## Title

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# Do mindfulness interventions cause harm? Findings from the Learning to Apply Mindfulness to Pain (LAMP) Pragmatic Clinical Trial

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## Abstract

**Background:** Although mindfulness-based interventions (MBIs) are widely used in clinical and nonclinical settings, there has been little systematic study of their potential risks. To address this gap, we examined differences in psychological and physical worsening among participants in the usual care and intervention conditions of a 3-group, randomized pragmatic trial (Learning to Apply Mindfulness to Pain [LAMP]) that tested the effectiveness of 2 approaches to delivering MBIs to patients with chronic pain.

**Methods:** The sample consisted of 374 male and 334 female patients with chronic pain enrolled in the LAMP trial who completed a 10-week follow-up survey, 61% of whom had a mental health diagnosis. Psychological and physical worsening was assessed by a checklist asking whether participants experienced specific symptoms since beginning the study. We used multivariable logistic regression models with imputed data to determine whether predicted probabilities of increased symptoms differed between usual care and the 2 MBIs.

**Results:** Participants in usual care were more likely to report experiencing increased psychological and physical worsening than were those in the MBIs, including an increase in disturbing memories; sadness, anxiousness, and fatigue; isolation and loneliness; and feeling more upset than usual when something reminded them of the past.

**Conclusions:** MBIs do not appear to cause harm, in terms of increased symptoms, for this population of patients with chronic pain and high levels of mental health comorbidities.

**Clinical trial registration:** Preregistration with an analysis plan at www.ClinicalTrials.gov: NCT04526158. Patient enrollment began December 4, 2020.

**Keywords:** chronic pain; mindfulness; veterans; meditation-related adverse effects.

## Background

Mindfulness-based interventions (MBIs) are increasingly used in clinical and nonclinical populations.[1] Although MBIs have been extensively and rigorously studied, with a large experimental literature documenting their benefits for a range of outcomes, there is a lack of systematic research investigating their potential harms, which has led to diverging perspectives about their safety.[2–9]

Concern about possible meditation-related adverse effects (MRAE) has grown, particularly in light of case reports and observational studies documenting harm.[2,5,10–12] However, such study designs are limited in their ability to determine cause and effect. Additionally, reports of more severe MRAE, which have included depression, psychosis, mania, depersonalization, and traumatic re-experiencing, have occurred mainly in the context of intensive or long-term practice, such as during or immediately after a multi-day and immersive meditation retreat.[6,13] By contrast, there has been less evidence of MRAE associated with less intensive MBIs, such as Mindfulness-Based Stress Reduction (MBSR),[6] and in

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randomized control trials (RCTs). For example, a systematic review of 231 RCTs of MBIs (MBSR and Mindfulness-Based Cognitive Therapy) found no difference in rates of adverse events (AEs) between participants in the MBI and control conditions, and those AEs were rare (1% and 0.9%, respectively).[14] Likewise, an analysis of observational data from 2155 MBSR participants and data from 3 RCTs of MBSR ($n = 274$) found no evidence of harm and, for many measures, found that MBSR seemed to be protective[9] (but see Van Dam and Galante, 2023, for a critique).

Despite evidence pointing to the safety of MBIs, gaps in the literature remain.[2–5,7] Indeed, although the National Center for Complementary and Integrative Health's patient-facing website states that "meditation and mindfulness practices usually are considered to have few risks," it also notes that the lack of research precludes definite statements about safety.[15] Although documentation of AEs is required by the Consolidated Standards of Reporting Trials (CONSORT) guidelines, most published trials of MBIs do not report AEs.[7] For example, the previously mentioned systematic review of MBSR and Mindfulness-Based Cognitive Therapy trials found that 195 of 231 trials did not report AEs,[14] and a systematic review of 44 meta-analyses of MBIs found that adverse effects were discussed in only 15.[3] Moreover, because clinical trials in the European Union and the United States are required to report only AEs that are classified as serious, less severe AEs are rarely reported.[5,16,17] Additionally, the majority of MBI trials assess AEs through passive monitoring, based on participants' reporting AEs on their own, which likely leads to an undercount.[5,7] Although researchers have begun to actively monitor harms, they tend to focus on more serious AEs and use data from only participants who complete the intervention.[7] There is also scant research on individual difference factors, such as prior trauma or psychiatric conditions, that have been theorized to increase vulnerability to harm.[5,10,18]

The lack of rigorous research on MBI-related harms has important implications for research, practice, and policy. One chief issue is whether MBIs are safe for individuals with psychiatric conditions. Guidelines for MBSR include exclusion criteria for suicidality, psychosis (not treatable with medication), post-traumatic stress disorder (PTSD), major depressive disorder or other major psychiatric disorders (if the disorder interferes with participation), and social anxiety.[19] Guidelines in other institutions, however, such as the Veterans Health Administration, have few restrictions based on psychiatric conditions.[20] Although part of the rationale for these policies is to protect a vulnerable group from harm, restrictions that are too stringent, such as "blanket" restrictions based on mental health diagnoses rather than restrictions based on current functioning, might unnecessarily deprive individuals of the opportunity to benefit from participation in research studies or clinical programs using MBIs. This raises equity concerns, as groups that disproportionately experience psychiatric disorders, such as military veterans, women, and the socioeconomically disadvantaged, will be systematically excluded, and it also increases the likelihood that the results of MBI trials will not generalize to populations that would be most likely to benefit from MBIs in real-world settings.[21] Additionally, individuals with mental health disorders might be more highly motivated to participate and might accrue greater benefits than would those without.[1,7,22]

In sum, there is growing consensus on the need for more nuanced assessment of the potential harms of MBIs, which goes beyond reporting the serious AEs required by regulatory bodies. The present study helps address this knowledge gap by examining differences in perceived worsening of mental or physical functioning reported by participants in the control and intervention conditions of a randomized pragmatic trial of 2 MBIs for chronic pain, with harm defined as "outcomes worse than would have been expected in the absence of treatment."[9,23]

## Methods

### Design and participants

Data for this secondary analysis were obtained from the 10-week follow-up survey conducted as part of the LAMP (Learning to Apply Mindfulness to Pain) study, a 3-arm randomized clinical trial that tested the effectiveness of 2 approaches to delivering MBIs to patients with chronic pain.[24] A full description of the study aims and further details about the intervention and methods can be found in our study protocol publication.[24] The LAMP study was approved by the VA Central Institutional Review Board before data collection (C-IRB #18-21). All randomized participants provided verbal informed consent before enrollment, through the following approved protocol. Specifically, if a participant was deemed eligible after the screener, baseline, and chart review, a study staff member called the participant to review the study information sheet, which included the same elements required in a consent form but did not require a signature. Participants were required to agree that they wanted to enroll and participate in the LAMP study, which was considered verbal informed consent.

Participants were patients from the Minneapolis, Greater Los Angeles, and Durham VA Health Care Systems who had had 2 qualifying pain diagnoses in the electronic health record (EHR) within the same pain category on at least 2 occasions, at least 90 days apart, during the previous 2 years. These potentially eligible patients were mailed an invitation letter and brochure (initially by postal mail and then by email) and invited to log into the study website and complete a screening form to ascertain whether they met the following study criteria: a pain duration of ≥6 months, a pain severity score of ≥4 on the 0–10 numeric rating scale, access to a smartphone and internet, willingness to meet remotely online on the dates and at the time when sessions were held, willingness and ability to download the study mobile app, and absence of current enrollment in another study for their pain or in MBSR. Participants who met the study criteria had the opportunity to complete the online baseline survey. Of the 1945 patients who were eligible for the study according to the online study screener, we excluded 407 patients (21%) on the basis of chart review indicating active and uncontrolled psychotic symptoms, high risk for suicidality, severe depression, poorly controlled bipolar disorder, or a behavioral flag on their medical record indicating serious behavioral issues (see Table 1 in Supplementary Material for operational definitions). These patients were excluded for concerns about their own safety and that of other group members (eg, the need for psychological safety in the group), given that this program was designed to be delivered outside of a clinical setting and to be led by facilitators who were not required to have mental health training. A total of 419 female and 392

male patients were recruited from November 2020 to May 2022 and randomized to the Group MBI, Self-Paced MBI, or Usual Care conditions in a 1:1:1 ratio.

Both MBIs were 8 weeks in duration (preceded by a technical session) and aimed to address identified barriers to engaging in mindfulness interventions (eg, time, transportation), as well as the unique needs of veterans (eg, high prevalence of PTSD).[25] Participants were allowed to pursue usual care in the VA as they normally would. The MBIs consisted of prerecorded mindfulness educational and skill-building videos presented by instructors who were certified in MBSR, rated as "advanced" by the Mindfulness-Based Interventions: Teaching Assessment Criteria,[26] and trained in trauma-informed practices. Videos ranged from 7 to 15 minutes. Video content focused on essential elements of MBIs and provided veterans the opportunity to enhance their mindfulness-related knowledge and skills in regulating attention and emotions, establishing body awareness, and shifting self-perceptions.[26] Educational videos covered the following topics: Mindfulness and Pain, Working With the Mind–Body Connection, Being Kind to Yourself, Thoughts and Feelings, The Power of Perspective, Finding the Positive, Connecting Mindfully, and Finding Your Way. Skill training videos included mini-practices (1–2 minutes) to develop awareness of thoughts, feelings, and body sensations in everyday life; meditations (5–10 minutes) to develop awareness of thoughts, feelings, and body sensations; and mindful movement (7–9 minutes) to build body awareness and confidence in moving, as well as finding relief with simple exercises oriented toward mobility.

For the Group MBI, in-session video viewing was interspersed with workbook reflections and group discussions, led by trained facilitators who were not experts in mindfulness. Participants were encouraged to practice on their own between sessions, using a workbook, mobile app, and study website. The Self-Paced MBI consisted of the same curriculum and resources but did not include a group component. It was supplemented by 3 phone calls from a facilitator at the beginning, middle, and end of the intervention period to provide orientation and reminders, as well as identification of barriers to and facilitators of engagement.

The Usual Care arm was allowed to pursue usual care in VA system as they normally would according to their needs and preferences. They were not provided access to the MBI training during the intervention and follow-up period of the study (1 year). They were given access to MBI training materials after the entire follow-up period was complete.

## Measures

Data collection occurred at baseline and Week 10. Participants were paid $25 for each survey they completed.

## Baseline demographics and utilization of pain treatment

EHR data were used to assess gender and age. Survey questions assessed race, ethnicity, household financial situation, education, employment status, and utilization of pain treatment, including nonpharmacological treatment options. We also included a categorical variable for the medical facility from which a participant was recruited and a time variable (ie, cohort) to indicate when a participant was recruited.

## Mental and physical health

Survey measures assessed as part of the 10-week follow-up survey included the Brief Pain Inventory (BPI) interference and intensity scores[27]; the Patient-Reported Outcomes Measurement Information System (PROMIS)-29 Profile v.2.0 measures of physical function, anxiety, fatigue, sleep disturbance, and participation in social roles and activities[28]; depression, assessed by the Patient Health Questionnaire (PHQ)-8[29]; and PTSD, assessed by the Post Traumatic Stress Disorder (PTSD) Checklist for DSM-5 (PCL-5).[30] EHR data were used to capture mental health diagnoses. We used an algorithm used by prior researchers[31] to assess for the presence of mental health diagnoses in the sample. Specifically, EHR data were drawn from a 12-month period before the participant's index date. EHR records were flagged if they indicated a diagnosis of (1) a depressive disorder, (2) a bipolar disorder, (3) an anxiety disorder, (4) PTSD, (5) personality disorders, (6) schizophrenia, (7) a manic disorder, (8) attention-deficit hyperactivity disorder, (9) stress, (10) a substance use disorder (including alcohol but excluding tobacco), or (11) other serious mental illness. The definition for a diagnosis was at least 1 diagnosis code from an outpatient clinic or inpatient clinic. We constructed a dichotomous indicator for a mental health diagnosis of any kind, with a "1" representing having been diagnosed and a "0" representing no mental health diagnosis.

## Outcomes

We created a brief checklist of 7 negative outcomes selected on the basis of the prior literature and linked to established mechanisms of mindfulness meditation. This checklist was administered as part of the 10-week survey. Participants were asked, "Since you started your participation in the study, have you experienced any of the following? (Check all that apply): Increase in disturbing memories; feeling more upset than usual when something reminded you of the past; increased feelings of sadness; increased feelings of anxiousness; seizures; feeling more tired or fatigued than usual; feeling more isolated or lonely; physical or mental symptom (please specify) ___; none of the above."

## Statistical analyses

This was an exploratory analysis based on data from the parent trial, in which the sample size was based on power calculations for the primary analysis.[24] Eleven respondents (1.5% of the sample) had missing values for 10-week symptom data. Because symptoms were measured with a check-all-that-apply question, a participant was considered to have a missing value if the participant failed to respond to the question by not checking any of the options. To assess what predicted missingness, we created a binary indicator where a "1" denoted a missing value for the outcome and a "0" denoted a non-missing value. When regressing baseline demographic variables on that binary missingness indicator, we found that none of these measures predicted missing symptoms data. As a result, when conducting multiple imputation, we included only the covariates (ie, facility and cohort time) that were to be included in regression models. We used multiple imputation with chained equations (MICE), imputing 100 datasets with seed value set to 1337.

We used an intention-to-treat analysis with the 100 imputed datasets. For the effect of the Group MBI and Self-Paced MBI arms on symptoms, we fit multivariable logistic

regression models with the binary indicator for experiencing a given symptom as the dependent variable and the 3-level categorical variable for each arm as the independent variable. Each model was fit separately for the 9 symptom outcomes and included dummy indicators for facility and time of enrollment (ie, "cohort time") as covariates. To estimate whether the effect of the 2 intervention arms on symptom probability differed by mental health diagnosis, we interacted the 3-level intervention assignment variable with an indicator for a mental health diagnosis. Predicted probabilities were calculated from all models with the *mimrgns* community-contributed command,[32] whereas *P* values comparing the intervention arms with usual care were calculated with the *pwcompare* option of the *margins* command. All statistical analyses were conducted in Stata version 15.1.

## Results

### Study participants

Figure 1 delineates participant enrollment and follow-up. The 10-week survey response rate was 87% (93% Usual Care; 88% Group MBI; 82% Self-Paced MBI). Table 1 shows the demographic characteristics of the sample overall and by intervention arm. The sample was 53% male, with a mean age of 55 (SD, 13) years. Sixty-nine percent were White, and 25% were Black. Thirty-three percent were unemployed or

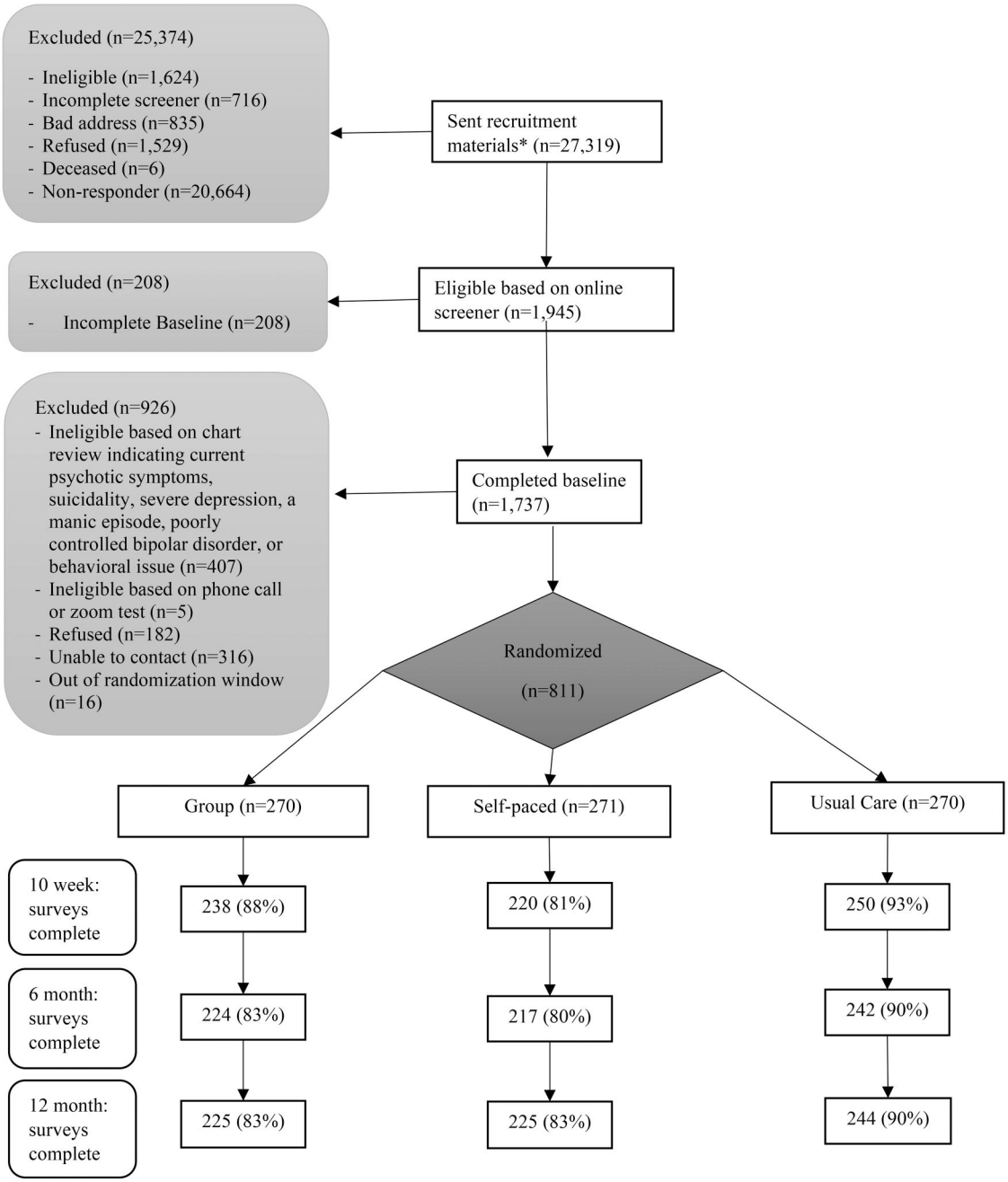


**Figure 1.** CONSORT flow diagram.

**Table 1.** Baseline demographic and health characteristics by condition among 10-week survey completers.

| | Group MBI ($n = 238$) | Self-Paced MBI ($n = 220$) | Usual Care ($n = 250$) | Total ($n = 708$) |
|---|---|---|---|---|
| Age, mean (SD) | 54 (13) | 56 (13) | 56 (12) | 55 (13) |
| Gender, *n* (%) | | | | |
| Male | 124 (52%) | 118 (54%) | 132 (53%) | 374 (53%) |
| Female | 114 (48%) | 102 (46%) | 118 (47%) | 334 (47%) |
| Hispanic or Latino, *n* (%) | | | | |
| No | 227 (95%) | 206 (94%) | 230 (92%) | 663 (94%) |
| Yes | 11 (5%) | 13 (6%) | 20 (8%) | 44 (6%) |
| Race, *n* (%) | | | | |
| White | 163 (69%) | 153 (70%) | 169 (68%) | 485 (69%) |
| Black | 62 (26%) | 52 (24%) | 60 (24%) | 174 (25%) |
| American Indian / Alaskan Native | 2 (1%) | 2 (1%) | 6 (2%) | 10 (1%) |
| Asian | 1 (0%) | 3 (1%) | 2 (1%) | 6 (1%) |
| Multiracial | 8 (3%) | 10 (5%) | 11 (4%) | 29 (4%) |
| Employment status, *n* (%) | | | | |
| Working | 98 (41%) | 82 (37%) | 98 (39%) | 278 (39%) |
| Not working | 72 (30%) | 74 (34%) | 91 (36%) | 237 (33%) |
| Retired | 68 (29%) | 64 (29%) | 61 (24%) | 193 (27%) |
| Household financial situation, *n* (%) | | | | |
| Live comfortably | 75 (32%) | 68 (31%) | 87 (35%) | 230 (32%) |
| Meet your basic expenses with a little left over for extras | 110 (46%) | 89 (40%) | 90 (36%) | 289 (41%) |
| Just meet your basic expenses | 47 (20%) | 53 (24%) | 61 (24%) | 161 (23%) |
| Don't even have enough to meet basic expenses | 6 (3%) | 10 (5%) | 12 (5%) | 28 (4%) |
| Education, *n* (%) | | | | |
| <4-year degree | 120 (50%) | 106 (48%) | 125 (50%) | 351 (50%) |
| 4-year degree or above | 118 (50%) | 114 (52%) | 125 (50%) | 357 (50%) |
| Scores, mean (SD) | | | | |
| BPI—Total | 6 (2) | 5 (2) | 6 (2) | 6 (2) |
| BPI—Interference | 6 (2) | 5 (2) | 6 (2) | 6 (2) |
| BPI—Intensity | 6 (2) | 5 (2) | 6 (2) | 6 (2) |
| Physical function (PROMIS) | 12 (3) | 12 (3) | 12 (4) | 12 (3) |
| Anxiety (PROMIS) | 10 (4) | 10 (4) | 10 (4) | 10 (4) |
| Fatigue (PROMIS) | 14 (4) | 14 (4) | 14 (4) | 14 (4) |
| Sleep disturbance (PROMIS) | 14 (4) | 14 (4) | 14 (4) | 14 (4) |
| Participation in social roles and activities (PROMIS) | 10 (3) | 11 (3) | 10 (3) | 10 (3) |
| Depression symptoms (PHQ-8) | 10 (6) | 9 (6) | 9 (6) | 9 (6) |
| PTSD checklist (PCL5) | 26 (19) | 27 (20) | 27 (20) | 27 (20) |
| Mental health diagnoses, *n* (%) | | | | |
| Depressive disorders | 93 (39%) | 91 (41%) | 91 (36%) | 275 (39%) |
| Anxiety disorders | 57 (24%) | 52 (24%) | 55 (22%) | 164 (23%) |
| Opioid use disorder | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| Drug/alcohol use disorders | 16 (7%) | 14 (6%) | 21 (8%) | 51 (7%) |
| Post-traumatic stress disorder (PTSD) | 56 (24%) | 55 (25%) | 67 (27%) | 178 (25%) |
| Any mental health diagnosis | 141 (59%) | 143 (65%) | 150 (60%) | 434 (61%) |
| Pain treatment in past 3 months, *n* (%) | | | | |
| Acupuncture | 33 (14%) | 42 (19%) | 46 (18%) | 121 (17%) |
| Manipulation | 74 (31%) | 83 (38%) | 91 (36%) | 248 (35%) |
| Massage | 101 (42%) | 96 (44%) | 99 (40%) | 296 (42%) |
| Yoga | 49 (21%) | 42 (19%) | 52 (21%) | 143 (20%) |
| Tai Chi / qigong | 13 (5%) | 15 (7%) | 11 (4%) | 39 (6%) |
| Exercise | 161 (68%) | 164 (75%) | 177 (71%) | 502 (71%) |
| Relaxation techniques | 104 (44%) | 102 (46%) | 124 (50%) | 330 (47%) |
| Meditation/mindfulness | 65 (27%) | 60 (27%) | 74 (30%) | 199 (28%) |
| Psychotherapy/counseling | 60 (25%) | 52 (24%) | 70 (28%) | 182 (26%) |
| Other pain treatments | | | | |
| Spinal injections | 25 (11%) | 21 (10%) | 29 (12%) | 75 (11%) |

BPI (Brief Pain Inventory): mean of items scored 0–10, where higher scores mean greater pain interference or intensity. PROMIS scales: Each is sum of 4 items scored 1–5. PHQ-8: sum of 8 items scored 0–3, where higher scores reflect greater depression. PCL5 (Post-Traumatic Stress Disorder Checklist): sum of 20 items scored 0–4 for a range of 0–80, where 31 is threshold for PTSD.

unable to work, 27% were retired, and 39% were employed. Half had a 4-year degree or higher. When describing their financial situation, 4% were unable to meet their basic needs. Sixty-one percent had at least one mental illness diagnosis in the EHR, the most prevalent of which was a depressive disorder (39%). There were no significant differences at baseline among the 3 arms on baseline measures, including measures related to the outcomes assessed at 10 weeks (eg, anxiety and depression symptoms, sleep disturbance, fatigue) and participants' use of pain treatments in the prior 3 months.

**Table 2.** Symptom probabilities (and confidence intervals) by intervention arm.

| Side effect | Group MBI | Self-Paced MBI | Usual Care |
|---|---|---|---|
| Increased feelings of anxiousness | 12%* (8% to 16%) | 11%* (7% to 15%) | 27% (21% to 32%) |
| Feeling more tired or fatigued than usual | 14%* (10% to 19%) | 15%* (10% to 19%) | 42% (36% to 48%) |
| Feeling more isolated or lonely | 9%* (6% to 13%) | 6%* (3% to 9%) | 23% (18% to 29%) |
| Increase in disturbing memories | 4%* (2% to 7%) | 7%* (3% to 10%) | 13% (9% to 17%) |
| Feeling more upset than usual when something reminded you of the past | 8%* (4% to 11%) | 7%* (4% to 10%) | 16% (11% to 20%) |
| Seizures | — | — | — |
| Increased feelings of sadness | 7%* (4% to 10%) | 6%* (3% to 9%) | 19% (14% to 24%) |
| Other physical or mental symptoms | 5%* (2% to 7%) | 2%* (<1% to 5%) | 13% (8% to 17%) |
| None of the above | 74%* (68% to 79%) | 77%* (71% to 83%) | 47% (41% to 53%) |

Estimates are predicted probabilities for reporting a given symptom at 10-week follow-up, generated from multivariable logistic regression models with facility and cohort time as covariates. Estimates marked with (*) are statistically significantly different from usual care at $P < 0.05$. No estimates for seizures are presented because of the small numbers of cases, preventing regression models from generating estimates (there were 0 reported seizures in the Group MBI, 1 seizure in the Self-Paced MBI, and 2 seizures in the Usual Care arm).

**Table 3.** Symptom probabilities (and confidence intervals) by intervention arm and diagnosed mental health status.

| Symptom | Group MBI | Self-Paced MBI | Usual Care |
|---|---|---|---|
| Mental health diagnosis = yes | | | |
| Increased feelings of anxiousness | 15%[a] (9% to 21%) | 14%[a] (8% to 19%) | 36% (29% to 44%) |
| Feeling more tired or fatigued than usual | 16%[a] (10% to 22%) | 15%[a] (10% to 21%) | 45% (37% to 53%) |
| Feeling more isolated or lonely | 12%[a] (6% to 17%) | 7%[a] (3% to 11%) | 30% (22% to 37%) |
| Increase in disturbing memories | 5%[a] (2% to 9%) | 8%[a] (4% to 13%) | 17% (11% to 23%) |
| Feeling more upset than usual when something reminded you of the past | 11% (6% to 16%) | 8%[a] (3% to 12%) | 19% (12% to 25%) |
| Seizures | — | — | — |
| Increased feelings of sadness | 11%[a] (5% to 16%) | 7%[a] (3% to 12%) | 23% (16% to 30%) |
| Other physical or mental symptoms | 6%[a] (2% to 10%) | 1%[a] (<1% to 3%) | 17% (11% to 23%) |
| None of the above | 69%[a] (61% to 76%) | 74%[a] (67% to 81%) | 41% (33% to 49%) |
| Mental health diagnosis = no | | | |
| Increased feelings of anxiousness | 6% (1% to 11%) | 5% (<1% to 11%) | 13% (6% to 19%) |
| Feeling more tired or fatigued than usual | 12%[b] (5% to 19%) | 13%[b] (5% to 20%) | 37% (28% to 47%) |
| Feeling more isolated or lonely | 5%[b] (1% to 10%) | 3%[b] (<1% to 7%) | 14% (7% to 21%) |
| Increase in disturbing memories | 2% (<1% to 5%) | 4% (<1% to 8%) | 7% (2% to 12%) |
| Feeling more upset than usual when something reminded you of the past | 2%[b] (<1% to 5%) | 5% (<1% to 10%) | 12% (5% to 18%) |
| Seizures | — | — | — |
| Increased feelings of sadness | 2%[b] (<1% to 5%) | 3%[b] (<1% to 6%) | 13% (6% to 20%) |
| Other physical or mental symptoms | 3% (<1% to 6%) | 4% (<1% to 9%) | 7% (2% to 12%) |
| None of the above | 81%[b] (73% to 89%) | 84%[b] (75% to 92%) | 56% (46% to 66%) |

Estimates are predicted probabilities for reporting a given symptom at 10-week follow-up, generated from multivariable logistic regression models with an interaction between intervention arm and a mental health diagnosis indicator, and with facility and cohort time as covariates.

[a] Value in an intervention arm that is statistically significantly different from usual care (at $P < .05$) among the subsample of participants with a mental health diagnosis.

[b] Value in an intervention arm that is statistically significantly different from usual care (at $P < .05$) among the subsample of participants without a mental health diagnosis.

No estimates for seizures are presented because of the small numbers of cases, preventing regression models from generating estimates (there were 0 reported seizures in the Group MBI, 1 seizure in the Self-Paced MBI, and 2 seizures in the Usual Care arm).

There were no significant differences in participants' use of pain treatments at the 10-week assessment (see Table 2, Supplementary Material), except for the use of relaxation techniques and meditation/mindfulness at 10 weeks, which was higher in the 2 MBI groups.

Participants randomized to the Group MBI arm and the Self-Paced MBI arm had statistically significant lower probabilities of all symptoms at 10-week follow-up than did the Usual Care group (Table 2). Seizures were not included because too few occurred to estimate an effect. Adjusted for cohort time and facility (and after the exclusion of seizures), among Group MBI participants, fatigue was the most probable symptom experienced at 10-week follow-up (probability 14% [confidence interval (CI): 10% to 19%]). Anxiousness was the second-most common symptom in this group (12% [CI: 8% to 16%]). Group MBI participants had a high likelihood of reporting that they had experienced none of the listed symptoms at 10-week follow-up (74% [CI: 68% to 79%]). Participants in the Self-Paced MBI arm had similar predicted probabilities for 10-week symptoms as the Group MBI participants. Across both intervention arms, the predicted probability of any one symptom did not rise above 15%. In the Usual Care arm, symptom probabilities ranged from 13% (CI: 8% to 16%) for disturbing memories to 42% (CI: 36% to 48%) for fatigue.

Table 3 shows predicted probabilities and $P$ values for symptoms across intervention arm and mental health

diagnosis status. When the differential effect of the intervention across mental health status was estimated, the pattern of results varied between those who did and those who did not have a mental health diagnosis. Overall, there were more statistically significant differences between the intervention arms and usual care among participants who had a mental health diagnosis.

Among the subsample without a diagnosed mental health condition, neither intervention arm showed a statistically significant difference in anxiousness compared with usual care (6% [CI: 1% to 11%] for Group MBI and 5% [CI: <1% to 11%] for Self-Paced MBI, compared with 13% [CI: 6% to 19%] for usual care). Increases in disturbing memories and other physical or mental symptoms also did not differ statistically significantly between the intervention arms and usual care. The Self-Paced MBI subsample also did not differ from usual care in "feeling more upset than usual when something reminded you of the past."

## Discussion

In a pragmatic randomized trial of MBIs among patients with chronic pain, those randomized to the usual care condition were significantly more likely to report experiencing poorer self-reported physical and mental functioning 10 weeks after the start of the study than were participants in either of the MBI study arms. With harm defined as outcomes worse with treatment than no treatment,[9,23] the Group and Self-Paced MBIs did not appear to cause harm, according to the outcomes we assessed, although this approach did not consider the broader array of possible AE harms. Instead, the MBI conditions appeared to have had a protective effect for this population of patients with chronic pain, the majority of whom had comorbid mental health disorders. These results are consistent with a recent study finding MBSR to have protective effects against physical and psychological harms.[9] Moreover, MBIs appeared to have more beneficial effects among participants who had a mental health diagnosis than among those without a diagnosis.

This study design addresses several criticisms of the extant literature on the harms of MBIs. First, it is one of the few studies to actively assess the risks of MBIs via survey methods, including the assessment of different domains of functioning independently, with a structured instrument.[7,23] It is also one of the few studies to prospectively assess harm among control and intervention participants, which mitigates threats to validity that occur in the absence of a control condition, when mental and physical deterioration among MBI participants is attributed to the MBI. Additionally, high survey response rates and the use of an intent-to-treat analysis allay concerns that those experiencing MRAE are more likely to drop out of treatment and hence not be included in analyses.[7,8] Another strength is the use of a pragmatic randomized trial, designed to test intervention effectiveness in more generalizable, "real-world" conditions with minimal exclusion criteria, versus "explanatory" trials, with more stringent exclusion criteria.[33] Accordingly, we included participants with mental health diagnoses (61% of our sample), such as depression, anxiety, PTSD, and substance use disorders, all of which are highly comorbid with chronic pain in this population.

This study calls into question the blanket exclusion of individuals with mental health disorders and psychiatric conditions from participating in MBIs in research and practice on the basis of having a mental health diagnosis, in contrast to a more nuanced approach based on an assessment of current functioning. It also calls into question similar policies in which such patients are routinely excluded from trials of nonpharmacological treatment for pain.[21,34] Given the potentially protective effect uncovered in the present study, overly restrictive criteria limiting patients with mental health disorders from participating in MBIs could have a net effect of increasing harm. In this way, such policies could exacerbate disparities, as individuals with psychiatric conditions are disproportionately likely to be part of marginalized and disadvantaged groups. There is also a need to advance an inclusive research agenda for individuals with more complex mental and behavioral health conditions, examining how MBIs could be adapted to benefit such individuals, while ensuring their safety and understanding the circumstances under which the benefits of MBIs are likely to outweigh the risks. For example, future research could examine a version of Self-Paced MBI, adapted to be delivered as part of individual psychotherapy, for those with more serious psychiatric conditions. These findings also underscore the risk involved in usual care that would not be discerned without a control condition and that is often not considered in risk/benefit analyses of interventions.

There are several limitations to this study and potential alternative explanations. Results from this treatment-seeking population of VA patients with chronic pain and high rates of mental health comorbidities might not generalize to other populations. Alternative explanations for the findings include the "nocebo effect," in which random assignment to the control condition leads to worsening negative expectancies.[8] However, that being assigned to a control condition would lead to such high rates of physical and psychological worsening seems implausible in this population who had many risk factors that likely contributed to deterioration, such as chronic pain, high levels of comorbid mental health conditions, and negative impacts from the COVID-19 pandemic. Another explanation is bias due to demand characteristics, such that participants in the MBIs were motivated to avoid reporting negative events. However, we minimized the likelihood of this by assessing outcomes almost entirely through online questionnaires. Additionally, because this study focused on group comparisons between control and MBI conditions, we were unable to ask participants to indicate worsening that they attributed to the MBI. Future research should incorporate measures specifically designed to assess mindfulness adverse effects, such as the recently developed Meditation Experiences Interview, which systematically assesses the frequency, duration, and intensity of a broad range of MRAE.[7] Studies should also assess potential longer-term adverse effects beyond the intervention period.[8]

It should be noted that the LAMP MBIs were specifically designed for a veteran population with high levels of psychiatric comorbidities, including PTSD, with a particular focus on addressing the psychological needs of female veterans, who have high rates of military sexual trauma, sexual abuse, and childhood trauma.[35–38] Programs were aimed at individuals new to mindfulness and were considered "entry level." Compared with the commonly studied MBSR programs, the MBI sessions in this study were shorter (eg, no more than 1 hour, compared with 2.5 hours), there was no daylong retreat, and guided meditations were purposely shorter (no

more than 10 minutes) to prevent psychological distress. The primary mindfulness expert (A.C.H.) had a background in trauma-informed mindfulness, and the consultant (J.G.S.) was a national expert on mindfulness in VA; their expertise informed the intervention design and facilitator training protocol. Videos, including guided meditations, were recorded in a female voice and a male voice. All videos reminded participants to be attentive to feelings of distress and provided instructions for relieving distress or discontinuing practice. Each group included 2 trained facilitators with backgrounds in trauma and counseling, one of whom led the session and one of whom monitored participants and was attuned to potential distress and trained to activate a manualized safety protocol if needed. Participants were encouraged to do what felt safe to them (eg, they could meditate with eyes open or closed). Shorter, guided meditations were used, and there was not a daylong retreat. Hence our findings that MBIs did not appear to cause harm might not generalize to MBIs that do not incorporate these types of safety considerations.

## Conclusion

In this pragmatic trial of patients with chronic pain, the majority of whom had comorbid mental health conditions, participants in 2 MBIs designed for a veteran population with high levels of psychiatric comorbidities (eg, trauma informed, with shorter, guided meditations) were significantly less likely to experience psychological and physical deterioration than were participants in usual care. These findings add to the nascent literature showing MBIs to be relatively safe,[6,14] although more research is needed.

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*Transparency and openness:* A limited de-identified dataset is available upon request and execution of required data use agreement(s).

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## Supplementary material

Supplementary material is available at *Pain Medicine* online.

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## Supplement statement

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## References

1. Creswell JD. Mindfulness interventions. *Annu Rev Psychol*. 2017;68:491-516.
2. Baer R, Crane C, Miller E, Kuyken W. Doing no harm in mindfulness-based programs: conceptual issues and empirical findings. *Clin Psychol Rev*. 2019;71:101-114. https://doi.org/10.1016/j.cpr.2019.01.001
3. Goldberg SB, Riordan KM, Sun S, Davidson RJ. The empirical status of mindfulness-based interventions: a systematic review of 44 meta-analyses of randomized controlled trials. *Perspect Psychol Sci*. 2022;17(1):108-130. https://doi.org/10.1177/1745691620968771
4. Van Dam NT, van Vugt MK, Vago DR, et al. Mind the hype: a critical evaluation and prescriptive agenda for research on mindfulness and meditation. *Perspect Psychol Sci*. 2018;13(1):36-61. https://doi.org/10.1177/1745691617709589
5. Farias M, Maraldi E, Wallenkampf KC, Lucchetti G. Adverse events in meditation practices and meditation-based therapies: a systematic review. *Acta Psychiatr Scand*. 2020;142(5):374-393. https://doi.org/10.1111/acps.13225
6. Binda DD, Greco CM, Morone NE. What are adverse events in mindfulness meditation? *Glob Adv Health Med*. 2022;11:2164957X221096640. https://doi.org/10.1177/2164957X221096640
7. Britton WB, Lindahl JR, Cooper DJ, Canby NK, Palitsky R. Defining and measuring meditation-related adverse effects in mindfulness-based programs. *Clin Psychol Sci*. 2021;9(6):1185-1204. https://doi.org/10.1177/2167702621996340
8. Van Dam NT, Galante J. Underestimating harm in mindfulness-based stress reduction. *Psychol Med*. 2023;53(1):292-294.
9. Hirshberg MJ, Goldberg SB, Rosenkranz M, Davidson RJ. Prevalence of harm in mindfulness-based stress reduction. *Psychol Med*. 2020;52(6):1080-1088. https://doi.org/10.1017/S0033291720002834
10. Aizik-Reebs A, Shoham A, Bernstein A. First, do no harm: an intensive experience sampling study of adverse effects to mindfulness training. *Behav Res Ther*. 2021;145:103941. https://doi.org/10.1016/j.brat.2021.103941
11. Cebolla A, Demarzo M, Martins P, Soler J, Garcia-Campayo J. Unwanted effects: is there a negative side of meditation? A multicentre survey. *PLoS One*. 2017;12(9):e0183137. https://doi.org/10.1371/journal.pone.0183137
12. Schlosser M, Sparby T, Voros S, Jones R, Marchant NL. Unpleasant meditation-related experiences in regular meditators: prevalence, predictors, and conceptual considerations. *PLoS One*. 2019;14(5):e0216643. https://doi.org/10.1371/journal.pone.0216643

13. Britton WB. Can mindfulness be too much of a good thing? The value of a middle way. *Curr Opin Psychol*. 2019;28:159-165. https://doi.org/10.1016/j.copsyc.2018.12.011
14. Wong S, Chan JY, Zhang D, Lee EK, Tsoi KK. The safety of mindfulness-based interventions: a systematic review of randomized controlled trials. *Mindfulness*. 2018;9(5):1344-1357.
15. National Institutes of Health. Meditation and mindfulness: what you need to know. Accessed March 23, 2023. https://www.nccih.nih.gov/health/meditation-and-mindfulness-what-you-need-to-know
16. Zorzela L, Golder S, Liu Y, et al. Quality of reporting in systematic reviews of adverse events: systematic review. *BMJ*. 2014;348:f7668. https://doi.org/10.1136/bmj.f7668
17. Kuyken W, Warren FC, Taylor RS, et al. Efficacy of mindfulness-based cognitive therapy in prevention of depressive relapse: an individual patient data meta-analysis from randomized trials. *JAMA Psychiatry*. 2016;73(6):565-574. https://doi.org/10.1001/jamapsychiatry.2016.0076
18. Goldberg SB, Lam SU, Britton WB, Davidson RJ. Prevalence of meditation-related adverse effects in a population-based sample in the United States. *Psychother Res*. 2022;32(3):291-305. https://doi.org/10.1080/10503307.2021.1933646
19. Santorelli SF, Meleo-Meyer F, Koerbel L. *Mindfulness-Based Stress Reduction (MBSR): Authorized Curriculum Guide*. University of Massachusetts Medical School, Center for Mindfulness in Medicine, Health Care, and Society; 2017.
20. Serpa JG, Taylor SL, Tillisch K. Mindfulness-based stress reduction (MBSR) reduces anxiety, depression, and suicidal ideation in veterans. *Med Care*. 2014;52(12 suppl 5):S19-24. https://doi.org/10.1097/MLR.0000000000000202
21. Ali J, Davis AF, Burgess DJ, et al. Justice and equity in pragmatic clinical trials: considerations for pain research within integrated health systems. *Learn Health Syst*. 2021;6(2):e10291.
22. Polusny MA, Erbes CR, Thuras P, et al. Mindfulness-based stress reduction for posttraumatic stress disorder among veterans: a randomized clinical trial. *JAMA*. 2015;314(5):456-465. https://doi.org/10.1001/jama.2015.8361
23. Dimidjian S, Hollon SD. How would we know if psychotherapy were harmful? *Am Psychol*. 2010;65(1):21-33. https://doi.org/10.1037/a0017299
24. Burgess DJ, Evans R, Allen KD, et al. Learning to Apply Mindfulness to Pain (LAMP): design for a pragmatic clinical trial of two mindfulness-based interventions for chronic pain. *Pain Med*. 2020;21(suppl 2):S29-S36.
25. Lehavot K, Katon JG, Chen JA, Fortney JC, Simpson TL. Post-traumatic stress disorder by gender and veteran status. *Am J Prev Med*. 2018;54(1):e1-e9.
26. Crane RS, Hecht FM. Intervention integrity in mindfulness-based research. *Mindfulness (N Y)*. 2018;9(5):1370-1380. https://doi.org/10.1007/s12671-018-0886-3
27. Cleeland CS, Ryan KM. Pain assessment: global use of the Brief Pain Inventory. *Ann Acad Med Singap*. 1994;23(2):129-138.
28. Cook KF, Jensen SE, Schalet BD, et al. PROMIS measures of pain, fatigue, negative affect, physical function, and social function demonstrated clinical validity across a range of chronic conditions. *J Clin Epidemiol*. 2016;73:89-102. https://doi.org/10.1016/j.jclinepi.2015.08.038
29. Kroenke K, Strine TW, Spitzer RL, Williams JB, Berry JT, Mokdad AH. The PHQ-8 as a measure of current depression in the general population. *J Affect Disord*. 2009;114(1-3):163-173. https://doi.org/10.1016/j.jad.2008.06.026
30. Weathers FW, Litz BT, Keane TM, Palmieri PA, Marx BP, Schnurr PP. The PTSD Checklist for DSM-5 (PCL-5). 2013.
31. Meis LA, Noorbaloochi S, Hagel Campbell EM, et al. Sticking it out in trauma-focused treatment for PTSD: it takes a village. *J Consult Clin Psychol*. 2019;87(3):246-256. https://doi.org/10.1037/ccp0000386
32. MIMRGNS: Stata Module to Run Margins after mi Estimate. Version revised 25 Jul 2022. Statistical Software Components S457795. 2014. Accessed April 10, 2023. https://ideas.repec.org/c/boc/bocode/s457795.html
33. Thorpe KE, Zwarenstein M, Oxman AD, et al. A pragmatic-explanatory continuum indicator summary (PRECIS): a tool to help trial designers. *CMAJ*. 2009;180(10):E47-E57. https://doi.org/10.1503/cmaj.090523
34. Heapy AA, Driscoll MA, Buta E, et al. Co-Operative Pain Education and Self-management (COPES) Expanding Treatment for Real-World Access (ExTRA): pragmatic trial protocol. *Pain Med*. 2020;21(12 suppl 2):S21-S28. https://doi.org/10.1093/pm/pnaa365
35. Driscoll MA, Higgins DM, Seng EK, et al. Trauma, social support, family conflict, and chronic pain in recent service veterans: does gender matter? *Pain Med*. 2015;16(6):1101-1111. https://doi.org/10.1111/pme.12744
36. Cichowski SB, Rogers RG, Clark EA, Murata E, Murata A, Murata G. Military sexual trauma in female veterans is associated with chronic pain conditions. *Mil Med*. 2017;182(9):e1895-e1899. https://doi.org/10.7205/MILMED-D-16-00393
37. Zinzow HM, Grubaugh AL, Monnier J, Suffoletta-Maierle S, Frueh BC. Trauma among female veterans: a critical review. *Trauma Violence Abuse*. 2007;8(4):384-400. https://doi.org/10.1177/1524838007307295
38. Turner AP, Harding KA, Brier MJ, Anderson DR, Williams RM. Military sexual trauma and chronic pain in veterans. *Am J Phys Med Rehabil*. 2020;99(11):1020-1025. https://doi.org/10.1097/PHM.0000000000001469


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