results of the study, because white matter integrity decreases with age and reduced inhibitory control. (Assessed before the phone-screening using the main study database.)
7. Current meditation or intense yoga practice of more than 30 min a week or meditation experience of more than 20 hours in the past 10 years. (Since this pilot is focused on investigating mechanisms, we will limit the sample to participants who are new to mindfulness techniques). (Assessed before the phone-screening using the main study database.)
8. Participants with body weight >230 lbs or BMI > 38 will require additional in-person screening and PI approval, because of potential tight fit in the MRI scanner. (Assessed during the phone-screening.)
9. Participants with vascular disease, such as peripheral vascular disease, varicose veins, or lymphedema, in both lower limbs. (Participants may be included with PI approval, if they have vascular disease only in the right limb, which will not receive cuff-pain stimulation and no signs of disease in the left limb.) (Assessed during the phone-screening.)

10. Based on clinical judgment and safety assessment by the PI, the participant is inappropriate for fMRI or unable to complete experiments. (Assessed only if after the phone-screening and other interactions with the patient, the study personnel has doubts about the patients' ability to participate in this additional study.)

C.1.c.3. Patient Participant HEART Pilot Additional Inclusion Criteria:

1. Participant must be currently enrolled in, or have completed, the MINDFUL-PC study.
2. Participant must have access to a smartphone that is compatible with the activity tracker application.
3. Participant must be willing to use the smartphone application and/or wear a wristband activity tracker every day for activity monitoring periods of the HEART study and be willing to take pictures of their food and drink intake.
4. Participant must be able to fill out the study questionnaires daily on a computer or compatible mobile device.

Screening will be conducted by study staff and research assistants. Decisions on the inclusion/exclusion will be made by the study staff under the supervision of the neuroimaging postdoctoral fellow and Principal Investigator in cases where no additional clarifications are needed. In cases where MRI safety needs further assessments, the postdoctoral fellow or imaging consultants at the Martinos Center for Biomedical Engineering will coordinate the assessment with the MRI physics staff at the Martinos Center, and will decide on inclusion or exclusion of the participant.

C.2. Recruitment:

C.2.a. PCP Recruitment:

PCP recruitment has been completed for this study as of February 10, 2017. No further PCP enrollment or study sessions will take place after this date.
The study aims to enroll 50-120 PCPs as participants. PCPs will be recruited through print/flyer advertisements in department offices and health centers, email invitations, announcements at departmental meetings, and a presentation at CHA medical grand rounds and family medicine grand rounds. The presentation for Medicine grand rounds will take place on October 1st, 2014, and the presentation for Family Medicine grand rounds will take place on September 30th, 2014. The study aims to enroll at least 25-40 PCPs into an intervention group (Group 1) and at least 25-40 into a control group (Group 2 and 3).

C.2.b. Patient Recruitment:

The study aims to enroll a total of 434-1,000 CHA patients as participants during the project. Patients will be recruited through print/flyer advertisements in health centers, CHA marketing materials, community informational meetings, and referral by PCPs and other members of the health care team. In addition, we aim to develop a video introduction about mindfulness to be played in patient waiting areas within health centers with translations into the primary languages of the health centers (Once developed these videos will be provided for review by the CHA IRB prior to implementation). This study aims to randomize 290 patients to an 8-week study intervention and another 144 to a control group.

C.2.c. Experimental fMRI Pilot Patient Recruitment:
The study aims to enroll a maximum of 30 patients into an experimental fMRI pilot study to be conducted at the Athinoula A. Martinos Center for Biomedical Imaging in Charlestown, MA. Participants will be informed about this fMRI pilot study during the reminder phone call before the MINDFUL-PC orientation session. Participants will be told that this is an optional pilot study and that they do not need to participate in this pilot study in order to participate in the larger study. Participants will also be informed that they will ONLY be able to participate in the fMRI pilot study if they get randomized to the MTPC intervention condition. In the email confirmation for the orientation session, we will further include the fMRI neuroimaging study flyer with information on the fMRI pilot study and the fMRI information sheet about the fMRI study. Participants will hear again about the fMRI pilot as part at the MINDFUL-PC orientation session at their primary care health center. Again participants will be told that this is an optional pilot study and that they will ONLY be able to participate in the fMRI pilot study if they get randomized to the MTPC intervention condition. Patients are further informed about inclusion/exclusion criteria related to the fMRI study and that the number of scanner time slots may be limited, so all participants who enroll and qualify may NOT be offered an opportunity to attend a scanning session. All participants interested in participating will be ranked on the call-list in numerical order based on the order that they expressed interest as well as their level of reliability and timeliness during previous recruitment steps and interactions. The call-list ranking is to ensure that this study enrolls participants who are most motivated and most likely to be able to complete the extra demands related to the fMRI scanning and additional visits, and also to ensure that the limited scan slots for this study are allocated efficiently. During the orientation session, participants will receive the flyer with information on the fMRI pilot study with

potential scan times and we will again make available the information sheet about the fMRI study to read and review at home. Phone screening of MRI inclusion/exclusion criteria will be completed after the orientation and randomization to the mindfulness group, for interested mindfulness group participants (see attached phone script). We will phone screen interested mindfulness group participants during the group-scheduling phone call. The phone screen will include questions based on the Martinos Center MRI safety screening form and the Edinburgh Handedness Inventory to verbally screen participants and make sure they fulfill MRI safety criteria and all other criteria related to the fMRI study. After the phone screening, and if participants fulfill all criteria, they are given the opportunity to ask any questions they might still have about the study. We will then schedule an fMRI measurement scan session. If the participant needs additional time to make an informed decision or if we have to make additional inquiries based on the MRI eligibility phone screening process, we will arrange a follow-up phone call with the patient (within 1-3 days of the group-scheduling phone call), to decide on study participation and potentially schedule the fMRI measurement session.

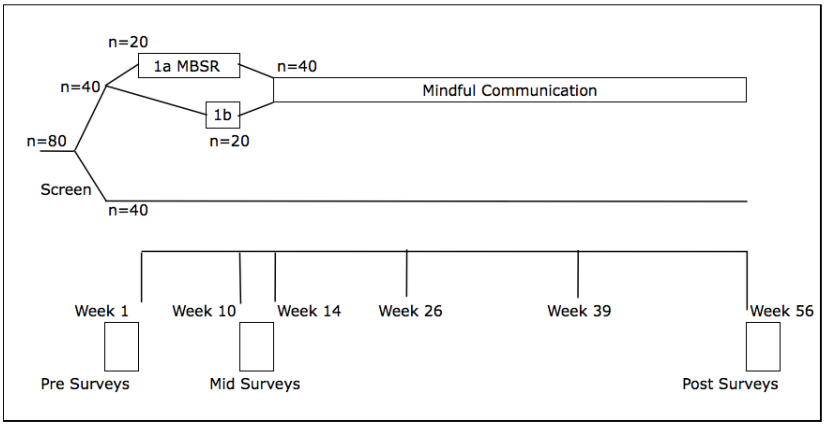
C.3. Experimental Design and Study Procedures:

C.3.a. Design Overview and Study Participants:

This study uses a mixed 2 x 2 factorial design embedding a randomized controlled trial within a naturalistic quasi-experimental implementation project.

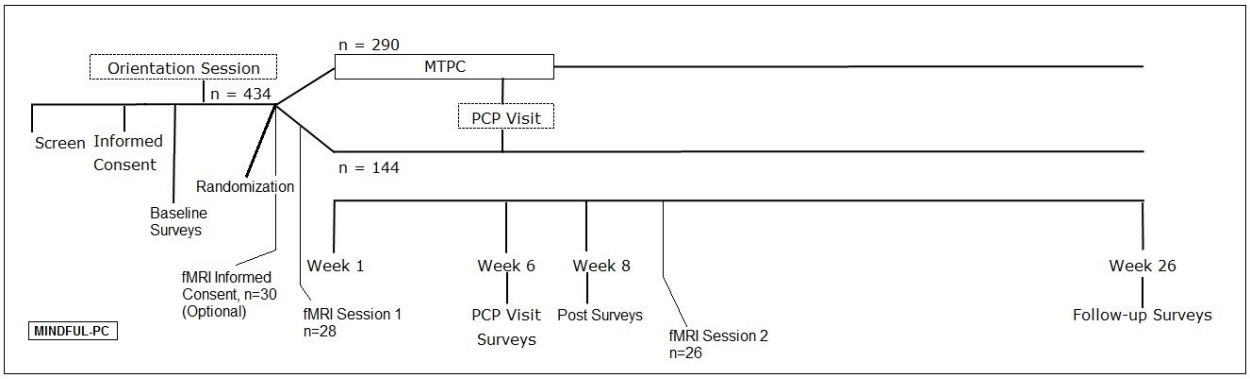
The implementation project, developed in collaboration with the CHA Center for Mindfulness and Compassion (CMC), will encourage CHA PCPs from across all CHA health care centers to participate in a mindfulness training program. All PCPs will be invited to participate in the study procedures, and those who enroll in the study will naturalistically be assigned to two different groups: those who engage in the mindfulness training program (Group 1) and those who decline to engage in the training program but are still willing to complete study procedures (Groups 2 and 3). The mindfulness training program includes an 8-week MBSR training course of 2.5 hours weekly with an 7-hour day of silent practice at the beginning of week 7 (Group 1a), or an abbreviated 18-hour weekend-long Mindfulness training course (Group 1b). Members of Group 1a will first receive MBSR training from senior MBSR teachers and Group 1b will receive training from CMC faculty and staff. After this MBSR training, members of Group 1a and Group 1b will be able to participate in a once-monthly 2.5 hour-long Mindful Communication course for 10 months during Year 1 of the study. We expect that this Mindful Communication training will eliminate between-group differences from MBSR course models, allowing us to collapse Groups 1a & 1b for research analysis. Both Group 1 and Group 2 will be invited to participate in several survey sessions: prior to starting the mindfulness training implementation project, between PCP study weeks 10 and 14, and then again after PCP study month 12 (see Figure 1a). Group 3 PCPs, enrolled after October, 2016, will not receive mindfulness training, and will only be required to participate in the initial survey session at baseline.

Figure 1a. Study flow schema for PCP participants:



Within this naturalistic implementation project, we will conduct a randomized controlled trial of CHA patients with a PCP referral. Patients will be randomized using a stratification algorithm to receive either MTPC training or one 60-min introduction to mindfulness session. This randomization will be based on the level of mindfulness training of the patient's primary care provider (Group 1 vs. Group 2 and 3). Those patients who are randomized to receive MTPC training (MTPC Group) will be instructed by behavioral health specialists who are trained as MTPC Group Leaders, as described later in section C.4.a. of the protocol. The MTPC group is a group psychotherapy intervention held within a primary care health center on 8 consecutive weeks with 10-12 enrolled patients with 2 hour-long sessions, including a 7-hr day of silent practice. As the level of desire to participate in mindfulness training may be a confounding factor, we will use a 60-min introduction to mindfulness group as a control in order to eliminate bias related to expectation and selection that could otherwise influence measures of treatment effect. In contrast, those patients who are randomized to receive only the 60-min introduction to mindfulness (Control Group) will be given preference to enroll in MTPC after the study's completion. Both groups of patients will complete surveys at the induction of the study, again after patient study week 8, and at study week 26 (see Figure 1b). Patients will complete an interview with a research coordinator to assess their maintenance of their action plan goal at week 26.

Figure 1b. Study flow schema for Patient participants



In this RCT, we will also conduct an optional experimental fMRI pilot study. This study will include a pre/post within-subjects design with 90 minutes of neuroimaging before and after completion of the MTPC group. Each scanning session will begin with setting up the equipment for autonomic monitoring (i.e., respiratory belts, finger plethysmograph, finger sensors for skin

conductance and a belt for monitoring breathing rate). The scanning session will consist of a localizer scan (3 min), an anatomical scan (7 min), and a resting state scan (7 min), followed by an inhibitory control task (the emotional Go/NoGo inhibitory control task; 15 min), a self-compassion task (15 min), a DTI-scan measuring white matter tracts (8 min), an interoceptive attention task (10 min) and an emotion/pain regulation task (10 min). The neuroimaging will take about 10 minutes for setting up autonomic monitoring outside the scanner and 75-90 minutes in the scanner.

C.3.b. Patient Screening

C.3.b.1. EPIC Chart Review

In order for patients to be screened for enrollment in the MINDFUL-PC study, they will be required to have a CHA PCP, and a referral from a CHA PCP or licensed CHA mental health clinician. The MINDFUL-PC Research Coordinator or other IRB-approved, EPIC-trained study staff will review the patient's EPIC chart for information on inclusion and exclusion criteria using the template attached. The Research Coordinator or other IRB-approved, trained study staff will consult with the Medical Director or Principal Investigator if there are any questions on the patient's eligibility, per their inclusion/exclusion criteria. Only the Medical Director or Principal Investigator will make decisions about patient exclusion.

C.3.b.2. Informational and Scheduling Phone Call

If the patient is eligible from this chart review process, the Research Coordinator or other IRB-approved, trained study staff will call the patient to inform them of their referral. During this screening phone call, the MINDFUL-PC Research Coordinator or other IRB-approved, trained study staff will inform the patient of the MINDFUL-PC study and ask screening questions using the phone script attached. Using information from these screening questions, the PCMH behavioral health care specialist, the MINDFUL-PC Principal Investigator, or the Center for Mindfulness and Compassion Medical Director will assess for the patient's eligibility for the study. If the patient is eligible but has not had a behavioral health evaluation within the past 6 months, or met with a behavioral health provider within the last 3 months, the patient will be scheduled for a 1-hour behavioral health evaluation with a behavioral health care specialist in the PCMH. The behavioral health care specialist will complete the MINDFUL-PC Patient Screening Form. If the patient has had a behavioral health evaluation within the last 6 months and met with their behavioral health provider within the last 3 months, the current behavioral health care specialist of record will complete the MINDFUL-PC Patient Screening Form without scheduling an additional evaluation. Once a patient is eligible for the study, the PCMH behavioral health care specialist will refer the patient to the MINDFUL-PC Research Coordinator, who will schedule the patient for an Informed Consent Session which will be followed by a mindfulness group orientation session.

C.3.c. Participant De-identification, Randomization, Allotment, and Blinding:

A unique numeric identifier and acrostic will be created for all participants (PCPs and patients) who have signed an informed consent and a list linking these identifiers with the participant's name, birthday, and MRN (if applicable) will be kept in a password-protected file by the principal investigator. All data will be linked to these coded identifiers and no direct patient identifiers will be transmitted from REDCap to SAS 9.3 for analysis.

For patient participants, the name, birthday, and MRN will be entered into an initial REDCap database strictly for the purpose of screening and consent process. Next, a unique numeric identifier and acrostic will be created for all participants (PCPs and patients) who have completed an informed consent and the linking list will be kept in a password-protected file by the principal investigator. All further study data collected in a second REDCap database will reference this unique numeric identifier and acrostic. All data will be linked to these identifiers and no direct patient identifiers will be transmitted from REDCap to SAS 9.3 for analysis. Through a collaboration with the CHA Quality Office and CHA information technology, we will generate medical record reports for participants who are in our study and this information will remain protected with the CHA system, and will not include any study data except name, MRN, and birthday.

Any patient participant who is eligible with a screen, has completed the informed consent form at the orientation session, and has completed the baseline assessment battery will be eligible for placement on our program list and ultimately randomization into either of the two groups using a stratification algorithm. Randomized patients will be stratified with two layers based on PCP group and health center location. PCPs who refer after the PCP portion of the study closes will be considered "non-trained" (equivalent to Groups 2 and 3) for purposes of randomization. We will begin with 4 health center regions (Malden, Revere, Somerville, and Cambridge) and health centers within each region will have their own list, but ultimately hope to expand so that each participating health center location with a mindfulness-trained behaviorist will have its own waitlist for new groups. When a new group is scheduled to open at a health center location, those patients with PCPs at that health center location will be randomized to either intervention group or control (First stratification layer—Location). Patients with a PCP from another health center but who have a specific language need may be included on the waitlist for capability of that health center. We hypothesize an increased rate of MTPC patient referrals from PCPs who are enrolled in the mindfulness training program versus those who only received information about mindfulness-based interventions. Therefore, within each group location, in order to achieve an optimal 2 x 2 factorial structure (see randomization schema figure), patients will be randomized using a second stratification layer based on the primary care provider's level of mindfulness training (Group 1 vs. Group 2 or Group 3) to either 8-week MTPC or one 60-min introduction to mindfulness, using a 2:1 randomization ratio, respectively (Second stratification layer—PCP Group), based on the second layer of stratification (See Table 1). Study staff will maintain the waitlists and then notify the patient participants of their acceptance into either group.

Table 1. Randomization Schema:

	MTPC Group	Control Group
Group 1: Providers with Mindfulness Training	145	72
Group 2 and 3: Providers with introduction & community referral	145	72

2 x 2 Factorial design testing main effects of patient training and primary care provider training, as well as the interaction of the combination.

This study will not be blinded; however, upon referral, all patients will receive a screening from the primary care behavioral health care provider, complete an informed consent, complete a set of pre-treatment baseline surveys and then will be informed that they will be given a random

number and placed on the waiting list for upcoming groups. They will be told about capacity restrictions, that there will be two groups consisting of different group lengths, and that if they would like to do more groups after completion of the program, they will be notified about groups that become available sometime in the next year or two.

C.3.d. Study Visits:

In this section, the flow of study visits will be described for both PCPs and Patient participants.

PCP Study Visits have been completed as of February 10, 2017. No additional PCP study visits will take place after this date.

C.3.d.1. Overview of PCP Study Visits (SEE TABLE 2 IN APPENDIX A):

Phone Screen Visit (PCP Group 1a or Group 1b):

PCPs who express interest in the MBSR program or the weekend 18-hr mindfulness retreat will be screened by phone or email by the study Research Coordinator who will register PCP participants for the study at one of the Patient-Centered Medical Homes. At the time of registration, the PI, Research Coordinator or a research assistant will conduct a brief screening interview to determine the PCP's eligibility for the study. This will take 10 minutes by phone or email.

Phone Screen Visit ([PCP Group 2 and 3]):

PCPs who express interest in referring patients to mindfulness groups will be asked to fill out an eligibility questionnaire on paper or through a secure REDCap link. Eligible PCPs will be given the opportunity to continue on to the informed consent session.

Informed Consent Visit (PCP Study week 1 [Group 1a, s, or Group 2 and 3] or Week 10 [Group 1b]):

PCP participants will be provided with written descriptions in English of the research study procedures, timeline and participant commitments electronically through a secure REDCap link for review prior to enrollment. PCPs will be given an opportunity to email and/or call the study staff for answers to any questions about the consent document and they will be asked to complete a consent quiz to ensure understanding of the most crucial points.

PCPs will be given the opportunity to review and sign the informed consent form and ask any remaining questions about the research either online through a secure REDCap link or in-person at their primary care location [Groups 1a, 1b, 2, and 3], or during the first hour of the first group [Groups 1a and 1b]. The Principal Investigator, Research Coordinator, or other IRB-approved, trained study staff will review each PCP's consent quiz and will be fully responsible for any issues related to informed consent, and will ensure that participants receive adequate oral and written information about the aims, procedure, possible risks and benefits of the study. When participants are ready, they will be asked to sign a written or electronic informed consent form approved by the CHA Institutional Review Board (IRB). Signed paper informed consent forms will be stored in a double-locked filing cabinet. Electronically signed informed consent forms will be printed out and stored in a double-locked filing cabinet. This document includes a full description of the study procedures and associated risks. Participants will receive an additional electronic or paper copy of the signed informed consent form for their own records. Participants must give written informed consent in order to participate in the study. Participation in the study is voluntary. All participants will be notified that they are free to discontinue from participating

in the study at any time. All participants will be asked to complete and sign a section acknowledging that sessions will be audio-recorded for research purposes. No study-specific procedures or investigations will be performed before the participant has signed and dated the Informed Consent Form. Consent quiz forms will be reviewed prior to starting study procedures, a score of at least 90% on the consent quiz is required to start the study. The principal investigator will review any errors on the consent quiz with PCPs prior to starting the study. The Principal Investigator will store the original, signed Informed Consent Form. The informed consent portion of the visit should take 30 minutes.

Pre-treatment Assessment Visit (PCP Study Week 1 [Group 1a,Group 2, and Group 3] or 10 [Group 1b]):
PCP participants will complete a 20 minute long set of survey batteries before beginning the program. PCPs will be given the opportunity to complete survey batteries on paper or electronically through a secure REDCap link. Paper surveys will be stored in a double-locked filing cabinet, and will be transferred electronically to the secure REDCap database by IRB-approved MINDFUL-PC study personnel with double-audit to minimize errors in data entry. In this survey session, PCP participants will complete the PCP Baseline Battery, the PCP Mindfulness Self-Report Battery, the PCP Clinical Assessment Battery, and the PCP Experience of Caring Battery.

Mindfulness-Based Stress Reduction (MBSR) course (PCP Study weeks 1-10):
PCPs who choose to enroll in the mindfulness training course may participate in Mindfulness-based Stress Reduction (MBSR) training with 8 sessions lasting 2.5-hours over 9 weeks with a 7-hour day of silent practice. The first hour of the first week's group will be for completing the consent and pre-treatment assessment visit.

Mindfulness Weekend Intensive Retreat (PCP Study Week 10):
PCPs who do not elect to receive MBSR training with 8 weekly sessions will be able to participate in an intensive 18-hour weekend retreat. The first hour of the first day will be for completing the consent and pre-treatment assessment visit.

Mid-Training Assessment Session (Completed between PCP Study Weeks 10-14):
After 8 weeks or the intensive weekend retreat, PCPs will be asked to fill out another survey battery electronically through a secure REDCap link, or on paper. Paper surveys will be stored in a double-locked filing cabinet, and will be transferred electronically to the secure REDCap database by IRB-approved MINDFUL-PC study personnel with double-audit to minimize errors in data entry. In this 20-minute session, PCP participants will complete the PCP Mindfulness Self-Report Battery, the PCP Clinical Assessment Battery, and the PCP Provider Resilience Battery. The Adverse Event Reporting Form will also be completed.

Mindful Communication Course (PCP Study Weeks 14-56):
PCPs assigned to receive Mindfulness training will then take a course in Mindful Communication for the next 10 months. They will receive 10 monthly sessions of 2.5-hour Mindful Communication instruction.

Post-Treatment Survey Session (PCP Week 56):
After completing 10 months of Mindful Communication [Group 1a or 1b], at Study Week 56 [Group 2], PCPs will be asked to complete another series of surveys electronically through a

secure REDCap link, or on paper. Paper surveys will be stored in a double-locked filing cabinet, and will be transferred electronically to the secure REDCap database by IRB-approved MINDFUL-PC study personnel with double-audit to minimize errors in data entry. These surveys will take approximately 20 minutes. In this session, PCP participants will complete the PCP Mindfulness Self-Report Battery, the PCP Clinical Assessment Battery, the PCP Provider Resilience Battery, and the Adverse Event Reporting Form.

C.3.d.2. Overview of Patient Study Visits (SEE TABLE 3 IN APPENDIX A):

Screening Visit:
Behavioral health care providers in primary care will screen patients who express interest in participating in a MTPC group and already have a referral from an eligible CHA PCP. In order for patients to be screened for enrollment in the MINDFUL-PC study, they will be required to have a referral from a participating PCP. We will create a new EPIC referral process for PCPs, such that when a PCP checks off Mental Health, under Question 2 "Where will the patient be seen for Psychiatry," the PCP will be able to select MINDFULNESS. Then, under "Services Requested," a PCP will be able to specify his or her health center region: "MINDFUL-PC Malden", "MINDFUL-PC Revere", "MINDFUL-PC Somerville", or "MINDFUL-PC Cambridge". This streamlined EPIC order will be sent to the MINDFUL-PC Research Coordinator via CHA Central Intake.

The "6-3 Rule": All patients must have a 1-hour behavioral health evaluation within the past 6 months documented by a CHA clinician in EPIC in order to be eligible to participate in the study. In addition, all patients must have had a visit with their behavioral health care provider within the last 3 months. If a patient has not received a behavioral health evaluation within the last 6 months or has not had a behavioral health care visit within the last 3 months, he or she will be scheduled for a 1-hour behavioral health evaluation with one of the licensed clinicians who have been trained to lead MTPC groups or a licensed clinician who has been trained to conduct screening evaluations for the MTPC groups.

In order to be eligible to participate in the MINDFUL-PC study, all patients must have a CHA PCP, and a referral from their CHA PCP or a licensed CHA mental health clinician. .

In order to be eligible to participate in the MINDFUL-PC study, all patients must have a MINDFUL-PC Patient Screening Form completed by a behavioral health care provider upon performing a behavioral health evaluation. Patients must fill out a Patient Eligibility Questionnaire electronically via an e-mail link to a secure REDCap form or by voice over phone. This questionnaire will be reviewed by the MINDFUL-PC PI or Center for Mindfulness and Compassion Medical Director, who will then assess the eligibility of the patient and schedule a 1-hour behavioral health evaluation, if appropriate. The behavioral health clinician will conduct a behavioral health evaluation to determine the patient's eligibility for the study and to enroll patients into the program. Data from the screening interview, MINDFUL-PC Patient Screening Form, and Patient Eligibility Questionnaire will be entered into a secure REDCap form.

Since the research study is overlaid on an implementation pilot program, we will rely on the assessment of the referring mental health clinician (either a masters or doctoral level clinician) to identify patient diagnoses and the presence of any severe mental illness. The Research Coordinator or other IRB-approved study staff with non-clinical training, but background in

psychology will be reviewing diagnoses on the submitted screening forms. Any diagnoses that suggest major mental illness will be reviewed with the PI daily. The PI is a board-certified psychiatrist and will decide if a patient with mental illness will be included and excluded from the study. If the decision is unclear from the referral documentation, then the principal investigator will contact the screening behavioral care provider to discuss the patient's appropriateness for the study. If the patient passes the screening interview, he or she will be offered to be scheduled to attend the Mindfulness Orientation Session.

Mindfulness Orientation Session (Prior to Randomization; To be scheduled prior to PT Study Week 1):
This will be a 2.5 hour session. For the first 1.5 hours, interested patients consent to participate in the study and will then complete the pre-treatment survey session. For the remaining hour, patients will be invited to attend a 1-hour orientation to MTPC. Patients will be paid 20 dollars for completion of surveys and attendance of 60 minute orientation session.

Informed Consent Session:
Prior to the beginning of the Mindfulness Orientation Session, patients will be asked to complete an Informed Consent Form. This session will be held either prior to the Mindfulness Orientation Session within a clinical space at each participating CHA primary care health center or at the CHA Center for Mindfulness and Compassion. Patients will complete informed consent and consent assessment in-person upon arrival at the orientation. Because this intervention is well-established with more than 1000 studies demonstrating the safety and efficacy of Mindfulness-based interventions [30], the group represents a low-risk psychoeducational experience. To ensure all patients have access to study personnel and an opportunity to ask questions, patients will complete the informed consent form in-person during an Informed Consent group Session prior to the beginning of the Mindfulness Orientation Session. With the permission of primary care site leadership, we will provide food for patients during the informed consent session. The MINDFUL-PC Research Coordinator or Program Manager and other trained study personnel will be present at this Informed Consent Session in order to answer any individual questions. The informed consent document will include a full description of the study procedures and associated risks. The participant will also be asked to complete an Informed Consent Assessment to ensure comprehension of the study procedures, rights of participants, as well as understanding of the risks and benefits of the study. The patient will not be able to sign the document without having completely correct answers on the consent assessment. After completion, participants will be given an additional copy of the signed informed consent form for their own records. Participants must give written informed consent in order to participate in the study. Participation in the study is voluntary. All participants will be notified that they are free to discontinue from participating in the study at any time. All participants will be asked to complete and sign a section acknowledging that sessions will be audio-recorded for research purposes. No study-specific procedures or investigations will be performed before the participant has signed and dated the Informed Consent Form. The signed informed consent forms will be stored in a binder in a double-locked cabinet at the Center for Mindfulness and Compassion. Only IRB-approved study staff will have access to this cabinet.

Patients who scored less than 90% on the informed consent assessment will meet individually with the Research Coordinator or other approved study personnel who will administer the Rapid Estimate of Adult Literacy in Medicine—Short Form (REALM-SF) form [31] to assess patient literacy levels. This is a 7-item word recognition test, which takes about 2 minutes, offers a valid

quick assessment of patient health literacy and has excellent agreement with the 66-item REALM instrument in terms of grade-level assignments. Patients are instructed to read seven words aloud for a member of the study team. Patients who pronounce fewer than four of the words correctly read at a literacy level of 4th to 6th grade.

Initially, in pilot groups in the year 2015, only patients with an English reading proficiency of at least a 7th grade level will be included. Patients with less than a 7th grade reading level in English will be excluded from pilot groups in 2015. In 2016, we will begin to offer MTPC groups in other language, to serve patients with limited English proficiency (LEP). It is our goal to offer MTPC groups in Portuguese, Spanish by mid-2016, and to pilot a LEP group for English speakers with low levels of literacy. Once the study protocol and informed consent documents are approved by the IRB, we plan to develop translations of the consent form into at least the 3 most common languages at CHA. The translated informed consent forms will be translated by the CHA Department of Translation Services (DTS) and approved by the IRB. Written consent will be given by the non-English speaking participant on a translated Informed Consent Form, and the participant will receive a copy for his or her own records.

Patients can reach study staff during the Informed Consent Session to review any difficulties with the consent assessment or other questions, so that patients have an opportunity to ask any necessary questions about the research study prior to completion of the consent. Patients will be given the opportunity to review the protocol with a trained study staff member if they fail the consent assessment. Patients will also be given an opportunity to correct their answers on the consent assessment. If they can't pass the assessment after reviewing it and the protocol with the coordinator, then they will evaluated by study staff for the presence of low literacy versus cognitive deficits disrupting their ability to complete study tasks. If they have cognitive deficits that disrupt the ability to complete study tasks, then they may be unable to participate in the study. Patients with a score of 90% or higher on the Informed Consent Quiz will be eligible for participation in the study. The Principal Investigator is fully responsible for any issues related to informed consent, and will ensure that the participant receives adequate written information about the aims, procedure, possible risks and benefits of the study and opportunity for oral discussion of questions if needed.

<u>Pre-treatment Survey Session Visit:</u>
The Research Coordinator or other approved study personnel will inform the patient participant that he or she must complete a series of surveys before the start of the 1-hour MTPC group orientation. Patients will complete the surveys through a link to the secure REDCap database using an electronic device in the primary care health center, or using paper surveys, which will be entered into REDCap by our IRB-approved study staff. Any paper surveys will be stored in our double-locked filing cabinet in the CMC Research Office. Electronic devices will be provided for patients to take surveys at each participating CHA health center.

In this session, patient participants will complete the Patient Baseline Battery, the Patient Mindfulness Self-Report Battery, the Patient Clinical Assessment Battery, the Patient Self-Management Battery, and the Patient-PCP Relationship Battery. These surveys are expected to take the average patient 60 minutes to complete.

<u>MTPC Orientation Session:</u>

Patients who have consented to participate in the study and have completed the pre-treatment survey session will be invited to stay for the 60-minute mindfulness orientation session. During this session, interested patients will meet for one visit with a behavioral care provider in groups of up to 30 participants. This group will be held within a clinical space at each participating CHA primary care health center. It will be one hour in length and the behavioral care provider will offer a list of mindfulness resources available in the community. Patients will be reminded that, after this session, they will be randomly assigned to either the 8-week or referral to community resources and electronic resources and placed on a 6-month waiting list. Details about this intervention can be found in section C.3.e.3.

Scheduling Phone Call:
Once an eligible individual has demonstrated an understanding of the study procedures and potential risks of participating, provided written informed consent, completed pre-treatment assessments on REDCap, and attended the MTPC orientation session, then he or she will be placed onto the waitlist for randomization for the respective health center and assigned a randomization ID by health center. This ID will be entered into a randomized algorithm with stratification, which will be used to allot the participant to a study group. The Research Coordinator or another approved member of the research personnel will contact the patient by phone to schedule him/her for the specified study group, and a scheduling email will be sent. Patient participants will be assigned either to an 8-week MTPC group or to a 6-month waiting list for the MTPC group, and will be informed of their placement during the phone call. Patients will also be encouraged at this time to ask any questions they might have.

If a participant cannot attend the assigned group, he or she will have to wait to be rescheduled for at least 6 months from the completion of his/her pre-treatment assessments.

Biweekly Engagement Phone Call (PT Study Week 1-8):
All patient participants will receive an ongoing 3-5 minute Participant Engagement phone call from a member of the study staff. This call will be made according to the brief phone script attached. This call will be made every two weeks during Study Weeks 1-8. The purpose of this outreach call will be to provide support for patients in both groups, help participants cultivate a relationship with study staff, give participants a place to ask questions, and support participants in completing study visits. The call will have five talking points: 1) How have you been in the last 2 weeks? 2) Have you had any issues with completing the weekly Mindfulness Practice Diary or the Mindfulness Resources Use Diary? 3) Have there been any issues with your participation in the study in general? 4) We appreciate your contribution to the research study and encourage you to continue filling out the diaries – just as a reminder you will receive $20 for each survey session and $20 if you complete all the weekly diaries. 5) Is there anything else you'd like to share with us? Study staff will complete a call log for all engagement calls, and issues raised in these calls will be discussed twice a week in research staff meetings.

Mindfulness Intervention (MTPC Intervention Group; PT Study Week 1-8):
Patients in the 8-week MTPC program will meet with a behavioral care provider for 8 weeks in groups of approximately 6-12 participants, to receive 2 hours of instruction in MTPC. MTPC groups will be generally held in the evenings in clinical spaces within each participating CHA primary care health center. Between weeks 6 and 7 there will be a weekend 7 hour long day of silent practice at locations within the local community or within a nearby CHA hospital facility space. The total duration of the program is 23 hours over 8 weeks with additional expectations

for daily home practice by participants. Details about this intervention can be found in section C.3.e.4.

Action Plan Study Session (Completed between PT Study Weeks 6-7):
During Patient Study Weeks 6-7, all patients participating in the MINDFUL-PC program will fill out an Action Plan Worksheet and watch a brief SMART goal video (for example: https://www.youtube.com/watch?v=1-SvuFIQjK8), which is designed to support the creation of a short-term health goal. Patients randomized to the 8-week MTPC group will receive instruction and support during the group in developing health goals for a short-term action plan, and communicating these goals effectively to people in their life who might be important stakeholders in their health. Duration: 15 minutes.

After completing the Action Plan Worksheet, patient participants will complete the Action Plan Assessment (APA-10), a 10-item scale that evaluates patient behavior in the domains of self-determination, motivation, shared decision-making, and barrier appraisal. This survey will be completed online in REDCap or on paper, and is expected to take the average patient 5 minutes to complete.

Post-treatment Survey Session Computer Visit 1 (Completed between PT Study Weeks 8-12):
After eight weeks, participants in both groups will be asked to complete another series of surveys online on REDCap or on paper. Patient participants will again be given the option to either complete the surveys on a device at their PCMH or outside of the office on a computer of their choosing. Electronic devices will be provided to patients in the 8-week MTPC group so that they may complete their surveys at their PCMH in the hour following their final weekly meeting. Paper survey answers will be transferred to a secure REDCap database by MINDFUL-PC study staff, and all paper surveys will be stored in a double-locked filing cabinet. Research assistants (to be hired later) will be available at several scheduled 1-hour sessions at PCMH sites to bring electronic devices and offer support for survey completion. Patients assigned to the 6-month waiting list may visit their PCMH to use a device to complete their surveys during one of these scheduled sessions.

In this session, patient participants will complete the Patient Mindfulness Self-Report Battery, the Patient Clinical Assessment Battery, the Patient Self-Management Battery, the Patient-PCP Relationship Battery, the Action Plan Initiation Survey (APIS-5), the Weekly Mindfulness Practice Diary, the Patient Satisfaction Survey, and the Adverse Event Reporting Form. These surveys are expected to take the average patient 65 minutes to complete.

Post-treatment Survey Session Computer Visit 2 (Completed at PT Study Week 9):
In this session, patient participants will complete the Action Plan Initiation Survey (APIS-5). This survey is expected to take approximately 5 minutes to complete.

Post-treatment Survey Session Computer Visit 3 (Completed at PT Study Week 10):
In this session, patient participants will complete the Action Plan Initiation Survey (APIS-5). This survey is expected to take approximately 5 minutes to complete.

Post-treatment Survey Session Computer Visit 2 (Completed at PT Study Week 16):
In this session, patient participants will complete the Action Plan Initiation Survey (APIS-5). This survey is expected to take approximately 5 minutes to complete.

Follow-up Survey Session Computer Visit (Completed between PT Study Weeks 24-26): After six months, both patient groups will complete a survey about attitudes about primary care providers. Patient participants will again be given the option to either visit their PCMH to complete the surveys on a CHA device, on paper, or complete the surveys outside of the office on a computer of their choosing. Patients requiring interpreters or electronic devices can schedule a meeting visit at their PCMH to complete the surveys. These surveys are expected to take the average patient 70 minutes to complete.

In this session, patient participants will complete the Patient Mindfulness Self-Report Battery, the Patient Clinical Assessment Battery, the Patient Self-Management Battery, the Patient-PCP Relationship Battery, the Action Plan Initiation Survey (APIS-5), the Weekly Mindfulness Practice and Resources Diaries, and the Adverse Event Reporting Form.

Waitlist patient participants must complete the following study requirements in order to be eligible for a spot in the next MTPC group once their 6-month study participation has ended: three 45-minute study survey batteries, the Action Plan Worksheet, 1 of 3 Action Plan Follow-Up Surveys, and 6 of 8 weekly Mindfulness Practice/Resource surveys.

Action Plan Interview (Completed after PT Study Week 26): After completing the study, participants will have an opportunity to give comments about their experience in the MINDFUL-PC program.

This interview will last for 20-30 minutes and will be conducted according to the Action Plan Interview Guide. Participants will be invited to interview via e-mail. Interviews will be recorded using a USB-based device that attaches directly to the telephone line. No identifying information beyond first name will be used in the interviews. Participants will always be asked permission before turning on the recording device – if they decline permission, no recording will be made. Recording devices will be stored in the secure research office double-locked filing cabinet when not in use, and will only be accessed by IRB-approved study staff. Recording files will be kept on CHA's secure study G Suite server and will only be accessible by IRB-approved study staff. Recordings will be transcribed using a transcription service with whom we have a HIPAA BAA agreement in place following IRB approval, such as Spext.com. A sample of the email communication to participants is presented below:

"Dear (Participant Name),

Thank you so much for your participation in the MINDFUL-PC study. We would like to invite you to share your experience with the MINDFUL-PC Program, especially the action planning process. This will take place in a 20-30 minute phone call with one of our research staff. Your response is confidential, and will be incredibly useful feedback on how we can make this program better for future participants. You may decline this invitation if you do not wish to share your experience. If you are interested, please let us know and we will arrange a time with you."

The calls will be conducted by a research assistant who has a strong background in qualitative research methods and phone interviewing and who has also fully grasped the objectives of the Action Plan Interview Guide (see supporting materials). If needed, other team members may be

trained to conduct the action plan interview by learning the objectives in the Action Plan Interview Guide, sitting in on two Action Plan Interview calls, and conducting one "test" call with another study staff member.

C.3.d.3. Overview of Patient Study Visits in Experimental fMRI pilot study (SEE TABLE 4 IN APPENDIX):

Orientation Session Reminder Phone Call and Email Confirmation:
Participants will be informed about the fMRI pilot study during a phone call before the MINDFUL-PC orientation session. In the email-confirmation for the orientation session, we will further include the flyer with information on the fMRI pilot study and the information sheet about the fMRI study. We will also let participants know about the possibility to enroll as part of the **concurrent cohort** in an optional health behavior tracking study, the Health, Eating, Activity, and Rest Tracking (HEART) pilot study.

Orientation:
During the orientation session, patients will be informed on the voluntary, additional fMRI pilot study. Patients will also be informed that they will only be able to participate in the fMRI pilot study if they get randomized to the MTPC condition and are eligible to this fMRI study. Randomization will be conducted based on the MINDFUL-PC study protocol. Patients will hear basic information about neuroimaging (e.g. safety, experience in the scanner, such as noise, limited space to move, etc.) and they will receive a flyer with information on the inclusion/exclusion criteria for the fMRI study, as well as further information on MRI and fMRI, and contact information for reaching neuroimaging personnel at the Martinos Center. Participants will also be given an informational flyer and a brief verbal description of the HEART study. Participants wishing to participate in the HEART study may do so without participating in the fMRI pilot study.

Group Scheduling Phone Call:
During the scheduling phone call for the mindfulness group only, patients are asked about their interest in the optional fMRI pilot study. We will then screen interested mindfulness group participants verbally, using a phone screening interview based on the Martinos Center MRI Patient Screening form and the Edinburgh Handedness Inventory (see phone script Pt Protocol - Randomization Status Phone Call). We will assess if participants fulfill all criteria related to the fMRI study. Participants will be given the opportunity to ask questions they have regarding the study, the flyer, the information sheet or other aspects regarding the fMRI. Some screening questions represent an immediate exclusion from the study (see phone screening script), other items represent potential risks, and require further clarification. In this case, the responsible Operations Manager and Chief MRI Technologist at the Martinos Center for Biomedical Engineering will be contacted by the neuroimaging post-doctoral fellow, with the necessary information to decide the safety for fMRI scanning for a patient with a certain condition. In case the responsible Operations Manager cannot confirm MRI safety, the patient will be excluded from the fMRI study. Participants will also be asked if they have used any illicit drugs in the past 30 days, and any drug use could result in exclusion from the study based on the clinical judgment of the PI. If a patient fulfils all eligibility criteria, we will then schedule an fMRI measurement scan session. If the patient needs additional time to decide about participating in this study or if we have to make additional enquiries based on the MRI eligibility screening, we will arrange a

follow-up phone call with the patient (within 1-2 days of the group-scheduling phone call), to decide on study participation and potentially schedule the fMRI measurement.

C.3.d.4. Overview of Patient Visits in HEART pilot study (see Table 4 in APPENDIX)

HEART Pilot Study Informed Consent Session:

Concurrent Cohort:

Participants are first notified of the opportunity to enroll in the HEART study during the MINDFUL-PC confirmation phone call to attend MINDFUL-PC orientation. Following this, at the in-person orientation, participants will be led through the verbal and written consent process for MINDFUL-PC. Once they have signed their MINDFUL-PC consent forms, they are eligible for the HEART study and will be given the HEART study information packet, as well as the HEART study informed consent form. A doctoral level member of the research staff will then guide participants through a verbal introduction of the HEART study, informing them of the invitation to voluntarily participate, reviewing study inclusion and exclusion criteria, and providing a chance to ask any questions. If after this in-person review, interested participants will be invited to sign the HEART study consent form. If an interested participant does not understand or agree to study requirements after the verbal introduction and a chance to ask questions, the doctoral level research staff member conducting the orientation session will decide to exclude the participant from the HEART study.

Upon completion of the HEART study informed consent form, participants will be given an additional copy of the signed informed consent form for their own records. The signed informed consent forms will be stored in a binder in a double-locked cabinet at the Center for Mindfulness and Compassion. Only IRB-approved study staff will have access to this cabinet.

The study staff member will then create a unique Participant ID, specific to the HEART study, for each participant, which will be used for all data collection in the HEART study. The form that contains the linking information between each Participant ID and each participant will be stored in a double-locked filing cabinet in the CMC Research Office, and will only be accessible by IRB-approved study staff. The participant will also be assigned a study-specific Gmail address and password, which will serve as their login credentials for the smartphone activity tracking application. To ensure confidentiality, the Gmail address will have no identifiable information or information related to their Participant ID.

At the end of the MINDFUL-PC orientation, participants who express interest in participating in the HEART study will be scheduled by one of the research assistants to come for an in person 45-minute Behavioral Measures visit, which will be conducted on an individual basis. In this visit participants will complete three behavioral measures tasks, install any required smartphone applications, be introduced to wristband activity trackers if applicable, and be given a chance to ask any questions. Participants are reminded that they will repeat the Behavioral measures visit once more during weeks 8-9 of the study.

HEART Pilot Study Sessions:
Concurrent Cohort:

Timing: HEART study participants participating in the **concurrent cohort** will complete the behavioral tasks 1 week prior to MTPC Session 1 of the intervention (Part 0) (applies to both waitlist and intervention arms), and will complete daily behavioral tracking surveys during Part 0, and for 4 weeks starting at MINDFUL-PC Study Week 5 (Parts 1 and 2). Part 1 is study weeks 5-6, and Part 2 is Study Weeks 7-8. Participants will complete the second behavioral tasks visit between Study Weeks 8 and 9.

Inclusion/Exclusion criteria: Participants must either be newly enrolling in the MINDFUL-PC study or be joining a MINDFUL-PC primary care group after having completed their 6-month study requirements in the low-dose comparator group. Participants must have access to a smartphone that is compatible with the activity tracking application, participants must be willing to attend the two behavioral task sessions, to use the smartphone application and/or wristband tracking device each day during the study collection periods, and participant must be willing to fill out online surveys at home.

HEART Study Tasks: Participants will do the following tasks on a daily basis for the duration of the HEART study:

- **Mindfulness Practice Diary:** Fill out the MINDFUL-PC weekly mindfulness practice diary and resource use diary daily for 1 week prior to MTPC Session 1 of the intervention and then for 4 weeks during Weeks 5 through 8.

- **Activity Tracking:** Install and use a smartphone application related to activity tracking, e.g., Argus or a similar version of commercially available activity tracking app, etc., and use this app every day for 1 week prior to MTPC Session 1 of the intervention and then for 4 weeks during Weeks 5 through 8. The Argus App is compatible on both Android and iOS platforms. Participants will install any required smartphone applications during their first Behavioral Tasks visit, with the guidance of a research study staff member. Participants will sign into the application using a coded Participant ID. During feasibility testing, we will assess the utility of wristband trackers. If feasible and appropriate for the study, the principal investigator may decide for all participants to also be given a wristband activity tracker to wear on the wrist each day. Data will be collected using a coded Participant ID. If they are given a wristband, then the participant will need to return the wristband to the study team upon completion of the study in order to receive final reimbursement

- **Food, Activity, and Sleep Tracking (FAST) Questionnaire:** Participants will be asked to fill out the FAST Questionnaire on a daily basis for 1 week prior to MTPC Session 1 of the intervention and then for 4 weeks during Weeks 5 through 8. This questionnaire will contain questions adapted from the Automated Self-Administered 24-Hour Dietary Assessment Tool (ASA24) and the National Sleep Foundation Sleep Diary.

- **Behavioral Tasks Session**

  Participants will be asked to complete the Behavioral Tasks component during an in-person behavioral tasks session that takes place prior to Week 1 of the MINDFUL-PC

study and then again between Weeks 8 and 9. This behavioral tasks session will be scheduled during the orientation session to the MINDFUL-PC and HEART studies. During this behavioral tasks session, participants will first download any required smartphone applications for activity tracking with the guidance of a research study staff member. Then, they will complete three behavioral tasks in the following order: the Heartbeat Detection Task (HBDT), 5-Trial Adjusting Delay Hypothetical Discounting Task (HDT), and Sustained Attention to Response Task (SART). Each task is described in brief below (see Section C.3.f.7 for more a detailed description):

- **Heartbeat Detection Task (HBDT)**: Participants are asked to count their heartbeat during three varying time intervals (30s, 30s, 60s). In parallel, individuals' heart-rate will be measured by Kardia Mobile technology. Participants will place their index and middle fingers of both hands on top of the Kardia Mobile device and will be instructed to count their heartbeat for a period of 30 or 60 seconds. The readings from this device are linked to the Kardia Mobile App, which will be on a screen faced away from the participant[1]. Participant data stored in the Kardia Mobile app will be identified with the HEART Study participant ID, which will not be linked to any identifying information.

- **5-Trial Adjusting Delay Hypothetical Discounting Task (HDT):** This is a brief delay discounting task performed on a computer that assesses an individual's impulsivity by presenting a series of 5 discrete choice questions between some amount of a delayed commodity (in this case, dollars) and half that amount available immediately (e.g. "Gain $1000 in 3 weeks or gain $500 now"). Individuals choose whether they would rather receive a smaller amount of money now, or a larger amount in the future[2, 3].

- **Sustained Attention to Response Task (SART)**: Participants will complete a series of computerized tests focused on sustained attention, response inhibition, and self-regulation. They are asked to press a key in response to rapidly displayed integers (1-9) and withhold a response to a designated "no-go" integer[4].

These tasks will be conducted in a quiet, closed, and gently lit room located at the Center for Mindfulness & Compassion (26 Central St, Somerville, MA 02143) or at a CHA primary care location. Participants will sit on a chair with their feet flat on the floor, forearms on the table, and with a desktop or laptop computer screen in front of them. The research staff member will explain each task to the participant before conducting the trial, and will provide a one-minute break between each task.

<u>fMRI Pilot Study Informed Consent:</u>
Participants will be given the informed consent form for the fMRI study at the fMRI session. During the fMRI session, we give participants time to read the consent and answer any questions they might have regarding the informed consent form. We will ask the participant to sign the informed consent in the presence of a doctoral-level staff.

<u>Pre-fMRI Session Preparation Phone Call:</u>

Participants will be contacted 96 hours prior to the session and reminded to abstain from alcohol and cannabis for at least 72 hours and from other illicit drugs throughout the study. If a person is not ready to comply with this rule the PI may exclude the patient from the fMRI pilot study (while the patient can still participate in the main study).
Participants will be given $10 towards the taxi fare or public transport costs to and from the Athinoula Martinos Center for Biomedical Imaging. Participants can also receive free parking at the Martinos Center. If a participant expresses discomfort or insecurity to reach the neuroimaging site, study staff can offer to accompany participants to the Athinoula Martinos Center for Biomedical Imaging.

Pre-fMRI Session Reminder Phone Call:
Patients will again be contacted 24 hours prior to the session and reminded to abstain from alcohol or cannabis and to make sure patients are still able to come to the scheduled fMRI visit.

Pre-treatment fMRI Session Visit:
At the fMRI visit, participants will be asked to complete a salivary oral fluid toxicology test for alcohol and illicit drug use. For alcohol-testing we will use the One Step Alcohol Saliva Test Strip (Confirm Biosciences). Participants will apply saliva directly to the reaction pad for 10 seconds. After 2 minutes the test will inform us about alcohol blood level concentration. For illicit drug testing, we will use the SalivaConfirm Premium - 5 Panel Instant Oral Cube Drug Test Kit (Confirm Biosciences), which tests for the use of Amphetamine and Methamphetamine (detects use within the last 72 hours), Cocaine (last 24 hours), Opiates (last 48 hours), Marijuana (last 14 hours). Participants will put the sponge end of the collection stick into the mouth and soak into saliva for 3 minutes. If the patient is positive representing any level of intoxication with substances, then the patient will be excluded immediately from the experimental fMRI study, and will not undergo the fMRI scan. The excluded patient can still participate in the main MINDFUL-PC study. Women will be asked during the screening phone-call if they are pregnant or planning to conceive, which would result in exclusion from the fMRI study. Women of childbearing potential (without active contraception) are further offered to take a urine pregnancy test at the fMRI visit, to confirm that they are not currently pregnant (TestCountry's Strip Pregnancy Tests). Results are available within 5 minutes. A positive pregnancy result on site will result in immediate exclusion from the fMRI study, but not from the MINDFUL-PC study. After toxicology and pregnancy testing, participants will fill in the Martinos Center Patient Screening Form. This form is mandatory before every scan session. All items have been screened during the Group Scheduling Phone Call so that potential risks can been assessed, before scheduling the fMRI visit. If however the Martinos Center Patient Screening Form shows any contra-indications for fMRI, the responsible Operations Manager and Chief MR Technologist at the Martinos Center will be contacted immediately. In case the responsible Operations Manager can not be reached or cannot confirm MRI safety, the patient will be excluded immediately from the fMRI study, and will not be scanned.

Before the fMRI measurement, study staff will place sensors and a belt on the participant to measure heart rate, breathing rate, and skin conductance during fMRI tasks. Participants will complete structural scans, a resting state scan, inhibitory control task, self-compassion task, diffusion tensor scan, interoceptive attention task and emotion/pain regulation task. The pain regulation task involves a pressure cuff which is placed on participant's calf and is inflated for periods of 30 seconds to a medium intense pain, as rated by the participants (50 out of 100, with 100 being the worst pain imaginable). After the scan, patients will answer questions regarding

experiences during the task (tiredness, pain, concentration, experience during the resting state and tasks). Patients will also schedule a time slot for their post-treatment fMRI Session Visit.

Post-treatment fMRI Session Visit:
Patients will complete salivary testing for illicit drugs and alcohol to prevent anyone who is intoxicated from participating in the fMRI session. If the patient is intoxicated with alcohol or cannabis, then the patient will be asked to reschedule for the experimental fMRI follow-up session to prevent a wasted session; however, given the initial fMRI data collection, post-treatment fMRI scanning will still be obtained if the patient can return in a sober state. All participants will need to complete the fMRI testing within 2 weeks after completion of the MTPC group. Patients will complete the same sequence of structural and resting state scans, an inhibitory control task, self-compassion task, diffusion tensor imaging, interoceptive attention task and emotion/pain regulation task.

C.3.e. Study Interventions:

C.3.e.1. MBSR:
Mindfulness-based Stress Reduction (MBSR) [32] was created by Jon Kabat-Zinn, Ph.D., in 1979. The program includes eight weekly classes, each 2.5 hours in duration, as well as a 7-hr day of silent practice. MBSR emphasizes both 'formal' and 'informal' mindfulness meditation practices. Formal methods include sitting meditation, walking meditation, body scan meditation, and gentle hatha yoga. Informal practices emphasize mindfulness in daily life, and include awareness of breathing, awareness of pleasant and unpleasant events, and purposeful awareness of everyday activities like eating, walking, and interpersonal communication. MBSR involves weekly home assignments for both formal and informal practice. Classes have a common flow and involve group exercises, guided formal practice, and opportunities for group and individual dialogue about difficulties and developments of formal and informal practices.

C.3.e.2. Mindful Communication:
Mindful Communication [33] offers a 10-month continuation phase following MBSR for medical providers, which meets monthly for 2.5 hours. This course emphasizes three major components: *mindfulness*; *narrative medicine*, "the creation and sharing of reflective stories that explore the profound and meaningful experiences one has as a physician"; and *appreciative inquiry* which focuses on examining and framing patterns of individual thinking and behavior as "strengths and capacities to be enhanced and extended." Each class has a common flow of activities maintained from MBSR, as well as an overarching theme. Themes include "teamwork", "uncertainty in medicine", "aspiration", and "suffering in medicine."

C.3.e.3. Mindfulness Orientation Session:
This hour-long informational session will involve both experiential and informational introduction sections. The class will begin by answering the question "What is mindfulness?" and group leaders will offer evidence for supporting mindfulness. Group leaders will then guide the class in an experiential session. The orientation session is designed to foster a commitment to do the 30 minutes or more per day at home practice; to give the participants a 'taste' of the mindfulness practices that will be presented in the classes and to process with the prospective participant the experience of the practice; to inform the patient about the logistics of the class; to review the specific upcoming course schedule; to meet the specific leaders for the upcoming group; to learn about risks and benefits of the MTPC program; and to give patients an

opportunity to ask questions. The orientation session will conclude with an explanation of internal and external resources for continuing mindfulness education, and will offer patients a referral to these resources.

C.3.e.4 MTPC:

Mindfulness Training for Primary Care (MTPC), is a modified version of MBSR for delivery as group psychotherapy modality within patient-centered medical homes. MTPC offers a series of eight weekly, two-hour core sessions delivered in a group format with a seven hour day of silent practice between weeks 6 and 7. MTPC will follow the same structure as MBSR, but will also include a weekly topic to be discussed for 20 minutes per class for each of the 8 weeks and the integration of a PCP illness management/health maintenance appointment to be held during week 6-7 of the group. The weekly themes are as follows:

Part A: Sessions 1-4 are primarily focused on learning to pay attention.

Week 1: From Autopilot to Befriending the Body and Mind
Week 2: Perception and Rediscovering "Beginner's Mind"
Week 3: Pleasure and Freedom in Being Present
Week 4: Staying Present with Pain, Difficulty, Illness and Stress

Part B: Sessions 5-8 are focused on illness self-management and skills for changing health behaviors.

Week 5: Allowing What Is: The Bedrock Needed to Support Change
Week 6: Skillful Action and Skillful Communication
Week 6-7 Action Plan Worksheet: The purpose of this worksheet is to support the patient in generating his/her own short-term action plan.
Week 5-7 Full-Day Session: The purpose of this 7-hour full-day session is to integrate mindfulness practices learned in earlier sessions and deepen personal practice.
Week 7: Cultivating Kindness towards Self and Others
Week 8: The Rest of Your Life

C.3.f. Measures:

The **Rapid Estimate of Adult Literacy in Medicine—Short Form (REALM-SF)** [34] will be used to assess patient literacy levels. This is a 7-item word recognition test that offers a valid quick assessment of patient health literacy and has excellent agreement with the 66-item REALM instrument in terms of grade-level assignments. Patients are instructed to read seven words aloud for a member of the study team. Patients who pronounce fewer than four of the words correctly read at a literacy level of 4th to 6th grade. Duration: 2 min.

C.3.f.1. Baseline Battery for Patient Participants:

A **Survey of Meditation and Mindfulness Experience (SMME)** will assess the participant's previous experience with meditation and Mindfulness-based interventions, both over their lifetime and in the past two weeks. This will be a brief questionnaire. Duration: 5 min.

A brief **demographics survey** will note patient race, ethnicity, optional sexual and gender identity, primary language, income, and other quantifiable attributes. Duration: 5 min.

Patients who note that they smoke in the demographics survey will be prompted to complete **the Fagerström Test for Nicotine Dependence (FTND)** [35] on REDCap. This is a widely used self-rating scale that provides a quantitative measure of nicotine dependence and will be administered at the screening visit to determine level of nicotine dependence. The 6-item scale includes: smoking rate, time between waking and first cigarette, smoking when ill, difficulty refraining from smoking where it is forbidden, smoking more heavily in the morning, and reporting that the first cigarette of the day would be the most difficult to give up. A score greater than or equal to 6 indicates high nicotine dependence. Duration: 3 min.

C.3.f.2. Baseline Battery for PCP Participants:

A **Survey of Meditation and Mindfulness Experience (SMME)** will assess the participant's previous experience with meditation and Mindfulness-based interventions, both over their lifetime and in the past two weeks. This will be a brief questionnaire. Duration: 5 min.

The **Mindfulness Knowledge and Attitudes Questionnaire for Primary Care (MKAQ-PC)** is adapted from Mindfulness Knowledge and Attitudes Questionnaire Administered to Psychology and Medical Students from McKenzie et al. [36]. This is an 8-item scale that examines providers' previous experience with and general outlook on the incorporation of Mindfulness into health care. Some of the items ask providers to rate their experience with or knowledge of Mindfulness from (a) nonexistent to (e) extensive. Providers are also asked about their willingness to incorporate Mindfulness into patient care. An example item is "To what extent do you think MBIs may have further potential for treating a range of other health problems? (a) nonexistent (b) mild (c) moderate (d) good (e) extensive." Duration: 5 min.

A brief **demographics survey** will note PCP race, ethnicity, gender, and other quantifiable attributes. Duration: 5 min.

C.3.f.3. Mindfulness Self-Report Battery for Patient and PCP Participants:

The **Five Facet Mindfulness Questionnaire (FFMQ)** [37] is a 39-item scale that examines five factors that represent aspects of the current empirical conception of mindfulness. These five facets include: "observing, describing, acting with awareness, non-judging of inner experience, and non-reactivity to inner experience." An example item is "I pay attention to how my emotions affect my thoughts and behavior." Participants rate their degree of agreement with each of the items on a Likert-type scale ranging from 1 (*Never or very rarely true*) to 5 (*Very often or always true*), with higher scores indicating higher experience of mindfulness. Duration: 8 min.

The short-form **Self-Compassion Scale (SCS-SF)** [38] is an abbreviated 12-item form of the original 26-item Self-Compassion Scale. This scale evaluates six different aspects of self-compassion: Self-Kindness (e.g., ''I try to be understanding and patient toward those aspects of my personality I don't like''), Self-Judgment (e.g., ''I'm disapproving and judgmental about my own flaws and inadequacies''), Common Humanity (e.g., ''I try to see my failings as part of the human condition''), Isolation (e.g., ''When I feel inadequate in some way, I try to remind myself that feelings of inadequacy are shared by most people"), Mindfulness (e.g., ''When something painful happens I try to take a balanced view of the situation''), and Over-Identification (e.g., ''When I'm feeling down I tend to obsess and fixate on everything that's wrong.''). The scale is scored on a 5 point Likert scale (1 = Almost never; 5 = Almost always), and negative subscale items are reverse scored. Duration: 4 min.

The **Difficulties in Emotion Regulation (DERS) Scale** [39] is a 36-item self-report scale designed to assess emotional dysregulation. The scale assess 6 aspects of emotional dysregulation: non-acceptance of emotional responses ("When I'm upset, I become embarrassed for feeling that way"), difficulties engaging in goal directed behavior ("When I'm upset, I have difficulty thinking about anything else"), impulse control difficulties ("When I'm upset, I lose control over my behaviors"), lack of emotional awareness ("When I'm upset, I take time to figure out what I'm really feeling (reverse-scored)", limited access to emotion regulation strategies ("When I'm upset, it takes me a long time to feel better"), and lack of emotional clarity ("I have no idea how I am feeling"). Duration: 5 min.

The **Multidimensional Assessment of Interoceptive Awareness (MAIA)** [40] is a 32-item self-report scale designed to assess multiple aspects of interoception and interoceptive awareness. The scale assesses 8 aspects of interoceptive awareness: noticing ("I notice when I am uncomfortable in my body"), not-distracting ("I do not notice (I ignore) physical tension or discomfort until they become more severe"), not-worrying ("I start to worry that something is wrong if I feel any discomfort"), attention regulation ("When I am in conversation with someone, I can pay attention to my posture"), emotional awareness ("I notice that my breathing becomes free and easy when I feel comfortable"), self-regulation ("When I am caught up in thoughts, I can calm my mind by focusing on my body/breathing"), body listening ("I listen to my body to inform me about what to do"), and trusting ("I feel my body is a safe place"). Duration: 5 min.

C.3.f.4. Clinical Assessment Battery for Patient Participants :

The **Depression Anxiety Stress Scale (DASS-21)** [41] is a 21-item scale that evaluates distress in the subscales of depression, anxiety, and stress. Each subscale receives a total score that corresponds to a numerical value defining the aspect as mild, moderate, severe, or extremely severe. Each item is scored on a 4 point Likert scale (0 = Never; 5 = Almost Always) considering the participant's experience in the past week. An example item includes "I found it difficult to relax." Duration: 3 min.

The **Patient Health Questionnaire-2 (PHQ-2)** [42] is a 2-item scale that is used to screen for depression. PHQ-2 asks participants to indicate the frequency with which they have experienced the items on the scale in the past two weeks, ranging from 0 (*Not at all*) to 3 (*Nearly every day*). For example, the scale asks patients how often in the past few weeks they have felt "Little interest or pleasure in doing things." A participant's total score can be used to evaluate the probability that the participant expresses major depressive disorder or any depressive disorder. (*Note: The PHQ-2 will not be used with PCPs*). Duration: 1 min.

The **Perceived Stress Scale (PSS)** [43] measures the degree to which situations in life are stressful. Items are designed to evaluate how overloaded, unpredictable, and uncontrollable one finds one's life. Each item is scored on a 5 point Likert scale from 0 (*Never*) to 4 (*Very often*). An example question is, "In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?" Positively stated items are reverse scored before all scale items are summed to yield a total score. Duration: 3 min.

The **consumption subscale of the Alcohol Use Disorders Identification Test (AUDIT-C)** [44] is a 3-item modified version of the original 10-item AUDIT scale, used to identify harmful drinking behavior or alcohol use disorders in patients. Each question has a set of five possible answer choices, ranging in frequency. For example, the question "How often do you have six or more drinks on one occasion?" is followed by these five possible answers: "(a) Never; (b) Less than monthly; (c) Monthly; (d) Weekly; (e) Daily or almost daily." The points allotted to each score are: a = 0 points, b = 1 point, c = 2 points, d = 3 points, e = 4 points. A score of four or greater indicates harmful drinking behavior or alcohol use disorder in men. A score of three or greater indicates the same in women. The greater the score, the more likely the drinking behaviors are affecting the patient's health or safety. Patient participants will complete this survey before they begin the study group and again after 8 weeks. Duration: 1 min.

The **DSM-V Survey of Substance Use** is adapted from the DSM-5 Self-Rated Level 1 Cross-Cutting Symptom Measure [45]. The 23-item original measure is intended to be used in research or clinically to help clinicians rapidly identify areas of patient behavior that require further examination. This 11-item adapted version includes only the domain of substance use, which asks three questions about drinking, smoking, and substance use in the past two weeks. Items are rated on a 5-point scale of frequency, from 0 (*Not at all*) to 4 (*Nearly every day*). The survey includes questions such as "During the past **TWO (2) WEEKS**, about how often did you use any of the following medicines **ON YOUR OWN**, that is, without a doctor's prescription, in greater amounts or longer than prescribed? … Painkillers (like Vicodin, Percocet, Oxycodone)." The answers to each item will be summed to yield a total score. Duration: 3 min.

The **Patient Reported Outcomes Measurement Information System – Depression Short Form 8a (PROMIS-DSF)** [46, 47, 48] is an 8-item scale used to assess patient-reported health status for depression. PROMIS instruments are funded by the National Institutes of Health (NIH) and used to reliably and validly measure patient-reported outcomes for clinical research and practice. Participants are asked to rate their experience of the item in the past seven days on a 5-point scale from 1 (*Never*) to 5 (*Always*). With use of the PROMIS Assessment Center Scoring Service, a T score is generated from participant responses. A sample item includes "I felt that nothing could cheer me up." Duration: 4 min.

The **Patient Reported Outcomes Measurement Information System – Anxiety Short Form 8a (PROMIS-ASF)** [49, 50] is an 8-item scale used to assess patient-reported health status for anxiety. PROMIS instruments are funded by the National Institutes of Health (NIH) and used to reliably and validly measure patient-reported outcomes for clinical research and practice. Participants are asked to rate their experience of the item in the past seven days on a 5-point scale from 1 (*Never*) to 5 (*Always*). With use of the PROMIS Assessment Center Scoring Service, a T score is generated from participant responses. A sample item includes "My worries overwhelmed me." Duration: 4 min.

C.3.f.5. Clinical Assessment Battery for PCP Participants:

The **Depression Anxiety Stress Scale (DASS-21)** [51] is a 21-item scale that evaluates distress in the subscales of depression, anxiety, and stress. Each subscale receives a total score that corresponds to a numerical value defining the aspect as mild, moderate, severe, or extremely severe. Each item is scored on a 4 point Likert scale (0 = Never; 5 = Almost Always) considering the participant's experience in the past week. An example item includes "I found it difficult to relax." Duration: 3 min.

The Perceived Stress Scale (PSS) [52] measures the degree to which situations in life are stressful. Items are designed to evaluate how overloaded, unpredictable, and uncontrollable one finds one's life. Each item is scored on a 5 point Likert scale from 0 (*Never*) to 4 (*Very often*). An example question is, "In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?" Positively stated items are reverse scored before all scale items are summed to yield a total score. Duration: 3 min.

C.3.f.6. Self-Management Battery for Patient Participants:

The **Self-Efficacy for Managing Chronic Disease Scale (SECD-6)** [53] is a 6-item scale that is used to evaluate a participant's ability to self-manage care for a chronic disease. SECD-6 asks participants to rate their confidence in their own ability to do certain activities, on a scale from 1 (*not at all confident*) to 10 (*totally confident*). For example, the scale asks patients to indicate "How confident are you that you can do the different tasks and activities needed to manage your health condition so as to reduce your need to see a doctor?" A participant's score for the scale is calculated as the mean of the six items. Duration: 3 min.

The **Patient Activation Measure (PAM)** [54] is a 13-item scale that is designed to evaluate a participant's ability to be an effective and informed manager of his or her own health and health care. Participants are asked to rate their agreement with each statement on a 0-100 metric where 0 = the lowest possible activation and 100 = the highest possible activation as measured by this set of items. The PAM survey generates an overall score on a 0-100 scale for each patient, and can segment patients into one of four activation levels along an empirically derived continuum. Statements include: "I am confident that I can follow through on medical treatments I may need to do at home." Duration: 4 min.

The **Perceived Control Questionnaire (PCQ)** is adapted from a 5-item perceived control measure from Jerant et al. [55] and a previously validated survey from Armitage et al. [56]. This 5-item scale ask participants to rate their sense of control over chronic illness self-management on a 7-point scale from 1 (*None*) to 7 (*Total*). Items include "How much personal control do you have over your self-management behaviors?" Duration: 3 min.

Action Plan Worksheet/SMART Goal Video: Patient participants will complete the Action Plan Worksheet and watch a brief video about creating SMART goals (for example, https://www.youtube.com/watch?v=1-SvuFIQjK8) in PT Study Week 7. The Action Plan Worksheet is a 13-item worksheet that incorporates information about SMART goals to support patient participants to make a goal about their health in one of 3 categories (activity level/exercise, diet/eating/drinking, or mindfulness meditation practice). Patients are encouraged to share this worksheet with a person who may help the patient in accomplishing the goal, and/or a healthcare provider. Duration: 15 min.

Patients will complete the self-report **Action Plan Assessment (APA-10)** questionnaire after filling out the Action Plan Worksheet, at PT Study Week 7. This survey instrument is developed as an adaptation of two self-determination theory scales [57] [58] and incorporates elements of shared decision-making [59] and self-efficacy and barrier appraisal [60]. This 10-item scale evaluates patient behavior in the domains of self-determination, motivation, shared decision-making, and barrier appraisal. Participants are asked to rate their agreement with a statement on

a 7-point scale from 1 (*Strongly Disagree*) to 7 (*Strongly Agree*). A sample item includes "I have agreed to this action plan because I want to do it for myself." Duration: 5 minutes.

Patient self-reported **Action Plan Initiation Survey (APIS-5)** will be administered at post-treatment (PT Study Week 8, 12, and 16). This 5-item questionnaire is adapted from a measure used by Guck et al. [56]. In this questionnaire, patients are asked to list their action plan goals generated with their PCP, and determine whether they met or did not meet each goal. Patients are asked to categorize their goals into one of six categories: diet/eating/drinking, exercise/activity, sleep, medication, reducing substance use, and self-care. For each unmet goal, patients are asked to rate the cause of not meeting the goal on an attributional rating scale using a 7-point format. Higher scores indicate internal rather than external and uncontrollable rather than controllable attributions. A sample item includes: "Was the cause of not meeting this goal controllable by you?" where 1 is "Extremely controllable" and 7 is "Not at all controllable." Duration: 5 minutes. Participants in the HEART pilot study in the concurrent cohort will fill this out as per the main study timeline. Participants in the HEART pilot study alumni cohort will fill this out at the end of HEART study Weeks 4 and 5.

The **Three-Factor Eating Questionnaire-R18 (TFEQ-R18)** is an 18 item questionnaire that refers to current dietary practice and measures 3 different aspects of eating behavior: restrained eating (conscious restriction of food intake in order to control body weight or to promote weight loss), uncontrolled eating (tendency to eat more than usual due to a loss of control over intake accompanied by subjective feelings of hunger), and emotional eating (inability to resist emotional cues). The TFEQ-R18 consists of 18 items on a 4-point response scale (definitely true/mostly true/mostly false/definitely false). Responses to each of the 18 items are given a score between 1 and 4 and item scores are summated into scale scores for cognitive restraint, uncontrolled eating, and emotional eating. An example item includes "Sometimes when I start eating, I just can't seem to stop." Duration: 5 minutes.

C.3.f.7. HEART Pilot Study Battery:

Activity Tracking Smartphone Application: Participants will install a free activity tracking smartphone application, which is compatible on both Android and iOS platforms. One example is the Argus application by Azumio or another commercially available Smartphone application with similar features, which can track the number of steps taken. Participants will be asked to carry their phone on their person (can be in a bag or pocket) during the day to enable activity tracking.

The Argus application (http://www.azumio.com/s/argus/index.html) and other Azumio applications have been included in multiple NIH-funded studies, including the Big Data to Knowledge (BD2K) at Stanford University Mobilize Center (http://mobilize.stanford.edu/), and has shown feasibility as a compatible and safe method for collecting data in their clinical trials. We also may use wrist-worn devices offered by MD2K, which is a NIH-funded national initiative to use mobile sensor data in clinical trials (https://md2k.org/). Recognizing the rapid changes in the consumer market, we hope to keep flexibility in the activity tracking app used; Argus currently stands as a good example, and we will notify the IRB if we choose an app that is substantially different in function or safety profile.

Activity Monitoring Duration: 2 minutes daily

Wristband Activity Tracker: During feasibility testing, we will assess the utility of wristband trackers. If feasible and appropriate for the study, the principal investigator may decide for all participants to also be given a wristband activity tracker to wear on the wrist each day. We are considering use of one of several types of wristbands: Fitbit, Moov, Jawbone, Withings, MD2K Cerebrum, or Garmin Vivosmart. Recognizing the rapid changes in the consumer market, these are examples of what we may use and are listed here for flexibility of choice. Study staff will notify the IRB if we choose a wristband tracker that is substantially different in function or safety profile. Participants will be given instructions on how to wear, charge, and sync their wristband tracker. Data will be collected, stored, and extracted using a coded Participant ID. The participant will need to return the wristband in working condition to the study team upon completion of the study in order to receive final reimbursement. For information about confidentiality related to use of the wristband, please refer to section D.1a: Protection of Subject Privacy.

Food, Activity, and Sleep Tracking (FAST) Questionnaire: Participants will be asked to fill out a daily questionnaire about their food, activity, and sleep tracking. The survey is adapted from the Automated Self-Administered 24-Hour Dietary Assessment Tool (ASA24) and the National Sleep Foundation Sleep Diary.

The ASA24 was released in 2009 by the NIH and the National Cancer Institute as a web-based tool that enables multiple, automatically coded, self-administered 24-hour recalls. This tool was designed for use by research participants, clinicians, patients, and students. The ASA24 asks detailed questions about food form, preparation, portion size, and additions using an extensive branching logic database. The ASA24 was designed to be culturally sensitive and accessible by individuals using assistive technologies. Features of the ASA24 respondent website can be found here (https://epi.grants.cancer.gov/asa24/respondent/features.html). A demo version of the respondent site can be found here (https://asa24.nci.nih.gov/demo/).

The FAST Questionnaire asks participants what time they went to bed, what time they got out of bed, the total hours slept, any naps taken during the day, then about the timing and amount of alcoholic and caffeinated drink consumption. It also asks if they exercised throughout the day and then further asks how long they performed each type of exercise.

The food tracking portion asks subjects what main meals they ate in a day. For each main meal, subjects are asked how fast they ate, what they were doing while they ate, what food groups were included in their meals, and how much they ate. It also asks subjects if they ate any food outside of their main meals, and then asks how many times they eat each type of food.

Duration: 10 minutes.

Action Plan Creation – Participants in the **concurrent cohort** of the HEART pilot study will fill out the Action Plan Worksheet, the APA-10, and the APIS-5 as regularly scheduled for the main MINDFUL-PC study. Participants in the **alumni cohort** of the HEART study will fill out the Action Plan Worksheet and the APA-10 at the end of HEART study Week 3. They will fill out the APIS-5 at the end of HEART study Weeks 4 and 5.

Action Plan Creation Duration: 20 minutes

Action Plan Initiation Survey Duration: 5 minutes

Behavioral Tasks

Participants will be asked to complete the Behavioral Tasks component during an in-person behavioral tasks session that takes place prior to Week 1 of the MINDFUL-PC study and then again between Weeks 8 and 9. This behavioral tasks session will be scheduled during the orientation session to the MINDFUL-PC and HEART studies. During this behavioral tasks session, participants will first download any required smartphone applications for activity tracking with the guidance of a research study staff member. Then, they will complete three behavioral tasks in the following order: the Heartbeat Detection Task (HBDT), 5-Trial Adjusting Delay Hypothetical Discounting Task (HDT), and Sustained Attention to Response Task (SART). Each task is described in brief below. Each task is described in further detail below:

Heartbeat Detection Task (HBDT) [Total time: 10 minutes]: Participants are asked to count their heartbeat during three varying time intervals (30s, 30s, 60s). In parallel, individuals' heart-rate will be measured by Kardia Mobile technology. Participants will place their index and middle fingers of both hands on top of the Kardia Mobile device and will be instructed to count their heartbeat for a period of 30 or 60 seconds. Participants will place their hands on top of the Kardia Mobile devices and then will be given instructions on how to count their heartbeat (e.g. *"We will have you complete this task three times at varying time intervals. When I say 'begin' I want you to try your best to detect and count your heart beat. When I say 'stop' please let me know how many times you think your heart beat during the time interval. Try your best.").* The readings from this device are linked to the Kardia Mobile App, which will be on a screen faced away from the participant[1]. Participant data stored in the Kardia Mobile app will be identified with the HEART Study participant ID, which will not be linked to any identifying information. The Kardia Mobile app will be installed onto an iPad that is kept within the research office. Data from the Kardia mobile app will be wirelesswritten down by hand on a handout that is filed in the study binder and then entered by a study staff member into the secure CHA REDCap database once the behavioral tasks session has been completed.

Figure 1: Kardia Mobile device and interface. Participants place two fingers on either side of the Kardia Mobile Device, which will then produce a live reading of their EKG** (Image taken from alivecor.com)[1].

****Although Kardia Mobile can be used as an FDA-approved EKG**, in this study, we will not be conducting analysis on participants' heart rhythms and will not be able to determine whether a participant's heartbeat rhythm is irregular. This task does not, in any way, serve as a diagnostic test for heart disease or heart rhythm abnormalities. If the reading does register any heartrate abnormalities, such as arrhythmia, we will not inform the participant of the readings as the research staff are not trained to deliver healthcare related information. We will also not document any information about abnormalities in the database. Only heartrate will be measured. This will be clearly stated in the consent form.

5-Trial Adjusting Delay Hypothetical Discounting Task (HDT) [Total time: 5 minutes]. This is a brief delay discounting task performed on a computer that assesses an individual's impulsivity by presenting a series of 5 discrete choice questions between some amount of a delayed commodity (in this case, dollars) and half that amount available immediately (e.g. "Gain $1000 in 3 weeks or gain $500 now"). Individuals choose whether they would rather receive a smaller amount of money now, or a larger amount in the future This task will be run using a Python script on a designated research study laptop which will be password-secured and stored in a double-locked cabinet in the CMC research office, only accessible by approved study staff. Participants will be identified by their HEART study Participant ID, and data will be transferred from this laptop to a CHA-secure research drive using secure CHA wireless[2, 3].

Sustained Attention to Response Task (SART) [Total time: 25 minutes]. Participants will complete a series of computerized tests focused on sustained attention, response inhibition, and self-regulation. They are asked to press a key in response to rapidly displayed integers (1-9) and withhold a response to a designated "no-go" integer. This task will be run using E-Prime software on the password-protected study laptop. Participants will be identified using their HEART study Participant ID and data will be transferred to a CHA-secure research drive using secure CHA wireless[4].

These tasks will all be conducted in a quiet, closed, and gently lit room located at the Center for Mindfulness & Compassion (26 Central St, Somerville, MA 02143). Participants will sit on a chair with their feet flat on the floor, forearms on the table, and with the computer screen in front of them. The research staff member will explain each task to the participant before conducting the trial, and will provide a one-minute break between each task.

C.3.f.8. Provider Resilience Battery for PCP Participants:

The **Maslach Burnout Inventory (MBI)** [61] is the primary scale for assessing burnout. This study will use the original measure, MBI-Human Services Survey, a 22-item scale created for professionals in the human services. This scale examines the perspective with which professionals view their occupation and the people they work with. Items are rated on a 7-point Likert scale from 0 (*never*) to 6 (*every day*). An example item is: "I worry that this job is hardening me emotionally." The survey contains subscales for examining the factors of emotional exhaustion, depersonalization, and personal accomplishment. Scores are summed for each subscale, and indicate high, moderate, or low levels of the subscale factor (for example, high emotional exhaustion). Scores are usually reported as an average rating for each subscale, rather than a total score. Duration: 4 min.

The 31-item **Workplace Wellbeing Scale (WWS)** [62] measures workplace satisfaction and can be used to compare data across various categories such as gender and occupational level. Items on this scale are evaluated as four subscales: work satisfaction, organizational respect for the employee, employer care, and intrusion of work into private life. Summed items for each subscale generate a numerical score that corresponds to low, medium, or high levels of each subscale (for example, low employer care is indicated by a score between 0-7 for the employer care subscale). The WWS includes questions such as "Does your work eat into your private life?" Each item is scored on a 5-point Likert scale from 0 (*Not at all*) to 4 (*Extremely*). Positive questions are reverse scored. Duration: 4 min.

The **Jefferson Scale of Empathy (JSE)** [63] is a 20-item scale that evaluates self-reported empathy among health care professionals. This study will make use of the JSE HP-version for practicing health care professionals. Items are scored on a 7-point Likert scale from 1 (*Strongly Disagree*) to 7 (*Strongly Agree*). An example item includes "I try to imagine myself in my patients' shoes when providing care to them." Duration: 5 min.

C.3.f.9. Weekly Mindfulness Practice Diary Card:

The **Weekly Mindfulness Practice Diary Card** will be completed for the week preceding its administration. Carmody et al. [64] emphasizes that improvements in mindfulness, symptoms, and wellbeing are significantly related to formal and informal mindfulness practice. This card asks participants to specify the type and duration of formal mindfulness techniques they completed each day for the past week, as well as the type and frequency of informal techniques each day. Formal mindfulness techniques include body scan, sitting meditation, loving kindness, and informal mindfulness practices include techniques like connecting with breath and mindful awareness of eating. A participant's total practice for the week will be calculated by study personnel, based on the information on the diary card that will collected by group leaders weekly. This will also be completed by all patient participants, despite their group assignment, during the Post-Treatment Survey Session at patient study week 8, as well as during the Follow-up Survey Session, at patient study week 36. Participants in the MTPC group will fill out the practice diary on a scantron sheet, and participants in the control group will fill out the practice diary on an online REDCap form. Duration: 6 min.

This card will be completed each week by PCP participants in Group 1 for study weeks 1-8, the mid-study survey session, Mindful Communication months 1-10, and the post-study survey session. PCP participants in Group 2 will complete this card for the week preceding the mid-study survey session and the week preceding the post-study survey session.

Patient participants in the MTPC Group and in the Waitlist Group will complete the mindfulness practice diary card every week for patient study weeks 1-8, throughout their MTPC training. Both groups of patient participants will complete this card for the week preceding the post-treatment survey session and the week preceding the follow-up survey session. Participants in the **concurrent cohort** of the HEART pilot study will also complete this survey for 1 week prior to MTPC Session 1 and for four weeks during MINDFUL-PC study weeks 5 and 9.

C.3.f.10. Mindfulness Resources Use Survey:

The **Mindfulness Resources Use Survey** is a 7-item weekly survey that asks about the frequency of use of community or mobile mindfulness resources as listed on the Community Resources handout given to all patients during the orientation session. This survey asks patients whether they have visited local mindfulness or meditation centers in person, whether they have used mindfulness guided recordings or apps online, and whether they have read any mindfulness-related books. It also asked about some related activities where people often practice mindfulness such as yoga, spiritual activities, and places of worship. A patient's total mindfulness resource utilization will be calculated by study personnel weekly. This survey will be completed by every study participant for Study weeks 1-8, and during the Follow-Up Survey Session at patient study week 36. Participants in the MTPC group will fill out the resources diary on a scantron sheet, and participants in the control group will fill out the resources diary on an online REDCap form. Participants in the **concurrent cohort** of the HEART pilot study will also complete this survey for 1 week prior to MTPC Session 1 and for four weeks during MINDFUL-PC study weeks 5 through 9. Duration: 5 min.

C.3.f.11. Reports from Electronic Medical Records for Patient Participants:

The **Physician Quality Reporting System (PQRS)** [65] is used by Center for Medicare and Medicaid Services to provide incentive payments that are dependent on quality measures in health care. This list includes several community and behavioral health outcomes for PCPs to complete and document. Patient electronic medical records reports will be generated on a monthly basis by the executive office of the Chief Quality Officer at CHA for several specific data points for all patients for the month that they enter the study and again at one year after entrance into the study. The PQRS variables include documentation of patient alcohol use, body mass index (BMI), patient health questionnaire (PHQ-2), HgAlc, LDL-C, smoking cessation attempts, cigarettes per day, frequency of meat eating, blood pressure, risky sexual behaviors, quantity of prescribed opioids and sedatives, and illicit drug use. If the research personnel cannot find patient health outcome values for the previous year, they will contact the patient's primary care provider via EPIC to encourage the provider to document the current relevant PQRS quality variables into the medical record prior to the start of the patient's participation in the study. After study week 18, study staff will again send an EPIC note to flag PCPs to remind them about entering their patients' upcoming annual health quality variables into EPIC, which will be assessed around week 26. Patients who were on the waitlist will be requested to have an appointment at PCP office to get PQRS data documented prior to return to study for new group orientation.

Patient responses to the **Patient Health Questionnaire-2 (PHQ-2)** during the course of standard primary care and the number of current psychotropic medications prescribed will be downloaded to the research database from EPIC on a yearly basis for up to 3 years after the start of the study

in order to assess for longitudinal effects on depressive mood and psychiatric symptoms among each group.

Number of medical visits will be collected though EPIC for each patient for the year before and the six months after randomization. This will include a record of the number of visits with the patient's PCP, the number of outpatient medical visits, the number of inpatient medical stays, and the number of visits to the emergency department (ED). Chronic disease self-management programs have been shown to reduce patient visits to the ED [39]. In order to account for effects of recent health issues and seasonality, ED visits from the past six months and the 7-12 month period prior to study entry will both be used as covariates in the analysis.

Patient no-show rates will also be collected through EPIC as frequency counts from the year before and the six months after randomization. Programs emphasizing patient activation and empowerment have been shown to increase attendance to scheduled patient visits [66].In order to account for effects of recent health issues and seasonality, attendance rates from the past six months and the 7-12 month period prior to study entry will both be used as covariates in the analysis.

Patient action plans, created by patients and providers at the PCP visit and reported in EPIC, will be reviewed and collected through EPIC. Goal-setting exercises can be used to support chronic illness management [67]. Using these data, a member of the MINDFUL-PC research study team will compile a coded list of patients and their action plan goals.

C.3.f.12. Satisfaction Battery for Patient Participants:

Patient participants will complete the **MTPC Program Satisfaction Survey** after 8 weeks of participation in the study. This 18-item survey contains two parts. First is a series of 12 questions scored on a 5-point Likert scale from 1 (*Strongly Disagree/Poor*) to 5 (*Strongly Agree/Excellent*), with statements such as "I found this program helpful." Next is a series of six open-ended questions in which patients enter a written response to statements including "The most important thing I learned during this program." Duration: 5 min.

C.3.f.13. Adverse Events Reporting Battery for Patients:

The **Adverse Event Patient Participant Self-Report Form** will be completed at the 8-week survey session and 6-month survey sessions. This form asks that parameters be described for each AE. The parameters are detailed below in D.2.

C.3.f.14. Experimental fMRI pilot study screening battery:

We will phone screen interested MINDFUL-PC group participants for fMRI eligibility, using an fMRI screening phone interview, including items from the **Edinburgh Handedness Inventory** (EHI) [61]. This is a 10-item standard measurement scale used to assess the dominance of a person's right or left hand in everyday activities. Left-handers have less lateralization of brain function and can confound fMRI studies.

Further eligibility questions are based on the Martinos Center Patient Screening Form. Questions are related to metal implants, pacemakers, aneurism clips and other implants and stimulators that might be unsafe for scanning. The form will also ask about pregnancy and breastfeeding, past severe head trauma, claustrophobia or other conditions that might exclude them from participating in the fMRI study. We will also screen for vascular disease in the legs, such as

peripheral vascular disease, lymphedema, and varicose veins, in order to exclude those for whom the cuff pain task may not be safe. The fMRI screening form will be assessed during the phone call. The duration of the phone screening is 10 minutes total. The Martinos Center Screening Form will be acquired again before each scan session, and this will take 3-5 minutes.

We will conduct **saliva toxicology** for alcohol and illicit drugs at the Martinos Center before each MRI session. Duration 5 min.

In case a woman is not on contraception and has doubts about current pregnancy status, she will be given the option to conduct a **urine pregnancy screen** before each MRI session. Duration 5 min.

We will conduct fMRI neuroimaging before and after the MTPC group. Each session will also include autonomic monitoring of heart rate, breathing rate, and skin conductance. Duration 90 min.

fMRI questionnaire: Patients who undergo fMRI neuroimaging will be asked to complete a set of fMRI questions that ask about fatigue, concentration, and presence of pain before and after the pain cuff task (Duration: 5min).

C.3.g. Instructor Experience, Fidelity, and Supervision:

We have developed a detailed plan for training, monitoring and supervising staff that will deliver the intensive behavioral training interventions, as well as for maintaining adherence to protocol.

All MTPC groups will be conducted by clinicians with at least a master's degree and successful completion of the MTPC training program (described below in section C.4.) Participant-observers will be CHA primary care staff, CHA mental health clinicians, CHA mental health care partners, or CHA trainees. MTPC groups, MTPC group leaders, and MTPC participant-observers will be supervised by the CMC clinical medical director (Todd Griswold, MD), and the intervention fidelity will be reviewed by the principal investigator (Zev Schuman-Olivier, MD) and expert MBSR teacher trainers, Zayda Vallejo and Elana Rosenbaum. Group Leaders will be invited to participate in weekly group supervision by web conferencing with Zayda and Elana while they are leading groups. MTPC sessions will be audio-recorded in order to rate fidelity (measured as competence and adherence) to the manual, as well as to provide feedback to MTPC Group Leaders to prevent therapist drift. At the end of each MTPC session, group leaders will fill out a survey of content covered in each MTPC session, rating each other for coverage of content. Group Leaders will review these surveys during supervision. A treatment satisfaction survey will be given at the end of group session #8 to assess for patient impressions of the treatment experience and the group leader's qualities, and these will be reviewed by the Research Coordinator and project manager after the end of each group. If a group leader has below average scores, then the principal investigator will be notified in order to take appropriate corrective measures.

C.3.h. Participant Withdrawal/Termination Criteria:
Withdrawal/Termination criteria for Patient Participants:
Participants may be discontinued from study treatment and assessments at any time. Specific reasons for discontinuing a patient participant from this study are:

1. Voluntary discontinuation by the participant who is at any time free to discontinue his or her participation in the study, without prejudice to further treatment
2. Safety reasons as judged by the investigator
3. Severe non-compliance to protocol as judged by the investigator
4. Incorrect enrollment (i.e., the participant does not meet the required inclusion/exclusion criteria) of the participant
5. Participant lost to follow-up
6. Revealing private information about the study
7. Active substance use disorder or intoxication during study procedures
8. English proficiency below a 7th grade reading level

Withdrawal/Termination criteria for PCP Participants:
Participants may be discontinued from study treatment and assessments at any time. Specific reasons for discontinuing a PCP participant from this study are:
1. Voluntary discontinuation by the participant who is at any time free to discontinue his or her participation in the study, without effect on the relationship with CHA
2. Safety reasons as judged by the investigator
3. Severe non-compliance to protocol as judged by the investigator
4. Incorrect enrollment (i.e., the participant does not meet the required inclusion/exclusion criteria) of the participant
5. Participant lost to follow-up
6. Revealing private information about the study
7. Active substance use disorder or intoxication during study procedures
8. PCP withdraws from practice at a CHA PCMH

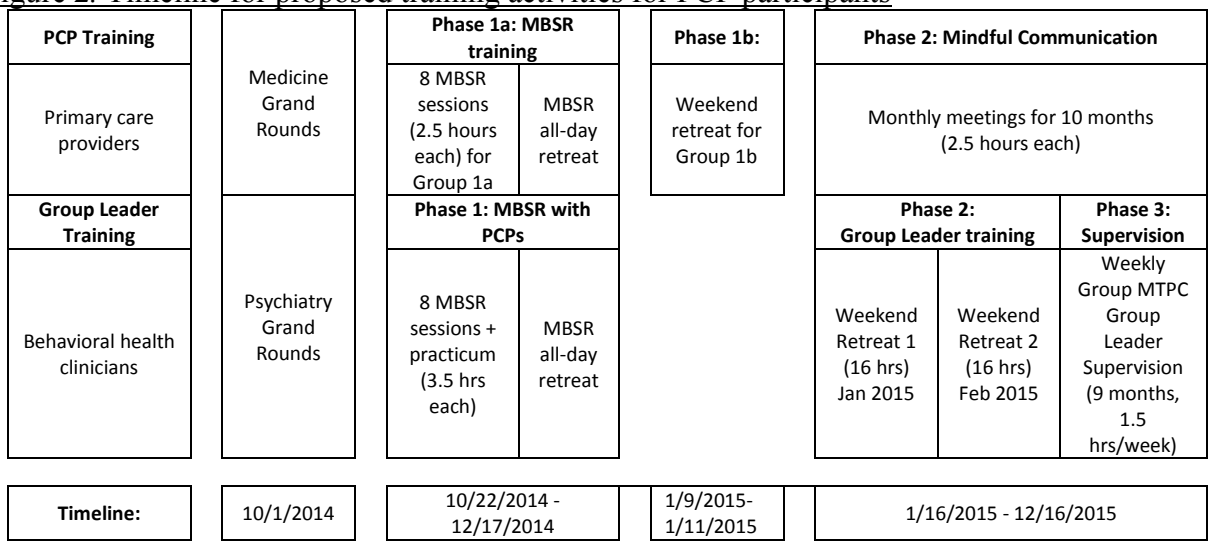
Participants who discontinue will be asked about the reason(s) for their discontinuation and the presence of any adverse events. If possible, they will be seen and assessed by the Principal Investigator. Serious and Unexpected Adverse events will be followed up.

If participants enrolled in MTPC groups are terminated from group treatment for any reason (except incorrect enrollment or safety concerns that endanger the study team), then they will still be expected to complete their outcome assessments, unless the participant revokes informed consent.

C.4. Implementation plan:

C.4.a. MTPC Group Leader Training (*See Figure 2 below*):
As explained above, this study with 2 x 2 factorial design involves both PCPs and patients as study participants. In addition, CHA behavioral health specialists will receive training during the course of this study to become MTPC group leaders who will provide MTPC groups for patient participants. PCMH behavioral health specialists will concurrently attend the 2.5-hr MBSR group with PCPs (Group 1a), and will also attend an additional 30-60 minute long educational practicum each week. After the conclusion of the 8-week MBSR course, behavioral health specialists will receive an additional 32 hours of training over two weekends to become staff MTPC group leaders. For the first year following their certification, these MTPC group leaders will receive weekly group supervision led by senior mindfulness teachers with supervision from the medical director of the Center for Mindfulness and Compassion who is a board-certified psychiatrist.

Figure 2. Timeline for proposed training activities for PCP participants



C.4.b. Current Implementation Staging Map:

Each primary care region will be assigned a hub based on space and staffing considerations. During training, primary care provider champions and behavioral care leaders will be identified within each regional primary care region to support recruitment and implementation at sites in their region. This program aims to begin patient enrollment in September 2015 at 2 regional hub primary care centers with groups starting around October 2015. After this first round of groups are completed, we will review the process to evaluate for improvements prior to a second round of groups. Additional health center group space will likely become available in late 2015 to add two additional centers as group sites, as well as the potential use of CHA hospital group rooms to provide MTPC groups, bringing the total to 6 PCMHs with on-site groups. We will begin recruitment for groups that meet the needs of cultural and linguistically diverse communities with several different groups for LEP patients starting in late 2016. We plan to offer MTPC groups in Spanish and Portuguese by early Fall 2016. Planning for a third implementation step will await development of space and a further roll-out in integration of mental health into the patient-centered medical homes in order to expand to the full set of sites.

The PCMHs included in the project will be: Cambridge [Cambridge Family Health, Cambridge Family Health North, East Cambridge Health Center, Windsor Street Health Center], Somerville [Broadway Health Center, Union Square Family Health, and Somerville Hospital Primary Care], MCREW [Everett Family Health Center, Revere Family Health Center, Malden Family Medicine Center]. Hub centers for the initial rollout are noted with asterisks. All implementation plans are still in flux and represent our best estimation for the implementation; however, decisions will continue to be made in ongoing collaboration with Lynn Budlong, VP for ambulatory operations and primary care, as well as the team leading the primary care behavioral health integration (including Christine Claypool, Emily Benedetto, Colleen O'Brien, and Bob Joseph).

Table 4. MTPC Implementation Schedule

Location	Estimated Start Month

First PCMH Step (Somerville Hospital Primary Care and Malden Family Medicine Center)	October 2015
Second PCMH Step (2-4 additional Centers)	June 2016
MTPC Groups in Portuguese and Spanish	September 2016
Third PCMH Step (3 Final Centers) (And continuing to add language-specific patient groups)	Awaiting development of space and roll-out of mental health integration into primary care

C.5. Data management and analysis:

C.5.a. Data management:

Research data will be obtained expressly for research purposes and will be in the form of responses to questionnaires and assessment tools. Signed informed consent forms, and informed consent assessments will be stored in a double-locked filing cabinet at the Center for Mindfulness and Compassion. Only IRB approved research team members will have access to this filing cabinet. All other study data will be collected and managed using REDCap electronic data capture tools hosted at The Cambridge Health Alliance [68]. REDCap (Research Electronic Data Capture) is a secure, HIPAA compliant, web-based application designed to support data capture for research studies. This platform provides the following elements: 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources. The REDCap software was developed by Vanderbilt University and has been obtained and installed for usage at the Cambridge Health Alliance.

Patient level and clinician level data for this study will be stored electronically in the REDCap platform. Only IRB approved research team members will have access to the REDCap data platform. Each team member will be granted access to the REDCap data system through a secure login.

C.5.b. Data Analysis:

We will use SAS 9.3 to conduct analyses for each of the specific goals or hypotheses associated with the study's primary aims:

1. *Implementation Goal*: Our implementation goals are a) to implement at least two MTPC groups in at least 8 CHA primary care sites within two years, b) to train at least 25 Primary care providers in Mindful Communication, c) to enroll a socioeconomically-diverse population of patients, and d) to enroll a culturally-diverse population of patients with at least 30% of patients completing the program being non-Caucasian or having a primary language other than English.

We will examine descriptive statistics for each of the stated implementation goals.

2. *PCP-Patient Relationship Hypothesis*: We hypothesize greater satisfaction with the PCP-patient relationship among patients with the combination of provider and patient mindfulness training compared with only one or neither training types.

Mixed Effects Modeling to evaluate for main effects of PCP mindfulness training and main effects of Patient training level (1 hour vs. 8 week) for each survey, as well as the interaction effect with relevant covariates.

3. *Health Outcomes Hypotheses*: We hypothesize reductions in depression, anxiety and stress as a main effect of MTPC. Finally, we hypothesize reductions in use of medications prescribed for symptom reduction (benzodiazepines, opioids, etc.), overall improvement in markers of health maintenance and chronic illness management (i.e. PQRS data). We hypothesize the highest levels of initiation and maintenance of self-management action plans among MTPC group with Mindfulness-trained providers.

Mixed Effects Modeling to evaluate for main effects of PCP mindfulness training, main effects of Patient training level (1 hour vs. 8 week) for each outcome, as well as the interaction effect with relevant covariates.

4. *Provider Resilience Hypothesis*: We hypothesize greater workplace well-being, reduced experience of burnout, and increased resiliency among providers as a main effect of provider MBSR + Mindful Communication training.

We will use Mixed Effects Modeling to evaluate for main effects of PCP mindfulness training and time for each survey and the interaction of the two.

5. Medical Regimen Adherence Hypotheses: We hypothesize a main effect of MTPC group status on levels of initiation and maintenance of medical regimen health behavior change, as measured by the APIS-5 self-report score. The highest levels will be demonstrated among the MTPC group participants with mindfulness-trained providers. We hypothesize that total formal mindfulness practice, post-study total mindfulness score, baseline mindful non-judgment score, and self-compassion will be associated with successful initiation and maintenance of action plans. Action plan initiation will be validated by increases in step count, and increases in number of active periods, changes in sleep, changes in mindfulness practice, and changes in nutritional habits.

Using an intent-to-treat analysis, we will use logistic regression and Mixed Effects Modeling to evaluate for main effects of MTPC, mindfulness-trained PCPS, and the interaction of the two on binary and continuous ratings of level of action plan initiation and maintenance. We will conduct exploratory linear regression models of post-study mindfulness and self-compassion and overall practice dose as independent variables with level of action plan initiation and maintenance as dependent variables.

The experimental fMRI pilot analyses methods are described below.

6. Self-Regulation Mechanisms Hypotheses: In 4 different fMRI tasks, we hypothesize (a) greater activation of ACC and OFC and decreased activation in the amygdala/hippocampus after MTPC intervention compared to before intervention (i.e, a pre/post increase) in an emotional Go/NoGo inhibitory control task, as in Perez 2016 [69], using validated emotional pictures (International Affective Pictures System, IAPS, [70]).The task includes 448 IAPS pictures (50% neutral and 50% unpleasant), which will

be presented briefly (1.5 seconds), while participants either react (Go) or withold a button press reaction (NoGo), depending on abstract symbols presented on top of the pictures; (b) greater activation of mid-posterior insula after (compared to before) MTPC in a self-compassion task (that contrasts a self-reassurance condition with a self-criticism condition), as in Longe 2010 [71]; (c) greater insula activation during an interoceptive attention task (that contrasts an interoceptive attention condition with an exteroceptive attention condition) as in Farb 2013[72], and d) increases in the rostral ACC (rACC) and ventromedial prefrontal cortex (vmPFC) during the **anticipation of pain** after compared to before MTPC and increased activation in the lateral prefrontal cortex (LPFC) and somatosensory areas **during pain** after compared to before the MTPC, as in Kim 2013 [73]. We hypothesize that all inhibitory control and interoceptive targets will be associated with higher levels of initiation of regimen adherence, while self-compassion, emotion/pain regulation, and interoceptive targets will be associated with higher levels of regimen maintenance.

We will follow current recommended methods for fMRI data analysis [74,75], especially in the case of longitudinal data [76-82]. Our approach is based on a priori regions-of-interest (ROI), a method more statistically powerful than whole-brain analyses since it limits the number of statistical tests to the voxels included in the ROI and thereby reduces Type I errors [83, 84]. Another advantage of using a ROI-based approach is that it enables precise spatial correspondence of the region of interest across subjects, since it does not involve normalizing different brains to a common atlas [87]. In this study, our ROIs are the following: OFC and amygdala/hippocampus (in the emotional Go/NoGo task), the mid-to-posterior section of the insula (in the self-compassion task, and emotion/pain regulation task), the anterior insula (in the interoceptive attention task) the DLPFC and rACC/vmPFC in the emotion/pain regulation task and Go/NoGo task.

The fMRI data will be analyzed using the following standard software packages: FSL [85, 86], FreeSurfer [87-90], AFNI [91, 92], and RETROICOR [93] for retrospective correction of physiological motion artifacts using our peripheral measures of cardiac and respiratory activity as independent assessments of physiological noise in the blood oxygen level-dependent (BOLD) signal. Following standard preprocessing steps (de-warping, slice timing correction, motion correction, removal of physiological noise signals), the statistical analysis of brain activation data will be performed using a linear mixed effects (LME) model, following recent recommendations for longitudinal fMRI analysis [76, 79, 80]. This approach is implemented in the AFNI software package with the group analysis program 3dLME [80]. This program will be used to solve the LME system (via built-in optimization procedures) and test our hypotheses. Of note, the LME approach is more general than the commonly-used General Linear Model (GLM), AN(C)OVA, regression, and t-tests, while including those as special cases. The LME approach is recommended for longitudinal fMRI data analysis because it includes in the model the covariance structure of serial measurements performed in the same subject, whereas the commonly-used GLM model assumes that there is no such correlation, which is incorrect in the case of longitudinal data [80]. In addition, the LME framework can offer superior statistical power in detecting longitudinal group differences [79, 80].

Self-Regulation hypothesis testing for the fMRI data will be performed as follows. For each of the 4 fMRI tasks, we will use a Linear Mixed Effects model of the BOLD signal in the ROIs associated with that task (described above), with 2 time points (pre- and post-intervention). The

model will include the following regressors of interest: gender, age, and the following pre-intervention scores: depression (PROMIS-DSF), anxiety (PROMIS-ASF), self-compassion (SCS-SF), and mindfulness (FFMQ); and the following regressors of no interest: head motion parameters and cardiac and respiratory components of physiological noise. Hypothesis will be expressed as: Is there any significant difference between the 2 time points in the task-specific ROI activation during a) NoGo trials versus Go trials, b) self-reassurance versus self-criticism, c) Interoception-versus-Exteroception, and d) expectation of pain and pain versus rest. The null hypothesis will be that the ROI activation at the 2 time points are not significantly different. Significance testing will be done using permutation/bootstrapping methods (see [79, 80]).

1. HEART pilot study analysis plan: The HEART pilot study aims to recruit 40 participants in the **alumni cohort** and 30 participants (10-20 in the waitlist arm and 20-40 in the intervention arm) in the **concurrent cohort** for a total of 70 participants. The data would be examined for correlations between the action plan initiation 7-item survey and pre-post differences in step count, the number of active periods, changes in sleep duration, changes in mindfulness practice, and change in nutritional habits depending on which action plan goal was specified in the patient action plan. We will also examine the percentage of action plan initiation events $\geq$5 on the APIS-5 that have a corresponding behavioral change evidenced in the daily data collection. Finally, we will also examine whether the activity changes are greater in the participants who selected exercise as compared to those who selected nutrition or dietary changes and vice versa.

C.5.c. Sample Size calculations:
Using an intent-to-treat analysis with 290 patients receiving mindfulness training and 144 patients with orientation only, there will be an 80% chance of detecting a significant difference at a two-sided 0.05 significance level. This assumes that the rate of action plan initiation is 0.54 in orientation only (based on Guck et. al. [70]) and the rate of action plan initiation among patients who receive mindfulness training is 0.68 (based on rates of initiation and maintenance of meditation practice in previous pilot MBIs [94]). After the first twenty participants complete the program, an interim analysis of these pilot data may be used to refine the sample size calculation for RCT.

D. Human Subjects Procedures and Confidentiality

D.1. Confidentiality:

D.1.a. Protection of Subject Privacy:
All of the materials collected are for research purposes only, and data will be kept in strict confidence. No information will be given to anyone without permission from the subject. Confidentiality will be ensured by use of identification codes. All data will be identified with a unique numeric identification code and an acrostic that are unique to the subject. Any data collected before a participant discontinues the study is available for use in this research project.

All research session data will be collected using standardized electronic forms on designed using the REDCap database hosted by Cambridge Health Alliance. REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing an intuitive interface for validated data entry and export procedures to common statistical packages. All data management will be conducted by the research team operating

from CHA. All data collection will take place under the supervision of the Dr. Schuman-Olivier and the Data Manager. Data will only be collected by members of the research team.

The name, birthday, and MRN will be entered into an initial REDCap database strictly for the purpose of screening and consent process. The list linking any personal identifying information with the participant's study number and acrostic will be kept in a encrypted computer file on a confidential shared drive. A unique numeric identifier and acrostic will be created for all participants who have completed an informed consent and this list will be kept in a password-protected file by the principal investigator. All data will be linked to these identifiers and no direct patient identifiers will be transmitted from REDCap to SAS 9.3 for analysis.

All further study data from survey sessions will be collected in a second REDCap database, which will reference this unique numeric identifier and acrostic. MTPC home practice data will be recorded on scantron forms, which will be scanned into a password-protected, secure Excel database.

Through collaboration with the CHA Quality Office and CHA information technology, we will generate medical record reports for participants who are in our study and this information will remain protected within the CHA system, and will not include any study data except name, MRN, and birthday.

fMRI data will be collected using the same unique numeric identifier and acrostic used for the MINDFUL-PC study, and will be maintained on a secure database server at the collaborating neuroimaging site (Martinos Center). Thus, only coded data will be stored on the database of the collaborating site. fMRI data analysis will take place at the Martinos Center. The exception is the addition of the patient's year of birth to the fMRI data. This is necessary in case a radiologist has to review the brain scans for potential incidental findings (compare https://www.nmr.mgh.harvard.edu/martinos/userInfo/safety/training_manual_082305.pdf). fMRI data analysis will require controlling for certain values, which will have been collected during the main study assessment visits (i.e., gender, age, pre-intervention levels of depression, anxiety, self-compassion, and mindfulness). Further, behavioral intervention results (e.g. initiation of regimen adherence and regimen maintenance) will be correlated with activation in hypothesized brain regions. These analyses don't require a full integration of fMRI data with the study file. The relevant data from the main study file will be communicated via REDCap between the two institutions, and the data will be integrated, using the MINDFUL-PC unique numeric identifier and acrostic. Data from the drug screenings and pregnancy test will not be added to participants' health records, and will only be retained in the participants' research records (REDCap database with unique numeric identifier and acrostic). We will apply for a Certificate of Confidentiality with the NIH to protect this data from being disclosed in any civil, criminal, administrative, legislative or other proceeding.

HEART pilot study data will be collected using a Participant ID (numeric identifier and acrostic) that is unique to the HEART pilot study. This Participant ID will be used for all smartphone applications and any other data tracking related to the HEART pilot study. The linking document specifying the link between the Participant ID and the identities of the participants will be kept confidential and will be stored in a password-protected file on a secure CHA drive, only accessible by IRB-approved study staff.

Because the data collected from the Argus app is not relating to sensitive information such as illegal activity or addiction, we determined it is not necessary to require secure Wi-Fi options for participants throughout the study. However, we will inform participants about the risks of using unsecure Wi-Fi and encourage them to use only secure Wi-Fi while using the smartphone app.

The study staff will notify the IRB if there is a need to have communication with the device or application manufacturers. While all smartphones have GPS capability, the research team will not be accessing any information related to current patient location that can be accessed through the GPS data. Similarly, while the photo function will be used to take pictures of food, the research team and the smartphone application will not be accessing any photos in the participant's photo album. The orientation protocol will show participants how to disable the smartphone's application's access to GPS, the participant's photo album, and to manage updates and push notifications. The study team will limit its use of data to only specified data points as outlined in the HEART study survey battery.

Data collected from the Kardia Mobile App will be written down by hand on a handout that is filed in the study binder which is locked in a double-locked cabinet and then entered into the secure CHA REDCap database by a member of the study staff.

Each participant will be given a HEART-study-specific study number, which will be used as an identifier in the Kardia Mobile app, the SART task, and the hypothetical discounting task (HDT). Therefore, the software developers will not have access to any identifiable data about any of the participants.

The SART task and HDT task will be done on a study laptop that is password secured and kept in a double-locked cabinet in the research office, accessible only by staff who have been IRB approved on the study. The data collected will be kept in an additional password protected file during retrieval and then transferred to a secure CHA drive after each study session is complete.

D.1.b. Database Protection:

Subject informed consent, screening forms, scantron sheets, and MTPC course documents will be stored in locked file cabinets within a locked office at Cambridge Health Alliance.

The REDCap electronic database will be secured with password protection on secure CHA servers. Data analysts will receive only coded information that is entered into the database under those identification numbers.

The data associated with the smartphone application, wristband tracker, and online surveys of the HEART pilot study will be stored only using the HEART study Participant ID in password-protected files saved on a secure CHA drive, or on the secure REDCap database. These coded data will be accessible to the associated smartphone application and wristband manufacturers, but these data will not be linked to participant identities. These data will be linked to the unique Participant ID and will not contain any identifying information.

Access to identifiable data will be limited to researchers directly involved in the study. All identifiable data will be destroyed 5 years after study completion and will not be maintained for future uses not specified in this research plan.

D.1.c. Minimization:
The risk of loss of confidentiality is judged to be minimal. Confidentiality will be maintained by numerically coding all data, disguising identifying information, and by keeping all data in the secure REDCap application. Any coded or de-identified data will be maintained in password-protected databases. Subject information will be accessible only to study staff. Information about study participants will not leave our institution in any form that would identify individual subjects. Data will be transmitted to SAS in a pooled form with subjects identified only by numeric code and acrostic. In addition, we will ask group participants to agree to a group confidentiality agreement. This agreement would require that information shared within the group remain solely within the group. PCP information would not be shared and there would not be responsibility for the PI to report this to CHA management.

D.1.d. Confidentiality During Adverse Event (AE) Reporting
AE reports and annual summaries will not include subject- or group-identifiable material. Each report will only include the unique MINDFUL-PC numeric identifier and acrostic.

D.2. Monitoring and Quality Assurance:

Following NCCIH request, a detailed Data and Safety Monitoring Plan (DSMP) was designed and an Independent Monitor was assigned. Please see appendix at the end of this document. Adverse event reporting guidelines are detailed in the DSMP and copied below.

D.2.a. Definition:

An adverse event (AE) is any untoward medical occurrence in a subject during participation in the clinical study. An adverse finding can include a sign, symptom, abnormal assessment (from vital signs or brain imaging), or any combination of these.

A serious adverse event (SAE) is any AE that results in one or more of the following outcomes:

Death
A life-threatening event
Inpatient hospitalization
A persistent or significant disability/incapacity
A congenital anomaly or birth defect
An important medical event based upon appropriate medical judgment.

D.2.b. Classification of AE Severity:

AEs will be labeled according to severity, which is based on their impact on the patient. An AE will be termed “mild” if it does not have a major impact on the patient, “moderate” if it causes the patient some minor inconvenience, and “severe” if it causes a substantial disruption to the patient’s well-being. Of note, a severe AE and a serious adverse event (SAE) are distinct terms. A subject could experience a severe AE that does not meet the above-listed definition of an SAE; alternatively, a subject could experience a moderate AE that meets the SAE definition.

D.2.c. AE Attribution Scale:

AEs will be categorized according to the likelihood that they are related to the study intervention. Specifically, they will be labeled definitely unrelated, probably related, possibly related, or definitely related to the study intervention.

D.2.c.1. AE Reporting and Follow-up:

This study will comply with the reporting requirements from the Cambridge Health Alliance IRB. The PI will report to the IRB, Independent Monitor, and NCCIH any of the following *unanticipated problems* and *adverse events* that occur 1) during the conduct of the study, 2) after study completion, or 3) after subject withdrawal or completion:

1. *Internal adverse events* that are *unexpected,* and related or *possibly related to the research* and that indicate there are new or increased risks to subjects;
2. *External adverse events* that are *serious*, *unexpected*, and related or *possibly related to the research* and that indicate there are new or increased risks to subjects that require some action (e.g., modification of the protocol, consent process, or informing subjects);
3. *Deviation* from the approved research protocol or plan without IRB approval in order to eliminate apparent immediate hazard to subjects or harm to others;
4. *Deviation* from the approved research protocol or plan that placed subjects or others at an increased risk of harm regardless of whether there was actual harm to subjects or others;
5. Any event that requires prompt reporting according to the research protocol or investigational plan or the sponsor;
6. Breach of confidentiality or violation of HIPAA (e.g., lost or stolen laptop);
7. Procedural error regardless of whether subjects experienced any harm;
8. Interim analysis, safety monitoring report, publication in a peer-reviewed journal, or other finding that indicates that there are new or increased risks to subjects or others or that subjects are less likely to receive any direct benefits from the research;
9. Complaint by/on behalf of a research subject that indicates that the rights, welfare, or safety of the subject have been adversely affected or that cannot be resolved by the investigator;
10. Incarceration of a research subject during participation in this study (which is not currently approved for involvement of *prisoners* as subjects);
11. *Noncompliance* with applicable regulations or requirements or determinations of the IRB identified by the research team or others that indicates that the rights, welfare, or safety of subjects have been adversely affected;
12. *Suspension* or *termination* of the research, in whole or in part, based on information that indicates that the research places subjects at an increased risk of harm than previously known or recognized;
13. Suspension or disqualification of an investigator by the sponsor, or others;
14. *Scientific misconduct*; or
15. Any other problem that indicates that the research places subjects or others at an increased risk of harm or otherwise adversely affect the rights, welfare or safety of subjects or others.

D.2.c.2. Procedures for collecting and reporting unanticipated problems:

All unanticipated problems (including AEs) will be collected by the PI or other study staff on an AE Tracking Log form, at the following time points: Baseline session, fMRI session (if applicable), on a weekly basis during the intervention (8 weeks), at post study session and at follow-up session, and additionally on an ad-hoc basis.

Reports of *unanticipated problems involving risks to subjects or others* will be submitted to the IRB, IM and NCCIH within 5 working days/7 calendar days of the date the investigator first becomes aware of the problem.

D.2.c.3. Reporting Unanticipated Problems that are Adverse Events:

Any unanticipated untoward or unfavorable medical occurrence, including abnormal sign, symptom, or disease, that indicates that the research places subjects at increased risk of physical or psychological harm than previously known or recognized will be submitted as an AE to the IRB, IM, and NCCIH. The PI will provide the following information in the report:
(1) a detailed description of the adverse event;
(2) the basis for determining that the event is unexpected in nature, severity, or frequency;
(3) the basis for determining that the event is related or possibly related to the research procedures;
(4) the basis for determining that the research places subjects at an increased risk of harm (i.e., a serious adverse event); and
(5) whether any changes to the research or other corrective actions are warranted.

D.2.c.4. Reporting Unanticipated Problems that are not Adverse Events:

All other unanticipated problems incidents, experiences, information, outcomes, or other problems that indicate that the research places subjects at an increased risk of physical, psychological, economic, legal, or social harm than was previously known or recognized will be submitted as an Other Event to the IRB. The investigator will provide the following information in the report:
(1) a detailed description of the unanticipated problem;
(2) the basis for determining that the problem is unexpected;
(3) the basis for determining that the problem indicates that the research places subjects at an increased risk of harm; and
(4) whether any changes to the research or other corrective action are warranted.

D.2.c.5. SAE Reporting:

SAEs that are unanticipated, serious, and possibly related to the study intervention will be reported to the IRB, IM, and NCCIH in accordance with requirements.

Unexpected fatal or life-threatening AEs related to the intervention will be reported to the NCCIH Program Officer within 7 days. Other serious and unexpected AEs related to the intervention will be reported to the NCCIH Program Official within 15 days.
Anticipated or unrelated SAEs will be handled in a less urgent manner but will be reported to the IRB, IM, and NCCIH in accordance with their requirements. In the annual AE summary, the IM Report will state that she has reviewed all AE and SAE reports.

D.2.c.6. Monitoring and Quality Assurance:

The PI and data manager will review data collection, data completeness and accuracy as well as protocol compliance on a monthly basis. Study progress and safety will be reviewed monthly (and more frequently if needed). Progress reports, including patient recruitment, retention/attrition, and AEs, will be provided to the Independent Monitor following each of the monthly reviews (see DSMP for details).

D.2.c.7. Possible Risk of Suicide:

This study will not be evaluating suicidality. Surveys will not ask patients or PCPs about their thoughts of suicide, and no data will be collected about suicidality for patients or PCPs.

Behavioral care providers will evaluate potential patient participants for suicidality in a pre-screen prior to participation in the study. If imminent risk of suicide or danger to self or others is evidenced during a screening evaluation, then the patient will be excluded from participation and will be referred to the emergency room or the appropriate level of care. The PI, Zev Schuman-Olivier, and the CMC medical director, Todd Griswold, will be contacted by page to help with clinical management.

If a participant describes feelings of suicidality while participating in a group, the licensed mental health clinician present during the group will help to manage this event with the current standard of care, and will make immediate contact with the CMC medical director, Todd Griswold, and the PI, Zev Schuman-Olivier. The participant will be referred to the emergency room or the appropriate level of care.

We will not ask any CHA staff members or PCP participants about suicidality. However, if during a group, any PCPs express any kind of imminent risk to self or others or any concern that might affect their capacity to work, the PI, Zev Schuman-Olivier, will be present to manage this event. In this case, the PI would refer a PCP to the EAP or the Physician Health Services if there was evidence of risk of imminent patient harm or neglect.

D.2.c.8. Adverse Events Communication with non-English speaking participants:

The CHA website has the ability to translate all pages into any language, so that any non-English speaking participant can read it. The CMC website will list the name of a point person for each language that the MINDFUL-PC program has the capacity to provide services. Patients will be able to look up a point person, who is a mental health clinician fluent in each language for which mindfulness services will be offered. The language point persons within CMC will be included as a contact on the informed consent in that language. Point persons will be associated with the CMC and the MINDFUL-PC implementation project, and will be able to contact the Research Coordinator, who can then arrange for an interpreter to help provide services to the patient.

D.2.d. Expected Risks:

D.2.d.1. Risks to Patients and PCP Participants:

1. Time spent learning mindfulness techniques

2. Increased anxiety due to difficulties in mental training program

Mindfulness practices can sometimes cause anxiety for those who practice. Support from the Group Leader and the group can help participants recognize that this anxiety is part of the

process, and can help people learn to manage these feelings. If meditation and mental exercises are causing a worsening of anxiety for participants, they will be encouraged within groups to change their approach to the practice. If they are unable to find a way to practice without eliciting an increase in symptoms, then they may be asked to stop practicing and to meet with either the CMC medical director or the principal investigator for an evaluation. The participant may ultimately be terminated from the study if they are experiencing an adverse reaction. These participants may continue to receive other treatments at CHA as part of their ongoing treatment plan.

In some very rare cases, meditation practice can lead to a dissociative state or to psychosis[95]. This is more likely in participants with current conditions of or a predisposition to psychosis. Patients experiencing active psychosis are excluded from participating in this study. If a participant begins to experience these feelings during his or her time in the study, then the participant may be asked to stop practicing and to meet with either the CMC medical director or the principal investigator for an evaluation. The participant may ultimately be terminated from the study if he or she is experiencing an adverse reaction. These participants may continue to receive other treatments at CHA as part of their ongoing treatment plan.

3. Physical discomfort due to gentle movement aspect of training

The training will involve gentle movements similar in form to hatha yoga. Some participants could experience physical discomfort during this aspect of training. If a participant feels discomfort, he or she will be encouraged to engage in a less straining manner. If discomfort continues, then the participant will be asked to sit out of this brief element of training and discuss the areas of discomfort with their PCP before return to practice of physical postures. Severe discomfort is not expected, but could possibly occur. In this case, the participant will be treated for this pain, and encouraged to return to practice stationary forms of mindfulness.

4. Feelings of embarrassment or anxiety when asked personal survey question.

Some survey questions are of a sensitive or personal nature, and may cause the participant to become upset. In some rare cases, participants may require mental health support upon feeling upset by the survey questions. A patient's referring integrated behavioral health clinician will be contacted if the patient needs additional mental health support. The PI and CMC medical director will remain available to field questions from PCPs about their experience with mindfulness and any adverse experiences. PCPs with adverse events that may influence their fitness to safely practice will be referred to the Employee Assistance Program (EAP) or Physician Health Services. Todd Griswold, MD, clinical supervisor of the MINDFUL-PC implementation project, will help to monitor and coordinate behavioral health care for participants.

5. Risk of loss of confidentiality

D.2.d.2. Risks to Patients in fMRI study:

1. MRI

The MRI system used in this study has been approved by the FDA and will be operated within the parameters reviewed and accepted by the FDA. MRI is not associated with any known

adverse effects except in people with non-MR-compatible features such as certain kinds of implants, tattoos, jewelry or other devices. Subjects will be excluded from this study if they have any MRI contraindication. The MR Safety Form will be administered prior to every MRI scan to confirm eligibility and subjects will be checked with a metal detector prior to entering the scanner. Some patients find it unpleasant or feel anxious when confined in the enclosed space of the scanner. Subjects will be able to converse with a staff member via a microphone and speaker system, and can request that the scan be stopped at any time for any reason. Subjects will be required to wear earplugs and have additional padding around their ears to prevent discomfort due to scanner noise (https://www.nmr.mgh.harvard.edu/martinos/userInfo/safety/index.php).

2. Pain task

In some cases, cuff pain stimulation can result in mild bruising associated with inflation of the cuff. The pressure from this cuff is controlled to be within a safe and tolerable range. If participants feel distress while wearing the cuff, the procedure will be stopped. Patients will be assessed for peripheral vascular disease, varicosities, and lymphedema prior to application of cuff pain to prevent the possibility of worsening of symptoms.

3. Emotional Go/NoGo task

This task will employ negative and unpleasant pictures to test the relation between emotional processing and attention performance, from the IAPS. Pictures include scenes of mutilations, car accidents, natural catastrophes, contamination or violence. For this task, we will use 50% neutral, and 50% unpleasant pictures. We do not include pictures of sexual content, spiders, or snakes. IAPS pictures are frequently used to study emotion processes, and are also commonly employed in patient studies and during fMRI. However, the pictures could induce discomfort during the task. Patients will receive information about these pictures in the information sheet and informed consent form. They will further complete a practice task outside of the scanner, with IAPS pictures of similar content. Thus, any concern can be addressed already before the scan, and if patients feel too uncomfortable, we will decide to abstain from conducting this task in the scanner. The participants are further reminded in the informed consent and orally that they can stop any task or their participation, should they feel too uncomfortable with any of the procedures. After the task, participants will be asked about their current condition and mood. In case of enduring discomfort caused by the pictures, they are instructed to contact the Principal Investigator, Dr. Zev Schuman-Olivier, at 617-591-6056 or the Behavioral Health Communication Center for CHA Psychological Services (617- 665- 1560) and the respective contact information is listed on the informed consent form.

3. Possible discovery of findings related to medical imaging

If the brain images collected in this study show what seem to be abnormalities – as judged by the neuroimaging post-doctoral fellow or neuroimaging consultants at the Martinos Center on the day of the scan session, a radiologist will be consulted within 1 business day to review the scan, following standard procedures at the Athinoula A. Martinos Center for Biomedical Imaging (compare
https://www.nmr.mgh.harvard.edu/martinos/userInfo/safety/training_manual_082305.pdf) . If the radiologist thinks there may be a medical abnormality in the scan, the subject will be contacted by the PI or the CMC medical director, and will be provided referrals and/or a list of options for follow-up medical care. Similarly, if cardiovascular anomalies and/or cardiac arrhythmias were evidenced by the vital signs recordings – as judged by the neuroimaging post-doctoral fellow or neuroimaging consultants at the Martinos Center on the day of the scan

session, the subject will be contacted by the PI or the CMC Medical Director and referred for follow-up medical care.

Potential risks for participants in the HEART pilot study:

1) Feelings of embarrassment or anxiety when asked personal survey questions or due to behavior tracking. Some survey questions are of a sensitive or personal nature, and may cause the participant to become upset. In addition, tracking behaviors related to activity, sleep, mindfulness practice, or eating and drinking may cause a participant to feel embarrassed or become upset. In some rare cases, participants may require mental health support upon feeling upset by the survey questions or behavior tracking. A patient's referring integrated behavioral health clinician will be contacted if the patient needs additional mental health support. The study staff, PI and CMC medical director will remain available to field questions from participants about their experience with mindfulness and any adverse experiences.
2) Extra time associated with completing the behavioral task tracking. Participants will be asked to spend time tracking behaviors each day during the HEART pilot study.
3) Participants will be asked to carry their smartphone during the day for activity tracking. This may cause participants inconvenience.
4) Mild discomfort due to wristband tracker. Participants may experience mild discomfort when wearing the wristband activity tracker. Participants who are experiencing discomfort will be encouraged to speak with study staff who will help participants adjust the wristband if necessary. If discomfort is not tolerable to participants, they will be encouraged to discontinue wearing the wristband at any time.
5) Potential to impact development of mindfulness as participants enrolled in MTPC will be doing the tracking during weeks 5-8 of their training.
6) Despite efforts to prevent data breaches, any use of electronic devices and internet data transmission can result in a breach of confidentiality.
7) Eye strain from performing Behavioral computerized tasks.

D.2.e. Potential Benefits:

D.2.e.1. Benefits to Patient Participants:

1. Learn techniques for improved behavioral control and psychological wellbeing
2. Improve health maintenance and self-management of chronic illness
3. Greater satisfaction with the provider-patient relationship
4. Decrease anxiety, depression, insomnia, and pain
5. Reduce substance use and tobacco smoking
6. Reduced reliance on prescription opioids and sedatives
7. Feeling of greater behavioral control over risky behaviors in general
8. Improve quality of life, with reductions in stress and anxiety
9. Reduce stress associated with chronic illness

D.2.e.2. Benefits PCP Participants:

1. Learn techniques for improved behavioral control and psychological wellbeing
2. Reduce burnout and increase resiliency
3. Increase patient-centered communication, improve provider empathy and increase patient satisfaction

4. Reduce stress, anxiety, depression, and insomnia

D.2.e.3. Alternatives to Participation:

Participation in this research study is voluntary. Patient participants can choose not to participate, and their decision will in no way affect the quality of care they receive at CHA or their working relationship with CHA; however, they will be unable to participate in the MTPC groups until after completion of the study if they choose not to participate in the study. PCPs will not be required to participate in this study, but they will need to at least enroll in the control group if they intend to refer patients to the study. Participants may elect at any point to discontinue their participation in this study.

D.3. Human Subjects and Confidentiality:

D.3.a Human Subjects Procedures:

D.3.a.1 Equitable Selection of Subjects:

People of all races and ethnicities will be included in this study.

D.3.b. Recruitment Procedures:

D.3.b.1. PCP Recruitment:

PCP enrollment is complete as of February 10th, 2017. No additional PCPs will be enrolled after this date, and no further PCP study sessions will take place. The study aims to enroll 50-80 PCPs as participants. PCPs will be recruited through print/flyer advertisements in department offices and health centers, email invitations, announcements at departmental meetings, and a presentation at CHA medical grand rounds and family medicine grand rounds. The study aims to enroll at least 25 PCPs into an intervention group (Group 1) and at least 25 into a control group (Group 2 and 3).

The principal investigator is not in a supervisory role for anyone in this study. Behavioral health providers are not study subjects and this training program is integrated in the mental health integration into primary care. Therefore, mental health providers in primary care will be encouraged to participate in the program by their supervisor.

The primary care providers will be encouraged to participate primarily through grand rounds presentations, but we will take care to inform supervisors not to pressure providers to participate in the Mindfulness group as it must be fully voluntary. Since this is primarily an implementation project, supervisors may encourage staff to participate in the program and refer patients, but supervisors will be reminded that non-participation at any level cannot affect employment.

D.3.b.2. Patient Recruitment:

The study aims to enroll a total of 434-1,000 CHA patients as participants within 18 months of beginning the project. Patients will be recruited through print/flyer advertisements in health centers, CHA marketing materials, community informational meetings, and referral by PCPs and other members of the health care team. In addition, we aim to develop a video introduction about mindfulness to be played in patient waiting areas within health centers with translations into the primary languages of the health centers (Note: *Once developed these videos will be provided for*

review by the CHA IRB prior to implementation). This study aims to randomize 290 patients to an 8-week study intervention and 144 to a control group.

The HEART pilot study aims to recruit 40 participants in the **alumni cohort** and 30-60 participants (10-20 in the waitlist arm and 20-40 in the intervention arm) in the **concurrent cohort** for a total of 70 participants (40 alumni, 20 intervention, and 10 waitlist). The absolute minimum total number would be 47 participants and the maximum total would be 100 participants (40 alumni, 40 intervention, and 20 waitlist).

D.4. Data Quality and Safety:

D.4.a. Data Quality and Management:

D.4.a.1. Description of Plan for Data Quality and Management:
The PI and data manager will review data collection, data completeness and accuracy as well as protocol compliance on a monthly basis.

Survey session data will be entered by subjects into REDCap. The data manager will review all REDCap data collection forms on an ongoing basis for data completeness and accuracy as well as protocol compliance.

All scantron data will be scanned by research coordinators and files will be reviewed by the data manager for completeness and accuracy prior to upload to the excel database.

Any surveys completed by pencil and paper will be entered by a research assistant. We will conduct ongoing verification audits for entry of any data transfer from paper forms. Discrepancies will be corrected by data manager and/or the PI, based on source documents. Any inconsistencies will be resolved. Exploratory analysis of data with simple range checks may be conducted periodically as a second audit of possible entry errors.

Frequency of Review**—The frequency of data review for this study differs according to the type of data and can be summarized in the following Data Quality Monitoring Table.**

Table 5. MTPC Data Quality Monitoring Table

Data type	Frequency of review	Reviewer
Study progress and safety	Monthly	Program Manager, PI
Data collection, data quality/completeness/accuracy, protocol compliance	Monthly	Data Manager, PI
Subject accrual (including compliance with protocol enrollment criteria)	Quarterly	PI, Independent Monitor
Status of all enrolled subjects, as of date of reporting	Quarterly	PI, Independent Monitor
Adherence data regarding study visits and intervention	Quarterly	PI, Independent Monitor

Data type	Frequency of review	Reviewer
AEs	Quarterly	PI, Independent Monitor
Protocol violations	Per occurrence	PI, Independent Monitor, NCCIH
SAEs	Per occurrence	PI, Independent Monitor, NCCIH

D.4.b. Subject Accrual and Compliance:

D.4.b.1. Measurement and Reporting of Subject Accrual, Compliance With Inclusion/Exclusion Criteria:
Review of the rate of subject accrual and compliance with inclusion/exclusion criteria will occur monthly by the data manager with reports to PI every 3 months to ensure that a sufficient number of participants are being enrolled and that they meet eligibility criteria and the targeted ethnic diversity goals outlined in the grant proposal (Targeted/Planned Enrollment Table).

D.4.b.2. Measurement and Reporting of Participant Adherence to Treatment Protocol:
Data on adherence to the treatment protocol will be collected twice weekly by research staff and reviewed quarterly by the PI, the study statistician, and the independent monitor. Adherence of patient participants will be evaluated by attendance at MTPC groups, PCP visit, and completion of all study sessions. Adherence for each session will be rated on the following scale: 0 = absence; 1 = completed; 2 = incomplete (with comments). An explanation of study staff attempts to understand and address participant adherence deficits will be documented and reviewed twice weekly.

D.4.c. Justification of Sample Size:
The goal of the study is to determine if Mindfulness Training provided in Primary Care results in a greater decreases in anxiety, stress, and depression than referral to community resources. The study is also powered to assess for effects of mindfulness training on provider-patient relationship. The current RCT is funded by AVDF and Gold Foundation and is sufficiently powered to address these aims.

Using an intent-to-treat analysis with 290 patients receiving mindfulness training and 144 patients with orientation only, there will be an 80% chance of detecting a significant difference at a two-sided 0.05 significance level. This assumes that the rate of action plan initiation is 0.54 in orientation only (based on Guck et. al.[5]) and the rate of action plan initiation among patients who receive mindfulness training is 0.68 (based on rates of initiation and maintenance of meditation practice in previous pilot MBIs[6]).

The experimental fMRI pilot trial will recruit primary care patients (n= max. 30 subjects) with anxiety or depression from the MTPC arm using a within-subject pre/post design, which is an adequate size for a pilot neuroimaging trial to be able to assess an effect size of the fMRI and medical regimen adherence measures needed to power the trial for the UH3 phase.

The HEART pilot study is underpowered to be able to compare between-group differences in outcomes, but the primary aims of the pilot study are 1) to demonstrate feasibility of using

commercially available activity/sleep/diet trackers and online daily surveys for ecological behavior tracking in a MBI RCT and 2) to use the daily behavior tracking to validate the action plan goal setting process and the self-report action plan initiation measure. To do this we aim to recruit the 70 participants from both the alumni and concurrent phases and then to examine the data for correlations between the action plan initiation 7-item survey and pre-post differences in step count, the number of active periods, changes in sleep duration, changes in mindfulness practice, and change in nutritional habits depending on which action plan goal was specified in the patient action plan. When conducting correlation analysis with 70 participants, using a= 0.05 type 1 error rate, we would have 80% to find a correlation coefficient of 0.33. If we have lower than expected recruitment and only had 47 participants for correlation analysis, using a= 0.05 type 1 error rate, we would have 80% to find a correlation coefficient of 0.4, which represents moderate correlation[96]. We will also examine whether the activity changes are greater in the participants who select exercise as compared to those who selected nutrition or dietary changes and vice versa.

D.4.d. Stopping Rules:

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

D.4.e. Designation of an Independent Monitor:

The Independent Monitor for this study is Dr. Paula Gardiner, MD at Boston Medical Center. Dr. Gardiner is not associated with this research project and thus works independently of the PI, Dr. Schuman-Olivier. Dr. Gardiner is not a part of the key personnel involved in this grant, and is qualified to review the patient safety data generated by this study because of her unique expertise in the area of mindfulness training for primary care patients.

D.4.f. Safety Review Plan:

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

D.4.g. Study Report Outline for the Independent Monitor (Interim or Annual Reports):

The study team will generate Study Reports for the Independent Monitor and will provide information on the following study parameters: rate of subject accrual and compliance with inclusion/exclusion criteria, Status of all enrolled subjects, Adherence data regarding study visits

and intervention, AEs, and Protocol violations. Study Report tables will be generated only from aggregate (not by group assignment) baseline and aggregate safety data for the study population. A separate Closed Safety Report, with masked group baseline and safety data, will be generated for the Independent Monitor(s) by a designated unmasked member of the team but will not be reviewed by the study team.

D.5. Informed Consent Procedures:

Written informed consent will be obtained from each subject at entry into the study. Informed consent is obtained by the following process:

D.5.a Consent for Primary Care Providers:
PCP participants will be provided with written descriptions in English of the research study procedures, timeline and participant commitments electronically for review prior to starting the course. PCPs will be given an opportunity to email or call the study staff for answers to any questions about the consent document and they will be asked to complete a consent quiz to ensure understanding of the most crucial points. The Principal investigator will review the consent quiz and verbally communicate with each PCP immediately prior to completion of pre-treatment surveys at the start the first group.

D.5.b. Consent for Patients for the main MINDFUL-PC study:

1. Patients will complete the Informed Consent Form in-person prior to the beginning of the Mindfulness Orientation Visit. The informed consent document will include a full description of the study procedures and associated risks. The participant will also be asked to complete an Informed Consent Assessment to ensure comprehension of the study procedures, rights of participants, as well as understanding of the risks and benefits of the study. The patient will not be able to sign the document without having completely correct answers on the consent assessment. Trained study staff will meet with the participant to review the assessment to confirm the subject understands the study, and to answer any questions the subject might have.

2. Patients who scored less than 90% on the informed consent assessment will meet individually with the Research Coordinator or other approved study personnel who will administer the Rapid Estimate of Adult Literacy in Medicine—Short Form (REALM-SF) form[7] to assess patient literacy levels. This is a 7-item word recognition test, which takes about 2 minutes, offers a valid quick assessment of patient health literacy and has excellent agreement with the 66-item REALM instrument in terms of grade-level assignments. Patients are instructed to read seven words aloud for a member of the study team. Patients who pronounce fewer than four of the words correctly read at a literacy level of 4^{th} to 6^{th} grade. Patients with less than a 7^{th} grade reading level in English will be excluded from initial groups and from experimental fMRI pilot.

3. The Research Coordinator and other approved study personnel will be present during the Informed Consent Session if patients have any questions during the consent process or the consent assessment. After completion, participants will be provided an additional copy of the signed informed consent form for their own records. Once the participant demonstrates understanding of the study and agrees to participate in the study, the consent will be signed in the presence of the doctoral level member of the study team and a witness. Participants must

give written, informed consent in order to participate in the study. Participation in the study is voluntary. All participants will be notified that they are free to discontinue from participating in the study at any time. All participants will be asked to complete and sign a section acknowledging that sessions will be audio-recorded for research purposes. No study-specific procedures or investigations will be performed before the participant has signed and dated the Informed Consent Form.

4. The NIH Common Fund Science of Behavior Change Initiative and NCCIH will be listed as co-sponsors of this study in the overall initial consent document signed prior to the Mindfulness Orientation Visit for all participants. If the MINDFUL-PC study continues after the NIH Common Fund/NCCIH grant ends, then references to NIH Common Fund and NCCIH as study sponsors will be removed from the overall consent document. No other intervention materials will mention NIH Common Fund and NCCIH other than the overall initial consent document and the neuroimaging pilot study consent document.

D.5.c. Consent for Patients for experimental fMRI pilot study:

After completion of the MINDFUL-PC consent form, the orientation session, and after being randomized to the mindfulness group, interested participants will be phone-screened by the Research Coordinator or other trained study staff based on the experimental fMRI inclusion and exclusion criteria during the group-scheduling phone call. Those who screened into the optional study are asked about any questions regarding the information sheet, flyer, and study in general. At the imaging session, participants are given enough time to study the informed consent and ask any question regarding the fMRI pilot study. Participants will then sign the informed consent before any other questionnaires or neuroimaging will be administered. It will be emphasized that any refusal to participate will not impact current or future treatment, nor participation in the broader study.

D.5.d. Consent for Patients for HEART pilot study:

Participants are first notified of the opportunity to enroll in the HEART study during the MINDFUL-PC confirmation phone call to attend MINDFUL-PC orientation. Following this, at the in-person orientation, participants will be led through the verbal and written consent process for MINDFUL-PC. Once they have signed their MINDFUL-PC consent forms, they are eligible for the HEART study and will be given the HEART study information packet, as well as the HEART study informed consent form. A doctoral level member of the research staff will then guide participants through a verbal introduction of the HEART study, informing them of the invitation to voluntarily participate, reviewing study inclusion and exclusion criteria, and providing a chance to ask any questions. If after this in-person review, interested participants will be invited to sign the HEART study consent form. If an interested participant does not understand or agree to study requirements after the verbal introduction and a chance to ask questions, the doctoral level research staff member conducting the orientation session will decide to exclude the participant from the HEART study.

Upon completion of the HEART study informed consent form, participants will be given an additional copy of the signed informed consent form for their own records. The signed informed consent forms will be stored in a binder in a double-locked cabinet at the Center for Mindfulness and Compassion. Only IRB-approved study staff will have access to this cabinet

D.6. Reporting Changes in Study Status:

During the funding of this study, any action by the IRB or one of the study investigators that results in a temporary or permanent suspension of the study will be reported to the NCCIH Program Official within 1 business day of notification.

D.7. Participant Reimbursement:

Participants will incur no fees as a result of participation in this study. All study-related visits and will be provided to the participants at no cost; however, given this is an implementation project and group visits will be offered as group psychotherapy, patient visits will be billed to their insurance companies and a co-pay may be involved. If a patient's insurance will not cover their participation in the group despite PCP referral, then the principal investigator will consider their inclusion individually on a case-by-case basis.

Patient participants will receive up to $140 in total compensation in the form of prepaid cards or cash cards for participating in the MINDFUL-PC study.

- Baseline: Up to $20
    - Patient participants will receive one $20 prepaid card after their first session of surveys.
- Week 8: Up to $40
    - They will receive a $20 card payment after their post-study week 8 session of surveys.
    - Participants will receive a $20 prepaid card at Study Week 8 for completing both the Weekly Mindfulness Practice Diaries and Weekly Mindfulness Resource Use Surveys every week during Study Weeks 1-8. If participants only complete 6 of 8 of the Weekly Mindfulness Practice Diaries or 6 of 8 of the Weekly Mindfulness Resource Use Surveys, they will receive a $15 prepaid card instead of a $20 prepaid card. If participants complete fewer than 6 of either of the weekly diaries, they will not receive compensation for this aspect of the study.
- Week 26: Up to $80
    - $20 for the 6-month follow-up session
    - $15 for the Action Plan Study Session
    - $15 total ($5 each) for the Week 9, Week 10, and Week 16 APIS-5 sessions
    - $30 completion bonus if all study participation items have been completed.
- Post Study: $15
    - They will receive $15 if they choose to do the Action Plan Interview

<u>Participant Reimbursement for the HEART Pilot Study:</u>

Patients will not be reimbursed for data plan usage relevant to this study. The Argus app and similar smartphone applications do not transmit data continuously, so the amount of data use is not high and will have a small impact on data usage.

Concurrent Cohort: Up to $195

$30 Behavioral Measures (pre)
$21 Part 0:

- $1/day each, for
    - Mindfulness tracking for 1 week ($7 total)
    - Smartphone/Accelerometer-based activity tracking for 1 week ($7)
- $1/day for Food, Activity, and Sleep Tracking (FAST) Questionnaire for 1 week ($7)

$84 Part 1 & 2

- $1/day each, for
    - Mindfulness tracking for 4 weeks ($28 total)
    - Smartphone/Accelerometer-based activity tracking for 4 weeks ($28)
- $1/day for Food, Activity, and Sleep Tracking (FAST) Questionnaire for 4 weeks ($28)

$30 Behavioral Measures (post)

$30 High Completion Bonus: If action plan paperwork is fully submitted and use of daily tracking on > 90% of the days for each activity above, participants will receive a $50 dollar bonus.

$20 Mid Completion Bonus: If action plan paperwork is fully submitted and use of daily tracking on 75-89% of the days for each activity above, participants will receive a $20 dollar bonus.

$

To be disbursed in **3** payments:

Payment 1: $30 after pre-Behavioral Measures visit
Payment 2: Up to $105 after completing Part 2
Payment 3: $60 after completing post-Behavioral measures visit, including the high completion bonus. If the participant has been given any devices (e.g. wristband sensor), then this payment will be disbursed only after the device is returned in working condition.

D.7.a. PCP Participant Reimbursement:
PCP Participants will incur no fees as a result of participation in this study. All study-related visits and procedures will be provided to the participants at no cost.

Reimbursement for transportation will not be provided to or from the study location; however, a van may be available for transportation for the day of silent practice day depending on location.

D.7.b. Experimental fMRI Pilot Participant Reimbursement:
Participants in the fMRI experiment will be paid $5 for completing the screening and informed consent and providing toxicology and pregnancy screenings if applicable at the pre-fMRI session, and $5 for completing the toxicology and pregnancy screenings at the post-fMRI session. Participants will be paid $50 after completion of each fMRI session. The total reimbursement for 2 fMRI visits and the screenings and informed consent will be $110. Participants will also receive free parking or $10 towards public transport or taxi costs for every fMRI visit. All payments for the fMRI study will be in cash.

D.8. MTPC Session Quality and Protocol Adherence:

Mindfulness group leaders will report on the quality of the sessions and the adherence to the protocol to the Program Manager or the Principal Investigator after each session. Every MTPC group will have an embedded unbiased observer who will rate group leader adherence and fidelity to the manual. In addition, all groups will be audio recorded. A trained rater will review 10% of group sessions for adherence, fidelity and competency. In order to prevent therapist drift, the program manager and/or principal investigator will review group adherence and fidelity ratings weekly. All MTPC group leaders will be asked to participate in weekly group supervision until they have successfully completed four 8-week sessions.

D.9. New Information:

Any pertinent new information will be communicated to study participants. In light of new information, participants may elect to discontinue their participation in the study.

D.10. Sources of Research Materials:

D.10.a. Sources of Research Materials for Patients:
The following research material will be obtained:
1. Responses to surveys
2. EPIC electronic medical records to assess for health outcomes
3. Audio tapes of MTPC sessions for fidelity ratings

The following data will be recorded:
1. Assessment measuring socio-demographic characteristics, depression, anxiety, stress, mindfulness, self-compassion, relationship with primary care provider, consumption of alcohol, and record of substance abuse.
2. Medical history for the year before and year after the study, including patient alcohol use, body mass index (BMI), patient health questionnaire (PHQ-2), HgAlc, LDL-C, smoking cessation attempts and cigarettes per day, frequency of meat eating, blood pressure, risky sexual behaviors, quantity of prescribed opioids and sedatives, and illicit drug use.
3. Attendance of medical visits, including number of visits with the patient's PCP, number of outpatient medical visits, number of inpatient medical visits, number of visits to the emergency department (ED), and no-show rates for the year before and the six months after randomization.
4. Patient action plan, created by a patient and his or her primary care provider at the PCP visit and reported in EPIC electronic medical records.

D.10.b. Sources of Research Materials for Patients in fMRI study:
The following research material will be obtained:
1. Toxicology testing (oral fluids)
2. Pregnancy testing (urine, females only, will be offered to female patients with childbearing potential)
3. Self-report measures as administered through a secure REDCap link
4. fMRI
5. Autonomic monitoring: heart rate, breathing rate, and skin conductance

The following data will be recorded:
1. Toxicology results for alcohol and illicit drugs.
2. Qualitative HCG result
3. Edinburgh Handedness Inventory
4. fMRI BOLD signal
5. Recordings of heart rate, breathing rate, and skin conductance during the full fMRI session

D.10.c. Sources of Research Materials for PCPs:
The following research material will be obtained:
1. Responses to surveys

The following data will be recorded:
1. Assessment measuring depression, anxiety, stress, mindfulness, self-compassion, and burnout.

D.10.d. Data Linkage to subjects and access to data:
The secure web application REDCap will be used for data collection. Data will be entered directly into REDCap by participants. Any data entry not conducted by participants will be conducted only by members of the research team. All data collection will take place under the supervision of the Principal Investigator (Dr. Schuman-Olivier, MD), the Project and Data Manager (Richa Gawande, PhD), or the Research Coordinator, Elizabeth Pine. All fMRI data collection will take place under the supervision of a doctoral-level neuroimaging collaborator, including the Neuroimaging Consultant and Director of the Center for Integrative Pain Neuroimaging (Vitaly Napadow, PhD), Neuroimaging Consultant in Department of Radiology (Gaelle Desbordes, PhD), or the neuroimaging postdoctoral fellow (Jacqueline Lutz, PhD). Substitute codes will be used to label all sources of subject information and access to identifiable data will be limited to researchers directly involved in the study. The Project and Data Manager, Richa Gawande, PhD, will be responsible for coding data and exporting coded data from REDCap to SAS 9.3. All identifiable data will be destroyed 10 years after study completion and will not be maintained for future uses not specified in this research plan.

D.11. Personnel:

D.11.a. Personnel present during study procedure:
At least one of the following personnel will be present during study procedures:
Zev Schuman-Olivier, MD, Principal Investigator; Richa Gawande, PhD, Program and Data Manager; Elizabeth Pine, BA, Research Coordinator; Angela Lozada, BA and Andrea Chen, MA Research Assistants and additional Research Assistants; CHA Behavioral Health Specialists.

D.11.b. Study team members responsible for the following activities:
At least one of the following personnel will be responsible for obtaining and documenting informed consent/parent or guardian permission/minor assent/legally authorized representative permission: Zev Schuman-Olivier, MD, Principal Investigator; Richa Gawande, PhD, Program and Data Manager; Elizabeth Pine, BA, Research Coordinator; and additional Research Assistants.

The following personnel will be responsible for providing on-going information to the study sponsor and the IRB: Zev Schuman-Olivier, MD, Principal Investigator.

At least one of the following personnel will be responsible for maintaining participant's research records: Zev Schuman-Olivier, MD, Principal Investigator; Richa Gawande, PhD, Program and Data Manager; Elizabeth Pine, BA, Research Coordinator; and additional Research Assistants.

In addition, the experimental fMRI pilot study will be conducted through collaboration with the following people: Gaelle Desbordes, PhD, Neuroimaging Consultant; Vitaly Napadow, PhD, Neuroimaging Consultant, Director of Center for Integrative Pain Neuroimaging; and Jacqueline Lutz, PhD, neuroimaging post-doctoral fellow.

D.11.c. Inclusion of study personnel:
This project is a research study built on top of an implementation pilot program. The senior MBSR teachers, CMC faculty, and mindfulness-trained behaviorists are all part of the underlying implementation program and they will not have access to study data or randomization codes. While behavioral health clinicians will provide some data which will be included in the screening and referral process, it will be MINDFUL-PC study staff under supervision from the principal investigator who will actually apply inclusion and exclusion criteria and send invitations for the study.

The MINDFUL-PC study staff will include Zev Schuman-Olivier, MD (Principal Investigator); Todd Griswold, MD (CMC Medical Director and MINDFUL-PC Clinical Implementation Supervisor); Richa Gawande, PhD (Program and Data Manager); Elizabeth Pine, BA (MINDFUL-PC Research Coordinator); Gaelle Desbordes, PhD, (Neuroimaging Consultant); Vitaly Napadow, PhD, (Neuroimaging Consultant); Jacqueline Lutz, PhD, neuroimaging post-doctoral fellow and additional Research Assistants.

APPENDIX A

Table 2. Study Visit and Assessment Schedule for PCP Participants

	Screen Visit	Pre-Study Session	Weeks 1-6	Week 7	Week 8	Weekend Retreat	Mid-Study Session	Months 1-30	Post-Study Session	Duration (min)
Group 1 Participants: MBSR and Mindful Communication										
Email or Phone Screen Interview	X									
Informed Consent										
Informed Consent Form*		X								20
Informed Consent Quiz*		X								10
Baseline Battery										
Demographic Survey*		X								5
MEAQ-PC*		X								5
Survey of meditation experience*		X								5
Weekly Mindfulness Practice Diary			X	X	X		X	X	X	35
Mindfulness Self-Report Battery										
FFMQ*		X					X		X	30
SCS-SF*		X					X		X	4
Clinical Assessment Battery										
DASS-21*		X					X		X	5
PSS*		X					X		X	5
Provider Resilience Battery										
Maslach Burnout Inventory*		X					X		X	4
Workplace Wellbeing Scale*		X					X		X	4
Jefferson Scale of Empathy (JSE)*		X					X		X	5
Adverse Events Reporting							X		X	5
Group 1a										
MBSR Course			X	X	X					1200
7.5-hour mindfulness retreat				X						480
Group 1b										
18-hour intensive mindfulness retreat						X				1080
Group 1										
Mindful Communication Course								X		1500
Visit Duration (min)	20	90	180	660	150	1080	90	150	60	
Group 2 Participants: No Training										
Email or Phone Screen Interview	X									
Informed Consent										
Informed Consent Form*		X								20
Informed Consent Quiz*		X								10
Baseline Battery										
Demographic Survey*		X								5
MEAQ-PC*		X								5
Survey of meditation experience*		X								5
Weekly Mindfulness Practice Diary							X		X	35
Mindfulness Self-Report Battery										
FFMQ*		X					X		X	30
SCS-SF*		X					X		X	4
Clinical Assessment Battery										
DASS-21*		X					X		X	5
PSS*		X					X		X	5
Provider Resilience Battery										
Maslach Burnout Inventory*		X					X		X	4
Workplace Wellbeing Scale*		X					X		X	4
Jefferson Scale of Empathy (JSE)*		X					X		X	5
Adverse Events Reporting									X	5
Visit Duration (min)	20	60	0	0	0	0	60	0	60	
* Represents surveys and/or instruments administered through REDCap.										

Table 3. Study Visit and Assessment Schedule for Patient Participants								
	Screen Visit	**Consent Session**	**Pre-Treatment Surveys**	**Group Orientation**	**Week 1-5**	**Week 6- 7**	**Action Plan**	**Week 8**
Patient Screening								
Patient Eligibility Questionnaire	X							
MINDFUL-PC Patient Screening Form[#]	X							
Informed Consent								
Informed Consent Form		X						
Consent Quiz		X						
REALM-SF[%]		X						
Baseline Battery								
Demographics Survey[#]			X					
SMME[#]			X					
FTND[#]			X					
Mindfulness Self-Report Battery								
FFMQ[#]			X					
SCS-SF[#]			X					
DERS[#]			X					
MAIA[#]			X					
Clinical Assessment Battery								
DASS-21[#]			X					
PHQ-2[#]			X					
PSS[#]			X					
AUDIT-C[#]			X					
DSM-V SSU[#]			X					
PROMIS-ASF[#]			X					
PROMIS-DSF[#]			X					
Self-Management Battery								
SECD-6[#]			X					
PAM[#]			X					
PCQ[#]			X					
APA-10[#]							X	
APIS-5[#]								
Action Plan Worksheet							X	
TFEQ-R18			X					
Weekly Mindfulness Practice								
Weekly Mindfulness Practice Diary					X	X		X
Weekly Mindfulness Resources Use Survey					X	X		X
MTPC Satisfaction Survey								
Satisfaction survey[#]								
Engagement and Adverse Event Reporting								
Adverse Event Reporting Form								
Participant Engagement Phone Call					X	X		X
Patient Study Visits								
60-minute Group Orientation				X				
2-hour MTPC Sessions					X^	X^		X^
Action Plan Study Session							X	
7-hour Full-Day Session						X^		
Action Plan Interview								
Visit Duration (min)	**10**	**32**	**83**	**60**	**660^**	**684^**	**20**	**132^**
Payments at study visits ($)			**20**					

^ Represents surveys, events, and time durations that only apply to MTPC group participants
% Represents surveys administered only to patients who score below 90% on the ICF assessment
# Represents surveys and/or instruments administered through REDCap
* Represents surveys, events, and time durations that only apply to 6-month waitlist participants

Table 3 (Cont'd). Study Visit and Assessment Schedule for Patient Participants							
	Post-Treatment Surveys	**Week 9**	**Week 10**	**Week 16**	**Follow-up Surveys**	**Optional Action Plan Interview**	**Item Duration (min)**
Patient Screening							
Patient Eligibility Questionnaire							5
MINDFUL-PC Patient Screening Form[#]							5
Informed Consent							
Informed Consent Form							20
Consent Quiz							10
REALM-SF[%]							2
Baseline Battery							
Demographics Survey[#]							5
SMME[#]							5
FTND[#]							3
Mindfulness Self-Report Batter							
FFMQ[#]	X				X		8
SCS-SF[#]	X				X		4
DERS[#]	X				X		5
MAIA[#]	X				X		5
Clinical Assessment Batter							
DASS-21[#]	X				X		3
PHQ-2[#]							1
PSS[#]	X				X		3
AUDIT-C[#]	X				X		1
DSM-V SSU[#]	X				X		3
PROMIS-ASF[#]	X				X		3
PROMIS-DSF[#]	X				X		3
Self-Management Battery							
SECD-6[#]	X				X		3
PAM[#]	X				X		4
PCQ[#]	X				X		3
APA-10[#]							4
APIS-5[#]	X	X	X	X	X		3
Action Plan Worksheet							
TFEQ-R18	X				X		5
Weekly Mindfulness Practice							
Weekly Mindfulness Practice Diary	X				X		6
Weekly Mindfulness Resources Use Survey	X				X		6
MTPC Satisfaction Survey							
Satisfaction survey[#]	X^						5
Engagement and Adverse Event Reporting							
Adverse Event Reporting Form	X				X		2
Participant Engagement Phone Call							5
Patient Study Visits							
60-minute Group Orientation							60
2-hour MTPC Sessions							960^
Action Plan Study Session							20
7-hour Full-Day Session							420^
Action Plan Interview						X	
Visit Duration (min)	**85**	**3**	**3**	**3**	**92**	**30**	
Payments at study visits ($)	**40**				**80**	**15**	

^ Represents surveys, events, and time durations that only apply to MTPC group participants
% Represents surveys administered only to patients who score below 90% on the ICF assessment
# Represents surveys and/or instruments administered through REDCap

* Represents surveys, events, and time durations that only apply to 6-month waitlist participants

Table 4. Study Visit and Assessment Schedule for HEART pilot study participants

Concurrent Cohort:

	Infomed Consent	**1st Behavioral Visit (Wk 0)**	**Part 0 (Wk 0)**	**Part 1 (Wks 5 & 6)**	**Part 2 (Wks 7 & 8)**	**2nd Behavioral Visit (Wks 8-9)**	**Item Duration (min)**
Informed Consent Session	x						30
Smartphone app/accelerometer-based daily activity tracking			**daily**	**daily**	**daily**		2
FAST Questionnaire			**daily**	**daily**	**daily**		10
Daily mindfulness practice diary			**daily**	**daily**	**daily**		3
Daily mindfulness resource use diary			**daily**	**daily**	**daily**		2
Behavioral Measures		**x**				x	20
Visit Duration (min)	**45**	**45**	**15/day**	**15/day**	**15/day**	**45**	
Payments at study visits ($)		**$30**			**$105**	**$60**	**$195**

Table 5. Study Visit and Assessment Schedule for fMRI Pilot Study Participants

	Screening	**fMRI session 1**	**fMRI session 2**	**Item Duration (min)**
Group Scheduling phone screen call				
fMRI pilot screening form	x			5
Edinburgh Handedness Questionnaire	x			5
fMRI appointment				
Informed Consent Form		x		20
Toxicology/Pregnancy screening		x	x	10
Autonomic measures electrodes/belt set-up		x	x	10
fMRI scan		X	X	90

fMRI questionnaire		X	X	5
Visit Duration (min)	**10**	**110**	**110**	
Payments at study visits ($)		**5 + 50**	**5 + 50**	
Travel Expenses ($)		**10 or parking**	**10 or parking**	

Choice of Smartphone Applications and Tracking Devices

The HEART Pilot study is intended to test the feasibility of using commercial behavior tracking smartphone applications and devices in the context of the action planning and initiation process of the MINDFUL-PC study, as well as to validate with objective behavioral measures, the self-report action plan initiation survey. We are not pilot testing the devices and applications themselves but are pilot testing their use in our studies. Due to the rapid innovations in the consumer market, we have left open the possibility of using other, improved but similar applications for activity, sleep, and diet tracking. The Argus App is among the current best possible apps for this purpose. Below is a list of similar alternatives.

We are considering the following smartphone activity tracking applications for inclusion in the study as alternatives to the Argus App:

- Pedometer for Android
- Stepz for IOS.
- Activ8 by 2M Engineering

We are considering use of the following activity tracking devices for inclusion in the study:

- Fitbit
- Moov
- Jawbone
- Withings
- MD2K Cerebrum
- Garmin Vivosmart

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