Title: A pilot study on mindfulness for pain and mental health outcomes

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Background

Veteran suicides occur at a disproportionately high rate compared to civilians, with an age-adjusted rate approximately 50% greater compared to non-veteran adults.[1] A prominent risk factor for suicidal thoughts and behaviors is chronic pain.[2] Veterans are more vulnerable to experience chronic pain, and report more severe pain relative to the general population.[3] Over 50% of veterans seeking treatment in the Veterans Health Administration (VHA) from 2000 to 2011 had at least one diagnosis of a musculoskeletal disorder.[4] A meta-analysis of chronic pain and suicidality found that current and lifetime suicidal ideation were reported in 9% and 21% of pain patients, respectively.[5] Relative to those reporting no pain, they found large effects among the relationships between pain and past-year suicidal ideation, suicide attempts, and suicides.[5] Ilgen et al.[6] found that pain conditions significantly predicted suicide despite adjusting for robust risk factors including psychiatric disorders, medical comorbidity, and demographics. The public health significance of chronic pain, in addition to the co-occurrence between pain and suicidal thoughts and behaviors, make veterans with chronic pain an ideal target for suicide prevention efforts. Interventions that both improve functioning and mitigate suicide risk in veterans with chronic pain are lacking.

Despite the increased risk of suicide among veterans with chronic pain, there are no randomized clinical trials examining suicide prevention efforts specifically targeting this common and high-risk group. To date, opioid analgesics are among the most common pain management approaches for veterans using the VHA.[7] Long-term opioid therapy for pain is associated with increased risk of developing and exacerbating SUD and psychiatric disorders, [8-11] unintentional overdose,[12] suicides and suicide attempts.[13,14] However, the CDC and VA/DoD have clinical practice guidelines indicating that non-pharmacological treatment for pain is preferred over opioid therapy, given its ability to have long-term positive outcomes with relatively fewer adverse outcomes.[15,16] Psychosocial approaches, such as cognitive therapies, may be a useful non-pharmacological approach to suicide risk and chronic pain. Meta-analyses on evaluating the impact of cognitive therapies on chronic pain and suicide risk, individually, have found medium effect sizes compared to treatment as usual (TAU) and comparable effects relative to other active interventions.[17,18] Interventions designed to address *both* suicide risk and chronic pain within one intervention are lacking.

Mindfulness meditation-based interventions (MMBIs) are especially well-equipped to address co-occurring chronic pain and suicide risk. The core components of MMBIs (e.g., mindfulness-based stress reduction (MBSR); mindfulness-based cognitive therapy (MBCT)), feature the practice of awareness through purposeful, non-judgmental attention to experiences. MMBIs have broad support across medical and psychiatric conditions.[19,20] MMBIs address several underlying mechanisms characteristic of depression, anxiety, PTSD, drug craving, and chronic pain, including increasing an individual's ability to disengage from repetitive negative thinking patterns, increasing emotional awareness, decreasing emotional reactivity, and reducing emotional and behavioral avoidance.[21,22] Growing evidence suggests that MMBIs reduce the intensity of pain and unpleasantness of pain through (a) changing the appraisal of painful sensations, (b) decreasing attentional fixation on and hypervigilance for pain-related stimuli, (c) decreasing emotional reactivity to pain, (d) increasing positive affect, and (e) decreasing habit behavior of thinking or behavioral patterns that maintain impairment and suicide risk.[23,24]

There have been numerous studies indicating significant treatment gains from MMBIs among patients with chronic pain. A meta-analysis on MMBIs among individuals with chronic pain indicate that they significantly decrease negative pain outcomes and depression, and increase quality of life compared to treatment as usual, passive controls, and educational control groups.[25] However, there is just one MMBI study to our knowledge that measured both pain and suicide-related outcomes. Serpa and colleagues[26] found that after receiving MBSR, there were significantly fewer veterans reporting thoughts of death or killing themselves, but there was no significant change in pain intensity. This study, however, was non-randomized, only one-quarter of participants reported thoughts of death or killing themselves at baseline, pain intensity levels were generally low to moderate, and there was no assessment of pain-related interference in functioning. Currently, there is no treatment manual that directly targets both suicide risk and chronic pain.

MBCT specifically is well-suited to address suicide risk and chronic pain within the same intervention. Studies of MBCT for pain (MBCT-P) have all demonstrated positive effects on clinical outcomes and several when compared to an active control.[25] Research indicates that it has decreased depression and functional

impairment in patients with fibromyalgia.[27] Studies have also found decreases in the frequency of headaches, pain interference, and pain catastrophizing, and an increase in self-efficacy among patients experiencing chronic headaches and migraines.[28,29] Dowd and colleagues recruited a sample of patients with a range of pain conditions and found that MBCT-P maintained decreased pain interference and pain catastrophizing through the 6-month follow-up.[30]

In terms of MBCT for suicide risk, several studies have focused on using the MBCT for Depression manual highlighting elements of suicide prevention (e.g. planning in suicidal crises, focusing on suicidal cognitions) among individuals with treatment-resistant depression and suicidal ideation.[31-34] While many of these studies did not examine suicide outcomes as the primary outcomes, two studies found that suicidal thoughts decreased over the course of treatment relative to controls[32] and that MBCT attenuates the relationship between depressive symptoms and suicidal thoughts.[31] Chesin and colleagues[35] devised a specific MBCT for Suicide intervention and found that participants rated the treatment as "satisfying to very satisfying," supporting the treatment's acceptability. Participants completed homework assignments, and the majority completed the treatment protocol supporting elements of the treatment's feasibility. Participants also reported significant reductions in suicidal ideation, depression, cognitive reactivity, rumination, and hopelessness.[35,36] Collectively, these studies highlight that incorporating elements of MBCT-P and MBCT for suicide to create a combined intervention is an ideal way to address functional impairment from pain and suicide risk.

In the proposed study, we are seeking to develop a combined intervention, MBCT-S/P, to focus on both improving functioning and mitigating suicide risk in veterans with chronic pain. We will combine unique elements of existing MBCT manuals and then test the new manual's feasibility and acceptability in a sample of veterans experiencing chronic pain and suicidal ideation. Participants will be randomized to either the MBCT-S/P condition (n=38) or the Education control condition (n=38) to assess additional aspects of study feasibility.

Aim 1: Examine the feasibility and acceptability of MBCT-S/P and an Education control condition in veterans at-risk of suicide with functionally impairing chronic pain.

We will assess: (1) treatment satisfaction and acceptability, (2) participant flow from recruitment through follow-up by condition, (3) participant adherence to treatment, and (4) therapist fidelity.

Aim 2: Assess parameters of suicide risk and pain outcomes among participants allocated to the MBCT-S/P condition and to the education control condition.

We will assess within-group means and standard deviations, and level of correlation of repeated outcome measurement across suicide risk (ideation, interpersonal needs, depression) and pain outcomes (pain interference, pain intensity, quality of life).

Method

Overview

The primary objective for the current study is to conduct a small, randomized clinical trial comparing an MBCT-S/P condition (n = 38) to an Education condition (n = 38) in veterans experiencing chronic pain who are at risk of suicide. This study will assess a variety of factors related to treatment feasibility and acceptability, including the research instruments and the psychometric properties of the primary outcome and secondary outcomes.

Study site and Recruitment

The study will take place at the Center for Excellence for Suicide Prevention. Recruitment and the intervention will occur at the Canandaigua and Syracuse VAMCs and the Rochester VA Outpatient Clinic.

Participants

This study aims to recruit 76 eligible participants from the VA Finger Lakes Healthcare System and Syracuse VAMC.

Inclusion criteria. Participants will include men and women, English-speaking veterans ages 18 years and older who understand informed consent. Participants must report pain that occurs on at least half the days for six months or more[37] and score at least a 4 on each item of the three items on a brief pain intensity and interference measure (PEG).[38] Consistent with our prior work, to meet the minimum threshold for suicide risk, veterans must meet *at least* one of the following: endorse at least a 1 ("several days") on item 9 ("thoughts of you would be better off dead, or thoughts of hurting yourself in some way" in the past 2 weeks) of the Patient

Health Questionnaire-9 (PHQ-9), *or* endorse *at least* "death ideation" in the last 3 months as measured by the Columbia Suicide Severity Rating Scale, *or* report a suicide attempt in the last 6 months. These criteria are predictive of suicide, are clinically meaningful, and will help include a broader spectrum of veterans who are at risk of suicide.[39-41]

Exclusion criteria. Veterans will be excluded on the basis of having significant medical and psychiatric conditions that may limit participation including an active severe SUD (at least 6 SUD symptoms within the last 3 months), documented schizophrenia, active psychosis or mania, upcoming surgeries, uncontrolled medical conditions (each confirmed through chart review), and intent to carry out a plan for suicide.

Table 1. Stop code, procedure codes, and ICD codes to identify potential eligible participants

Treatment	Stop codes/procedure codes/ICD codes
Physical (PT)/occupational therapy (OT)	PT: Stop codes 201, 205 and 177 with CPT codes 97113, 95833, 95834, 96125, 97116, 97150, 95832, G0151, 97036, 95831, 97140, 96000, 97112, G0238, 97799, 97750, 97001, 97002, 95851, 95852, 97533, 97530, 97110, G0237 OT: stop codes 206. 208, 230, 207, 213, 222, 223, 228; CPT codes 97755, 97537, G0152, 97003, 97004, 97535, 97545, 97546
Specialty pain clinic	Stop code 420
Complementary and Integrative Health/chiropractic	stop code 159, 436; CPT codes: 9890, 9891, 9892, and 9893.
Other active interventions (e.g., Move!, kinesiotherapy, recreation therapy)	Stop codes 214, 373, 327, 202; CPT codes H2023, 97005, 97006, S9451, S9970, G0176, S9449
Back/neck pain	*ICD-9:* 720-722.99, 723-723.99, 724-724.99, 737-737.99, 756.11, 756.12, 805-806.99, 846-846.99, 847.1-847.99; *ICD-10*: M43.27, M43.28, M43.6, M43.8X9, M45.9- M46.1, M46.90, M47.12, M47.812, M47.814, M47.817, M48.02, M48.10, M48.20, M48.30, M48.9, M50.20, M50.30, M51.34-M51.37, M51.9, M53.0, M53.1, M53.2X7, M53.3, M53.82, M53.9, M54.02, M54.08, M54.12, M54.13, M54.14-M54.17, M54.2, M54.30, M54.5, M54.6, M54.89-M54.9, M67.88; S13.4XXA, S13.8XXA
Arthritis	*ICD-9:* 274-274.99, 710-715.99, 716-719.99, 725.0-729.09, 729.2-729.99, 730-736.99, 738-739.99; *ICD-10*: M00-M02, M05-M08, M10-M14, M12, M15, M16-M19, M1A, M35.3, M36.2, M36.3
Neuropathic pain	*ICD-9:* 337.0-337.19, 355, 355.9, 356-357.99, 377-377.99; *ICD-10*: E08.42, E09.42, E10.42, E11.42, E13.42, G57.00, G58.9, G60, G61.9, G90, G99, H46-47
Fibromyalgia	*ICD-9:* 729.1-729.19; *ICD-10*: M60.9, M79.1, M79.7
Psychogenic pain	*ICD-9:* 307.8, 307.89; *ICD-10*: F45.41, F45.42
Migraines	*ICD-9: 346.0-346.9; ICD-10*: G43.0, G43.1, G43.4, G43.5, G43.6, G43.7, G43.8, G43.9, G43.A, 43.B, G43.C G43.D
Other headache or tension headaches	*ICD-9:* 784.0, 307.81; *ICD-10*: G44.1, G44.209, R51

Procedures

Recruitment. Veterans with pain diagnoses (identified using ICD codes[4,6]) and/or seeking pain-related services (identified using procedure codes or billing codes[42]) who are enrolled at the study sites will be identified using structured queries of VA administrative datasets (see tables below). Given that many of the veterans who meet the minimum threshold for suicide risk noted above will be at lower risk, additional recruitment efforts will target those at higher risk. We will use medical records to prioritize recruitment of veterans identified (a) in REACH VET, (b) with a high risk flag, (c) when available in the medical record, PHQ-9 item 9 scores greater than 1, and (d) when available, Columbia Suicide Severity Rating Scale responses of at least active suicidal ideation. The project coordinator will use these lists to identify potentially eligible participants. Among those who may be eligible, the project coordinator will contact one of veteran's providers and ask if an IRB-approved letter describing the study can be sent to the patient. The project coordinator will call all patients who receive a letter unless the patients call a number to opt out. Referrals for potential participants may also come from a combination of suicide prevention coordinators, clinicians, and providers in behavioral health, primary care, and other clinicians providing pain treatment. As done in previous research and clinical experiences by our research team, VA healthcare providers will be able to refer potentially eligible participants by distributing a study recruitment flyer, or by placing the investigators as additional signers on

notes using CPRS. Potential participants may be recruited from other studies that are IRB approved following completion of those other studies or if deemed ineligible. Only study staff that are approved on those studies will recruit those participants.

Screening. Study staff will screen by phone following a script. We are requesting a waiver of documentation of consent as Veterans will provide verbal consent to complete the screening measures. Veterans who report suicidal intent with a plan will undergo a standardized procedure. Veterans who meet initial eligibility who are interested in participating will be scheduled for a consent and baseline assessment appointment.

Consent Process and Baseline assessment. Veterans invited (in-person or telehealth) to the baseline assessment will be consented and will then complete a battery of measures administered by the coordinator. Telehealth options include phone, Teams, Cisco Webex, or VA Video Connect. Study staff will review the content of the consent and ensure comprehension. For consent processes completed via telehealth, study staff will send an RMS Azure VA encrypted email for Veterans. Study staff will review the content of the consent and ensure comprehension. The Veteran will then electronically sign the consent and send it back. The baseline assessment will start when the signed consent has been received. Participants will be remunerated $40 for completing the baseline assessment. Veterans can receive reimbursement through EFT or Direct Express debit card. Once the Veteran completes the enrollment paperwork, it will be immediately turned over to the Canandaigua or Syracuse VA cashier.

Randomization. Participants will be randomized to either the MBCT-S/P condition or Education condition. We will stratify the randomized assignment by gender given potential differences in predictors of suicidal ideation and pain outcomes in women compared to men.[44,45] We will use a block randomization procedure with block size of 4 to help ensure there balance between experimental and control condition.

MBCT-P/S condition. The active treatment to be evaluated in this study is MBCT-S/P, which will be developed by integrating elements of MBCT for chronic pain and suicide (manual included as an Appendix). MBCT-P is 8, ~60 minute-sessions structured to (a) review and discuss the previous session's homework, (b) practice skills by engaging in an activity and discussing the veteran's experience, (c) assign homework to continue learning about and practicing the skills, and (d) review the session's material. The primary goal of MBCT is to increase awareness of experiences to modify the way in which the individual relates to experiences. This allows the individual to have an opportunity to implement a strategy to respond to the experience, rather than operate out of habit.[46]

Table 2. Session breakdown of concepts and strategies learned

Session 1-5	Sessions 6-10
• Pain signals are affected by automatic experiences • Mindful eating to notice differ aspects of food • Body scan to notice sensations • Mindful breathing to notice body, break from autopilot	• Breath with no instruction • "Be" in experience instead of trying to change it • Notice changes in body during difficult experiences
• Interpretation affects emotions/sensation and stress response • Events that trigger beliefs then mood, behaviors; respond early • Pleasant experiences are missed; break the pain-stress cycle • Focus on breath with guidance on posture and labeling thoughts	• Different responses to same situation to see effect on mood • List of coping options for pain flares • Red flags for rising stress-pain • Plan to incorporate daily mindfulness practice
• Awareness of sights & sounds to break from autopilot • Breath to help identify changes in emotions and create stability • Awareness of stress & other experiences in the moment	• Attention to nourishing/depleting activities • Ways to ↑ nourishing and ↓ depleting activities • Self-care activities to use when red flag identified
• Thoughts and sounds come and go • Distance between unhelpful thoughts about pain • Slow movement noting changes in sensation	• How to practice skills from maintenance plan • Motivational strategies to encourage practice • Attention on various tactile aspects of an object

MBCT-P highlights the acceptance of pain; increased awareness of automatic thoughts related to one's response to pain; discriminating between nocioception, pain, and suffering; interrupting the relationship between negative emotions, fear of pain, and catastrophizing; refocusing attention from pain to pleasant experiences; and providing a rationale for and benefits of activity-rest cycles (activity pacing).[27,29,30,47] MBCT for Suicide places a greater emphasis on patterns and thoughts associated with suicidality and escalation of suicidal thoughts. This includes preparing an action plan to respond to suicidal crises by increasing awareness of warning signs, implementing coping skills, and having a list of personal and professional contacts who may assist in increasing immediate safety.[31,35,48] If participants need additional treatment, referrals will be made as

appropriate as with the Education condition. Rescheduling will be coordinated with the therapist. See Table 2 for session-by-session overview.

Education condition. We will use a health education control. The Education control provides information on the benefits of and guidelines for living a healthy lifestyle. The Education control is manualized and contains educational materials on topics such as diet, water consumption, exercise, social well-being and sleep. The topics will be delivered individually across 10 weekly, ~60 minute sessions. Importantly, the Education control is inert with respect to the outcomes of interest.[49-51] The Education condition, delivered individually by the study therapists, will help control for nonspecific conditions, such as providing attention or contact by the study staff, providing support or building rapport with study staff, managing participants' expectations of treatment outcomes, and provide behavioral activation because the veteran will need to attend in-person appointments. We anticipate that the Education condition contains enough pertinent and interesting material to engage the veteran over 10 sessions with support from previous studies indicating the information is useful and engaging and would recommend it to a friend.[49-51] Treatment satisfaction and the exit interview will provide key information about the Education condition should changes need to be made for the larger trial. As with the assessments, telehealth delivery of both MBCT-P/S and the education control will occur by phone, Cisco Webex, or VA Video Connect.

Therapist training and fidelity. The investigators will provide further training specific to the modified suicide- and pain-related elements of the intervention. The training will begin with a training session provided, which will involve a review of basic MBCT principles, rationale for using MBCT to reduce suicide risk and functional impairment based on empirical support, and a detailed description of MBCT-S/P with the manual and handouts. Although the Education condition provides basic health education information, the investigators will also provide training and supervision regarding the delivery of the Education condition, which will include strategies to decrease the cross-contamination of condition-specific content. Training for MBCT-S/P will include didactics, guided readings, role playing, and supervised training cases as needed until competency is met. We will monitor treatment fidelity by audio recording all intervention sessions via Webex, VA Video Connect, or a FIPS-compliant recorder. Once coders are reliable, we will randomly code 30% of these sessions to be coded separately by two independent raters with 20% of these double coded. We will use the fidelity tool during the delivery of the intervention to continue monitoring adherence and competence to deliver the treatment materials. Because the same therapists will also deliver the Education control, we will conduct random audio checks to ensure they are not delivering components of MBCT. During the treatment delivery, feedback will be given weekly to the therapist during supervision sessions to ensure fidelity to the intervention protocol is maintained.

Post-treatment assessments. Post-treatment assessments will be scheduled approximately within 1-month, 3-months, and 6-months following the treatment completion. Veterans will complete their exit interview at the first post-treatment assessment to describe their experiences related to the treatment. Participants will be remunerated $40 for the assessments using the same process as the baseline assessments. If participants drop out of treatment, they will still be eligible to complete the assessments unless they withdraw from participation. Assessments will be completed around the approximate time of when they would have been scheduled to complete the assessments.

Measures

The list of measures and their administration schedule is shown in Table 3.

Feasibility and acceptability: *Homework logs:* Participants will be instructed at the end of each session to track the days in which they practiced mindfulness skills since their last session using a tracking sheet. For each time practiced, they will also be asked to record the minutes in which they practiced the skills. *Session feedback forms***:** We will identify therapeutic components of each session and develop rating scale items to assess the helpfulness and relevance of the session topics for participants express their views for each session. *Exit interview.* The exit interview will comprise self-report measures and a semi-structured interview. The open-ended questions in the semi-structured interview will be administered by the trained research assistant. The interview will assess overall impressions and impact of treatment, relationship with the therapist, views of written materials and handouts, ways to improve the treatment, and any other additional feedback. The semi-structured format will allow specific content areas to be assessed, while also allowing participants to discuss other potentially important areas not included in the original interview. The interviews will be recorded for later evaluation by members of the research staff. Acceptability will also be assessed with items on a 5-

point rating scale in which participants indicate the extent to which they agree or disagree (from 1="Strongly Disagree" to 5="Strongly Agree") with statements about the relevance and helpfulness of treatment components. In addition to the exit interview, a modified version of the Abbreviated Acceptability Rating Scale (AARS) will be used to further assess treatment acceptability.[52] The Working Alliance Inventory assesses agreement on the tasks and tasks of therapy, and the development of a bond.[53]

Suicide risk: The Columbia Suicide Severity Rating Scale (CSSRS) will assess the presence and severity of suicidal ideation and behaviors in one's lifetime, over a specified period, and since the last visit.[39] The Interpersonal Needs Questionnaire (INQ-12) is a 12-item measure assessing thwarted belongingness (i.e., an unmet need for belonging) and perceived burdensomeness. The PHQ-9 assesses the frequency in which the respondent is bothered by nine symptoms of depression in the past two weeks.[54] The Beck Hopelessness Scale is a 20-item measure assessment hopelessness.[55] We will use the 5-item NIH Toolbox Loneliness Scale to assess loneliness.[56]

Pain outcomes: The Brief Pain Inventory[57] will be used to assess pain severity and pain interference. Pain severity consists of 4 items assessing current, average, worst, and least pain experienced. The pain interference subscale comprises 7 items assessing the extent to which pain interferes with various aspects of one's life (e.g., mood, sleep, daily activities).[57]The Veterans RAND-12 (VR-12) will be used to assess health-related quality of life and is comprised of physical and mental health component scores. There is strong psychometric support for the VR-12 across multiple disease systems in veterans.[58]

Potential mechanisms: The Five Facet Mindfulness Questionnaire (FFMQ) consists of 39 items that assess five elements of mindfulness: observing, describing, acting with awareness, non-judging of inner experience, and non-reactivity to inner experience. The Chronic Pain Acceptance Questionnaire (CPAQ)[59] is a 20-item measure that assesses two components of pain acceptance: pursuit of life activities regardless of pain and recognition that avoidance is not useful in adapting to chronic pain. Items are on a 0 ("never true") to 6 ("always true") rating scale with higher scores indicating higher levels of acceptance. The Tampa Scale of Kinesiophobia-11 (TSK) is an 11-item measure assessing pain-related fear of movement or injury. Research supports the scale's psychometric properties.[60] The Pain Catastrophizing Scale (PCS)[61] is a 13-item measure, with each item rated on a 5-point rating scale (0 = "Not at all" to 4 = "All the time"). The measure is divided into three subscales: magnification, rumination, and helplessness. Difficulties in Emotion Regulation Scale-16 (DERS-16) is a 16-item questionnaire used to examine general emotion regulation difficulties.[62] The *Pain Self-efficacy Questionnaire* (PSEQ) assesses one's confidence in performing activities while in pain.[63] To measure resilience, we will use the 6-item Brief Resilience Scale (BRS).[64]

Table 3: Schedule of measures

Measure	Screening	Base-line	1st follow-up	Subsequent follow-ups
Demographics	x			
PEG	x			
CSSRS*	x	x	x	x
COVID q's		x	x	x
ISI		x	x	x
BHS		x	x	x
BPI		x	x	x
CPAQ		x	x	x
COMM		x	x	x
FFMQ		x	x	x
INQ-12		x	x	x
PCS		x	x	x
PHQ-9**	x	x	x	x
TSK		x	x	x
NIH Loneliness		x	x	x
VR-12		x	x	x
BRS		x	x	x
PSEQ		x	x	x
PCL-5		x	x	x
DERS		x	x	x
AARP			x	
WAI			x	

*CSSRS items 1 and 2 used at screening. Lifetime and past 3 month CSSRS used at baseline and since last visit used for all follow-ups; **Item 9 used at screening.

Other data: We will assess participants' military background (e.g., service branch, years in service, deployment), gender, age, educational background, employment, income, ethnicity, and marital status. Demographics and military background will be collected at screening. Additional clinical characteristics will be assessed including insomnia severity as measured by the Insomnia Severity Index and PTSD symptomology assessed using the PTSD Checklist-5 (PCL-5).[65,66] Participants will also be asked about COVID-19 exposure, contraction, and impact in the past year at baseline, then will be modified to ask about since last appointment.

Additionally, the following data will be extracted from medical record: psychiatric and medical diagnoses; medications; and treatment utilization (e.g., primary care, behavioral health, pain management, emergency department). Because the medical record contains only VHA records and we will also ask participants about medication use and treatment utilization outside the VA. For training, the coordinator will code 12 charts unrelated to the study and then will meet with the PI to discuss and resolve issues. During the chart review for the study, the PI will overlap on 12 charts to facilitate agreement and ongoing discussion of differences will be addressed as needed.

Data analyses

A CONSORT flow chart of recruitment and retention will be completed for this project to track the number of veterans approached for screening, the number of those individuals meeting eligibility, and we will calculate the percent of eligible veterans who enrolled compared to those who were approached. We will also calculate the percentage of participants who complete the treatment protocol and those completing each of the follow-ups, by condition. Participant treatment adherence will also be assessed by tracking the number of days in which mindfulness skills were practiced between sessions and the average time per practice day will also be calculated. Reasons for drop-out will also be tracked, in addition to adverse events and serious adverse events. We will also evaluate the extent to which the treatment was delivered with fidelity and how long it takes the therapist to reach competence criteria using the modified MBCT-AAQS. Session-by-session participant feedback will be used to further examine potential reasons for drop-out and non-adherence, which can be integrated into our future study. This will be supplemented by the CSQ to assess overall acceptability of the treatment and exit interview to provide a richer understanding of participants' experiences during the treatment. For the analyses of semi-structured interviews, consistent with Consensual Qualitative Research,[67] we will use two raters to gain different perspectives, discuss their summarized responses, and reach a consensus on factors such as format, receptivity, and feasibility of the intervention. The PI will then check the work of the raters to further examine the domains, core ideas, and categories that describe the themes in the core ideas across domains. The data will be charted to help organize the results to make improvements to the study procedures, treatment, and participant engagement for the larger trial.

We will calculate means and standard deviations for outcomes at baseline, post-treatment, and follow-ups, in addition to change scores with the understanding that there will likely be large standard errors due to the relatively small sample size.[68] We will examine the distribution of the suicidal ideation severity scores to better determine how to use/analyze in a larger trial (e.g., dichotomize them at an appropriate cut point if highly skewed, treat as ordinal, treat as continuous). Our past trials suggest that suicidal ideation is highly skewed and kurtotic even amongst those with high ideation as an inclusion criterion. We will examine distributions for other measures as well to help refine use in the future trial. We will calculate within-group differences in the outcome measures as raw and change scores. We will examine correlations among baseline variables to examine if variables need to be included as stratification variables or as covariates in the future RCT testing the efficacy of MBCT-S/P vs. Education. This may also help identify potential moderators and mediators for the future larger trial. Keeping in mind that we will not perform any formal hypothesis testing due to inadequate sample size, for continuous outcome variables, we will use multiple regression models to examine treatment effects while controlling for demographics and/or baseline variables (e.g., PTSD). For dichotomous outcomes, we will use logistic regression analyses to examine the group effect while accounting for covariates.

We will also examine the extent to which our measures of client satisfaction (as measured by the AARP), therapist fidelity (scores on fidelity measures), and treatment adherence (sessions attended, days spent doing homework, time on homework) are associated with both pain and/or suicidal risk outcomes.

Data protections: Statistical data files will be kept on VINCI project servers maintained by VINCI OI&T personnel and only summarized data without PHI will be downloaded from VINCI to local storage media. Research staff will use an audited VINCI download utility to move summarized data for reports, presentations and publications from VINCI servers to local storage media. The VINCI download utility provides an audit path including a copy of the downloaded material. The data extraction tool will be adapted for use with software directly available on the VINCI platform (e.g. Microsoft Word and Excel) and study data will be stored and maintained on VINCI. All study personnel with access to sensitive patient data will stay current on their VA approved information security training and VA approved privacy policy training.

Additional protections: Several procedures for protecting participant confidentiality will be implemented to reduce the risk of revealing participant identity. All informed consent forms will contain identifying information.

In order to ensure confidentiality, each consent form will be labeled with a numeric identifier and will be stored in a double-locked file. These will be stored in separate double-locked files from other study materials. All electronic files, including therapy notes, will be maintained on a secure study folder behind the VA firewall. Only approved study team personnel will be granted access to this data. All identifiable information will be stored in a separate folder behind the firewall from the de-identified study ID and data.

Recorded interviews and intervention sessions may also contain identifying information. To ensure the protection of these materials, locked courier bags will be used to transport any sensitive study information (e.g., consents, audio recordings) between VA properties (e.g., from the Rochester VA Outpatient Clinic to the CoE) unless completed electronically for remote sessions. Upon arrival at the CoE, all recordings will be entered into the Audio Recording Log (noting study ID, date of upload, date of deletion from recorder, and staff responsible for upload/deletion), and uploaded to a secure study folder behind the VA firewall. Only approved study team personnel will be granted access to this data. In the unlikely event that a recording cannot be uploaded upon arrival at CoE, the study recorder will be stored in a double-locked file separate from other study materials. As an additional measure of protection, all study recorders are password protected and can only be turned on using a numerical password. Only study staff will be privy to this password.

During the consent process, participants will be informed of the limits of confidentiality, including if the participant is deemed to be a risk to self or others and if a child is abused or neglected. If participants report plans or intent to perform an act of violence or child abuse, the interviewer or study therapist will inform the PI. The PI will make a plan that could include a disclosure to clinical staff and making a child abuse report, depending on the nature of the information.

Data Safety and Monitoring Plan

Data Safety. To ensure safety of participants in the study proposed and validity and integrity of data collected, the PI (Ashrafioun) will oversee all data and safety monitoring functions and the research team will be advised that he will be the primary contact overseeing these activities. The investigators will meet regularly to monitor study progress and discuss the implementation of monitoring procedures. He will also meet regularly with the research coordinator and staff to review monitoring procedures and ensure all efforts are being taken to minimize risks to participants. We will have an independent Data Monitoring Committee (DMC) to help monitor safety issues. As indicated below, the PI will track all negative outcomes and incidents as well as conduct interim data analysis every 12 months after the study has started. The study design will be significantly modified (and even screening stopped) on the suggestion of the DMC that the study is creating potential harm to our participants.

The PI will regularly oversee all aspects of the study, including participant recruitment, informed consent, data collection, management, and analysis, as well as regularly assess the risk/benefit ratio associated with participation in the study. All research staff will participate in an intensive training to help them understand the importance of reducing the risk for participants and learning how to recognize and report any AE or SAE. SAEs may include: death, hospitalization due to worsening psychiatric symptoms or suicidal ideation, or all life threatening or disabling/incapacitating events among research participants. AEs may include, but are not limited to: physical injuries, worsened physical or mental health, or inadvertent disclosure of confidential research information.

If an SAE occurs, the PI will immediately contact the DMC and IRB, followed by a written report in 24 hours. He will make a decision whether there is sufficient evidence to suspend data collection, allow for further IRB review, modify the protocol, or make other changes to reduce potential risk to participants. The study will resume based on agreement of the PI, an IRB member (the chair will recuse himself because he is a co-I on the study), and the DMC. In the event that an AE that is not an SAE is reported to the PI, the PI will discuss the event with the DMC. Immediate evaluation will occur to determine if any extra steps can be taken to minimize the likelihood of that type of AE occurring again. If changes can be made, a report/amendment will be written and submitted to the DMC and IRB.

As part of a standard practice, the PI will supervise the implementation of one audit within 4 months after study recruitment and one regularly per year afterwards of the materials collected and produced as part of the study

at each site to ensure proper confidentiality and compliance with ethical principles, including informed consents, questionnaire data, and to make sure that the research staff are following established protocols. The PI will provide an annual summary report of all AEs to the IRB and the DMC as part of the annual review. If no adverse events have occurred, the report will state, “No adverse events affecting human participants have occurred during this project year.”

Data Monitoring. To ensure adequate participant recruitment and enrollment, each week, the PI will discuss the current number of participants contacted, screened, and enrolled from each site and compare those numbers to the expected based on our preliminary data. If after the first 4 months, it appears we are not reaching our expected number of participants, the PI will discuss potential barriers/obstacles and solutions with the DMC. Discussions regarding recruitment and enrollment will continue at each meeting with the DMC to ensure proper implementation of the study.

Data Monitoring Committee. The purpose of the DMC is to review protocols and consent documents for this study, monitor safety issues throughout the study, provide an overview of the quality of the accumulating data, and provide guidance on interim analyses and stopping rules. The DMC will be comprised of 3 individuals with no direct involvement in the study or conflict of interest with the research team conducting the clinical trial. The DMC will have expertise in: research and monitoring at-risk research participants; research in longitudinal clinical trials; and research expertise with chronic pain. The DMC responsibilities will include:

(1) Protect the safety of the participants
(2) Review, provide approval/disapproval, and provide suggestions to protocols, consent documents, and plans for data safety and monitoring.
(3) Monitor, provide suggestions, and report on ethical issues regarding protection of human subjects, and advise on ethical issues regarding AEs. The DMC will coordinate with the PI to report to the IRB any unanticipated problems involving risk. The DMC will provide potential solutions or other appropriate actions (e.g., altering inclusion/exclusion criteria, changing consent documents).
(4) Ensure appropriate balance between clinical care, safety, and patient confidentiality.
(5) Monitor data the progress of the trial. The DMC will periodically review outcome data for outcomes by treatment condition, including participant recruitment, retention, risks and benefits, and other factors that may affect outcomes. If differences in results between conditions appear to be clinically significant, the DMC will review whether the clinical trial should continue with or without further enrollment of new participants.
(6) Monitor and review any data relevant to quality control and safety.
(7) Make recommendations to the NCCIH about the continuation, termination, or changes to the trial based on benefits or adverse effects of the treatment.
(8) Communicate problems with the conduct, enrollment, sample size, and/or data collection to NCCIH

The PI will convene annually with the DMC for the duration of the study. The meetings will be held in-person or via video teleconference. The Board Chair and PI will decide on the format of the meetings. Additional meetings will be held on the recommendation of the Board Chair and PI and meeting logistics will be based on clinical urgency and the availability of the DMC. The PI will submit reports to the DMC a week prior to the scheduled meeting. Reports will include all data up to and including 2 weeks prior to the reporting deadline (except for SAEs, which are to be reported within 24 hours of an event). For each meeting at which the study is to be considered or monitored, the PI will present an overall progress statement containing the assurance that the PI has considered the clinical trial’s progress and that there is/is not evidence of safety issues that should be addressed by the DMC. The reports will also include information related to problems in recruitment, biases in attrition, biases with respect to AEs, or other operational problems that affect the integrity of the study. At the additional request of the DMC, interim analyses will be conducted to determine whether the emerging findings may lead to a discussion of discontinuing the trial early.

The DMC will be kept apprised of all SAEs and AEs on an ongoing basis and will decide whether individual patients should be removed from the protocol. Although research staff, under the PI’s supervision, are able to take whatever immediate action is necessary to safeguard the welfare of individual patients, the DMC will be called on whenever possible to make decisions as a result of a SAE. There may be rare instances where some

unanticipated situations occur that may affect participant welfare. In these situations, the IRB or the DMC may be contacted to help resolve the situation.

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