



NATIONAL DEFENSE RESEARCH INSTITUTE

Mindfulness Meditation for Chronic Pain

A Systematic Review

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Preface

The Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury is interested in determining the efficacy and comparative effectiveness of integrative medicine approaches for several health conditions. This systematic review assesses the safety and efficacy of mindfulness meditation as an intervention to alleviate chronic pain. The review will be of interest to military health policymakers and practitioners, civilian health care providers, and policymakers, payers, and patients.

None of the authors has any conflicts of interest to declare.

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Abstract

This systematic review synthesized evidence on mindfulness meditation interventions for the treatment of chronic pain (PROSPERO 2015:CRD42015025052).

In June 2015, we searched four electronic databases, as well as bibliographies of existing systematic reviews, to identify randomized controlled trials (RCTs) testing the efficacy and safety of mindfulness to treat adults with chronic pain. Two independent reviewers screened identified literature using predetermined eligibility criteria, abstracted study-level information, and assessed the quality of included studies. Outcomes of interest included changes in pain symptoms, use of analgesics, health-related quality of life, and adverse events. Efficacy meta-analyses used the Hartung-Knapp-Sidik-Jonkman method for random-effects models. The quality of evidence was assessed using the GRADE approach.

In total, 28 RCTs met inclusion criteria; three of these RCTs reported on safety. Interventions ranged in length from three to 12 weeks, and the median duration was eight weeks. We found low quality evidence (due to substantial unexplained heterogeneity among studies) that mindfulness meditation is associated with a small decrease in pain compared with control in 24 RCTs (SMD 0.26; CI 0.06, 0.46; 24 RCTs; I^2 62%; $n=1,456$); a sensitivity analysis excluding poor quality studies yielded similar effect estimates. This effect remained up to 12 weeks (SMD 0.27; CI 0.04, 0.50; 24 RCTs; I^2 65%), but was not statistically significant for follow-up periods beyond 12 weeks (SMD 0.37; CI -0.01, 0.74; I^2 75%; 11 RCTs). In subgroup analyses of comparators, mindfulness meditation statistically significantly reduced pain scores compared with treatment as usual (SMD 0.45; CI 0.02, 0.88; 7 RCTs; I^2 52%), but not compared with passive controls such as wait lists (SMD 0.28; CI -0.46, 1.02; 8 RCTs; I^2 77%) or with education or support groups (SMD 0.19; CI -0.11, 0.49; 8 RCTs; I^2 64%). The efficacy of mindfulness meditation on pain did not differ systematically by type of intervention, medical condition, or length or frequency of intervention. No systematic difference in effect on pain between monotherapy and adjunctive therapy was detected in a meta-regression.

Several studies reported non-pain outcomes; mindfulness meditation statistically significantly reduced depression (SMD 0.17; CI 0.03, 0.31; 10 RCTs; I^2 0%), improved mental health-related quality of life (SMD 0.44; CI 0.18, 0.69; 13 RCTs; I^2 51%), and improved physical health-related quality of life (SMD 0.30; CI 0.03, 0.57; 12 RCTs; I^2 55%). Of the three RCTs reporting adverse events, two stated that participants had no adverse events, and one stated that two participants experienced feelings of anxiety and anger toward their pain.

In sum, the review showed that mindfulness meditation improves pain symptoms, depression, and quality of life; however, there was evidence of substantial differences in study outcomes resulting in a low quality of evidence overall. We were unable to determine which patient subgroups or intervention characteristics were associated with greater efficacy, likely due to

small sample sizes and lack of statistical power. Additional trials with adequate power, greater efforts to prevent attrition, monitoring of adherence to meditation practice, active collection of adverse events, and better reporting of methods are suggested.

Table of Contents

Preface.....	iii
Abstract.....	v
Figures.....	ix
Tables.....	xi
Summary.....	xiii
Acknowledgments.....	xix
Abbreviations.....	xxi
Chapter One: Introduction	1
Background and Objective	1
Key Questions.....	3
Chapter Two: Methods	5
Sources.....	5
Search Strategy	5
Eligibility Criteria.....	5
Inclusion Screening	6
Data Extraction	6
Risk of Bias and Study Quality	7
Data Synthesis	8
Quality of Evidence	8
Summary of Findings	9
Chapter Three: Results.....	11
Results of the Search	11
Description of Included Studies	14
Design.....	14
Setting.....	14
Participants	14
Interventions.....	15
Comparators	15
Study Quality/Risk of Bias for Individual Included Studies	15
KQ 1: What Are the Efficacy and Safety of Mindfulness Meditation Interventions, as an Adjunctive or Monotherapy, for Adults with Chronic Pain Due to Migraine, Headache, Back Pain, Osteoarthritis, or Neuralgic Pain Compared with Treatment as Usual, Waitlists, No Treatment, or Other Active Treatments?.....	19
Chronic Pain Treatment Response Standardized Mean Differences.....	19
Analgesic Use.....	26
Health-Related Quality of Life.....	26
Functional Impairment (Disability Measures).....	27

Adverse Events Reported in RCTs.....	27
Study Characteristic Moderators and Risk of Bias.....	27
KQ 1a: Does the Effect Vary by the Type of Mindfulness Meditation Intervention?	27
Mindfulness-Based Stress Reduction	27
Mindfulness-Based Cognitive Therapy	28
Other Interventions	29
KQ 1b: Does the Effect Vary by Medical Condition Targeted (Migraine, Headache, Back Pain, Osteoarthritis, or Neuralgic Pain)?.....	30
Migraine or Other Headache	30
Back Pain.....	31
Fibromyalgia	32
KQ 1c: Does the Effect Differ When the Intervention Is Offered as an Adjunctive Therapy Rather Than as a Monotherapy?	33
KQ 1d: Does the Effect Vary Depending on the Duration and Frequency of Mindfulness Meditation (i.e., Dose Effect)?	34
Chapter Four: Discussion.....	35
Summary of Findings	35
KQ 1: What Are the Efficacy and Safety of Mindfulness Meditation Interventions, as an Adjunctive or Monotherapy, for Adults with Chronic Pain Due to Migraine, Headache, Back Pain, Osteoarthritis, or Neuralgic Pain Compared with Treatment as Usual, Waitlists, No Treatment, or Other Active Treatments?.....	35
KQ 1a: Does the Effect Vary by the Type of Mindfulness Meditation Intervention?	36
KQ 1b: Does the Effect Vary by Medical Condition Targeted (Migraine, Headache, Back Pain, Osteoarthritis, or Neuralgic Pain)?	36
KQ 1c: Does the Effect Differ When the Intervention Is Offered as an Adjunctive Therapy Rather Than as a Monotherapy?	37
KQ 1d: Does the Effect Vary Depending on the Duration and Frequency of Mindfulness Meditation (i.e., Dose Effect)?	37
Other Reviews in this Area.....	41
Strengths and Limitations	42
Implications for Future Research and Practice.....	43
Appendix A: Search Strategy.....	45
Appendix B: Excluded Full-Text Articles	47
Appendix C: Evidence Table of Included Studies	55
Appendix D: Studies Included in the Most Recent Systematic Review	83
References.....	85

Figures

Figure 3.1. Literature Flow Diagram	12
Figure 3.2. Mindfulness Meditation Versus Control, Pain Outcome, Longest Follow-Up	20
Figure 3.3. Mindfulness Meditation Versus Control, Pain Outcome, 0–12 weeks	21
Figure 3.4. Mindfulness Meditation Versus Control, Pain Outcome, >12 Weeks	22
Figure 3.5. Mindfulness Meditation Versus Treatment as Usual	23
Figure 3.6. Mindfulness Meditation Versus Passive Control	24
Figure 3.7. Mindfulness Meditation Versus Education or Support Group	25
Figure 3.8. MBSR Versus Control.....	28
Figure 3.9. MBCT Versus Control	29
Figure 3.10. Mindfulness Meditation for Migraine or Headache	31
Figure 3.11. Mindfulness Meditation for Back Pain.....	32
Figure 3.12. Mindfulness Meditation for Fibromyalgia	33

Tables

Table 1.1. Interventions Based on Mindfulness Meditation	2
Table 3.1. Evidence Base for Key Questions	13
Table 3.2. Quality Ratings	17
Table 4.1. Summary of Findings and Quality of Evidence Table	38
Table D.1. Studies Included in the Most Recent Systematic Review.....	83

Summary

Introduction

Chronic pain, often defined as pain lasting longer than three months or past the normal time for tissue healing, can lead to significant medical, social, and economic consequences; relationship issues; lost productivity; and larger health care costs. The high prevalence and refractory nature of chronic pain and the negative consequences of pain medication dependence drive investigation of innovative treatment modalities. Patients who seek a treatment plan for chronic pain that includes more than just medication are increasingly turning to complementary, alternative, and integrative medicine. One such modality that pain patients are using is mindfulness meditation. Based on ancient Eastern meditation practices, mindfulness is characterized by paying attention to the present moment with openness, curiosity, and acceptance. Previous systematic reviews on mindfulness meditation for chronic pain have been promising, but evidence was of low quality and additional studies have been completed since that time. This systematic review aims to synthesize evidence from trials of mindfulness meditation interventions to provide estimates of its efficacy in treating chronic pain (PROSPERO 2015:CRD42015025052). This report may be used by committees charged with updating U.S. Department of Veterans Affairs and Department of Defense guidelines for treatment of chronic pain.

Key Questions

This review was guided by the following key questions (KQs):

- KQ 1: What are the efficacy and safety of mindfulness meditation interventions, as an adjunctive or monotherapy, for adults with chronic pain due to migraine, headache, back pain, osteoarthritis, or neuralgic pain compared with treatment as usual, waitlists, no treatment, or other active treatments?
 - KQ 1a: Does the effect vary by the type of mindfulness meditation intervention?
 - KQ 1b: Does the effect vary by medical condition targeted (migraine, headache, back pain, osteoarthritis, or neuralgic pain)?
 - KQ 1c: Does the effect differ when the intervention is offered as an adjunctive therapy rather than as a monotherapy?
 - KQ 1d: Does the effect vary depending on the duration and frequency of mindfulness meditation (i.e., dose effect)?

Methods

To answer our key questions, we conducted a systematic search of electronic databases—PubMed, CINAHL (Cumulative Index to Nursing and Allied Health Literature), PsycINFO, and CENTRAL (Cochrane Central Register of Controlled Trials)—as well as bibliographies of existing systematic reviews and included studies, to identify reports of randomized controlled trials (RCTs) testing the efficacy and safety of mindfulness meditation used adjunctively or as monotherapy to treat adults with chronic pain.

Two independent reviewers screened identified literature using predetermined eligibility criteria, abstracted pre-specified study-level information, and assessed the quality of included studies. Outcomes of interest included changes in pain symptomatology, use of analgesics, functional status, health-related quality of life, functional impairment (disability measures), and adverse events.

Meta-analyses for efficacy outcomes were conducted using the Hartung-Knapp-Sidik-Jonkman method for random-effects models to estimate the relative risk (RR), standardized mean differences (SMDs), and 95-percent confidence intervals (CIs). We abstracted any adverse events reported. The quality of evidence was assessed using the Grades of Recommendation, Assessment, Development, and Evaluation (or GRADE) approach.

Results

In total, 28 studies met inclusion criteria. These 28 studies reported on the efficacy of mindfulness meditation, and three addressed safety. Risk of bias in included studies varied: Seven studies obtained a “good” quality rating, ten studies were rated “fair,” and 11 were rated “poor” quality.

Key Question 1

We identified 24 RCTs that met the inclusion criteria and reported continuous pain measures on the efficacy of mindfulness meditation for chronic pain. Intervention programs lasted from three to 12 weeks, with a median duration of eight weeks. Results of pooled analysis indicated a significant reduction on pain symptoms (SMD 0.26; CI 0.06, 0.46; 24 RCTs; I^2 62.1%). (Four studies were excluded from analyses because they did not report appropriate outcome data for meta-analysis.) A sensitivity analysis excluding poor quality studies yielded similar results (SMD 0.21; CI 0.00, 0.42; 15 RCTs; I^2 57.2%). This effect remained up to 12 weeks (SMD 0.27; CI 0.04, 0.50; 24 RCTs; I^2 64.6%), but was not significant for follow-up periods beyond 12 weeks (SMD 0.37; CI -0.01, 0.74; 11 RCTs, I^2 74.7%). The quality of evidence that mindfulness meditation is associated with a decrease in chronic pain compared with control is low overall, and for both short-term and long-term follow-up.

In subgroup analyses of comparators, mindfulness meditation significantly reduced pain scale scores compared with treatment as usual (SMD 0.45; CI 0.02, 0.88; 7 RCTs; I^2 51.5%), but

not compared with passive controls, such as waitlists (SMD 0.28; CI −0.46, 1.02; 8 RCTs; I^2 76.5%), or with education or support groups (SMD 0.19; CI −0.11, 0.49; 8 RCTs; I^2 63.9%). The quality of evidence is low for comparisons with treatment as usual and passive controls, but is very low for comparisons with education or support groups.

Several studies reported non-pain outcomes. There is high quality evidence that mindfulness meditation to treat chronic pain significantly reduced depressive symptoms (SMD 0.17; CI 0.03, 0.31; 10 RCTs; I^2 0%). There is moderate quality evidence that mindfulness meditation for chronic pain improves physical health-related quality of life as measured by the physical health summary measure of the 36-Item Short Form Health Survey (SF-36) (SMD 0.3; CI 0.03, 0.57; 12 RCTs; I^2 54.6%) and mental health-related quality of life as assessed by the mental health summary measure of the SF-36 or other instrument that measures such factors as affect, anxiety, vitality, role functioning, and social functioning (SMD 0.44; CI 0.18, 0.69; 13 RCTs; I^2 50.6%). When three RCTs were pooled, improvements in disability measures in the mindfulness groups were not significantly different from improvements in the control groups (SMD 0.47; CI −0.18, 1.12; I^2 0). Only one study reported on change in analgesic use; this study reported a significant decrease in the mindfulness group compared with control.

Of the three RCTs that reported adverse events, two stated that participants had no adverse events, and one stated that two participants experienced feelings of anxiety and anger toward their pain.

Key Question 1a

We did not identify head-to-head trials comparing different mindfulness interventions. The efficacy of mindfulness meditation did not differ systematically by type of intervention in indirect comparisons across studies. The effect of mindfulness meditation on pain was nonsignificant in the 15 RCTs examining mindfulness-based stress reduction (MBSR) (SMD 0.32; CI −0.06, 0.70; 15 RCTs; I^2 69.8%), in the four RCTs examining mindfulness-based cognitive therapy (MBCT) (SMD 0.16; CI −0.45, 0.76; 4 RCTs; I^2 63.6%), and in five RCTs examining remote (e.g., Internet, smart phone) interventions (SMD 0.06; CI −0.42, 0.55; 5 RCTs; I^2 56.7%). Meta-regression analyses showed that changes in pain outcomes with MBSR ($p=0.60$), MBCT ($p=0.58$), and remote mindfulness interventions via Internet or compact disc ($p=0.14$) were not significantly different from outcomes with other types of mindfulness meditation. The quality of evidence for the absence of differences between intervention types is very low due to the small number of studies per category and the lack of direct comparisons.

Key Question 1b

The effect of mindfulness meditation also did not vary systematically by medical condition. The effect of meditation on pain was not significant for participants with migraine or headache (SMD 0.38; CI −0.41, 1.17; 5 RCTs; I^2 80.6%), back pain (SMD −0.04; CI −0.39, 0.32; 4 RCTs; I^2 0%), or fibromyalgia (SMD 0.13; CI −0.12, 0.37; 8 RCTs; I^2 45.3%). Meta-regression

analyses also showed that changes in pain outcomes for patients with back pain ($p=0.28$), headache ($p=0.69$), and fibromyalgia ($p=0.24$) were not significantly different from outcomes for patients with other types of pain. The quality of evidence is low for migraine and back pain, and moderate for fibromyalgia.

Key Question 1c

The effect of meditation on pain did not differ systematically when offered as a monotherapy compared with as an adjunctive treatment. The effect was not significant for both monotherapy (SMD 0.21; CI $-0.02, 0.45$; 13 RCTs; I^2 55%) and adjunctive treatment (SMD 0.36; CI $-0.16, 0.89$; 11 RCTs; I^2 73.5%). A meta-regression found that pain outcomes did not differ significantly between interventions using mindfulness meditation as monotherapy or adjunctive therapy ($p=0.53$). The quality of evidence is low for mindfulness meditation as monotherapy and as adjunctive therapy.

Key Question 1d

The efficacy of mindfulness meditation did not differ systematically by frequency or duration of the treatment. In a meta-regression, efficacy did not vary significantly as program duration in weeks increased ($p=0.12$). The effect was not significant at a dose of less than one hour a week (low frequency; SMD -0.18 ; CI $-0.49, 0.10$; 3 RCTs; I^2 0%), or at a dose of one to four hours a week (medium frequency; SMD 0.44; CI $-0.16, 1.05$; 10 RCTs; I^2 77.5%). The effect for interventions requiring greater than four hours a week (high frequency) bordered on statistical significance (SMD 0.19; CI $0.00, 0.39$; 11 RCTs; I^2 4.5%), but the confidence intervals fit within those of the results for interventions requiring one to four hours of participation. A meta-regression found that pain outcomes did not differ significantly between low frequency ($p=0.17$) or medium frequency ($p=0.32$) and high frequency interventions. The quality of evidence is low for doses of less than one hour a week and one to four hours a week; the quality of evidence is moderate for more than four hours of practice a week.

Conclusions

Mindfulness meditation was associated with a small effect of improved pain symptoms compared with control groups in a meta-analysis of 24 RCTs. However, there was evidence of substantial heterogeneity among studies, resulting in a low quality of evidence for this outcome. Mindfulness meditation statistically significantly improved depression, physical health-related quality of life, and mental health-related quality of life; pooled analyses included ten, 12, and 13 studies, respectively. Those analyses detected less heterogeneity, so our confidence in the results is higher; quality of evidence was high for depression and moderate for physical and mental health-related quality of life.

Adverse events in the included RCTs were rare and not serious, but the vast majority of studies did not collect adverse event data. As reports of psychosis during meditation have appeared in the medical literature, we strongly suggest that future trials actively collect adverse event data.

Many trials were of poor quality. Due to the low quality of evidence supporting improved pain outcomes, additional trials are needed to increase confidence in this finding. These trials must have adequate power, greater efforts to prevent attrition, and better reporting of methods.

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Abbreviations

BPI	Brief Pain Index
CENTRAL	Cochrane Central Register of Controlled Trials
CI	confidence interval
CINAHL	Cumulative Index to Nursing and Allied Health Literature
GRADE	Grades of Recommendation, Assessment, Development and Evaluation
IBS	irritable bowel syndrome
ITT	intention-to-treat
MBCT	mindfulness-based cognitive therapy
MORE	mindfulness-oriented recovery enhancement
MBSR	mindfulness-based stress reduction
MPQ	McGill Pain Questionnaire
QOL	quality of life
RCT	randomized controlled trial
RR	relative risk
SD	standard deviation
SF-36	36-Item Short Form Health Survey
SMD	standardized mean difference
TAU	treatment as usual
USPSTF	United States Preventive Services Task Force
VAS	visual analog scale

Chapter One: Introduction

Background and Objective

Chronic pain, often defined as pain lasting longer than three months or past the normal time for tissue healing (Chou et al., 2015), can lead to significant medical, social, and economic consequences; relationship issues; lost productivity; and larger health care costs. Further, chronic pain is frequently accompanied by psychiatric disorders, such as pain medication addiction, depression, and anxiety, that make treatment complicated (Management of Opioid Therapy for Chronic Pain Working Group, 2010). Chronic pain is highly prevalent among service members who served in Operations Enduring Freedom and Iraqi Freedom; 44 percent of those who were deployed in combat deployment report chronic pain, compared with 26 percent of the general public (Toblin et al., 2014). Chronic pain is the most frequent symptom reported in the community and primary care setting, accounting for nearly 20 percent of all ambulatory visits to U.S. Department of Veterans Affairs facilities and is the most common cause of work disability in the military (Management of Opioid Therapy for Chronic Pain Working Group, 2010). In the veteran population, greater than 50 percent of Afghanistan and Iraq veterans report pain as their presenting complaint when signing in for care at a Veterans Health Administration facility. For those with poly-trauma, the prevalence is greater than 90 percent (Management of Opioid Therapy for Chronic Pain Working Group, 2010).

The high prevalence and refractory nature of chronic pain, in conjunction with the negative consequences of pain medication dependence, has led to increased U.S. Department of Defense interest in alternative interventions for chronic pain. Patients who seek a treatment plan that includes adjunctive therapy or alternatives to medication are increasingly turning to complementary and alternative medicine (Chiesa and Serretti, 2011). One such modality that pain patients are using is mindfulness meditation. The Army Surgeon General's Pain Management Task Force recommended that mind-body therapies such as mindfulness meditation be a Tier 1 therapy option (along with acupuncture, yoga, chiropractic care, therapeutic medical massage, and biofeedback) in the interest of providing a holistic, integrative approach to pain management (Office of the Army Surgeon General, 2010). Meditation is the intentional self-regulation of attention from moment to moment (Goleman and Schwartz, 1976). Based on ancient Eastern meditation practices, mindfulness facilitates an attentional stance of detached observation. It is characterized by paying attention to the present moment with openness, curiosity, and acceptance (Kabat-Zinn, Lipworth, and Burney, 1985). Clinical uses of mindfulness include applications in substance abuse (Chiesa and Serretti, 2014), tobacco cessation (de Souza et al., 2015), stress reduction (Goyal et al., 2014), and treatment of chronic pain (Kozasa et al., 2012; Cramer et al., 2012; Reiner, Tibi, and Lipsitz, 2013). The most

commonly used mindfulness meditation interventions are described in Table 1.1. (Mindfulness Awareness Research Center, 2015)

Table 1.1. Interventions Based on Mindfulness Meditation

Name	Description
Mindfulness-based stress reduction (MBSR)	In addition to mindfulness meditation, MBSR involves teaching of body scan or yoga to encourage open, nonjudgmental observation and acceptance of painful or unpleasant sensation, negative thoughts, or emotions instead of cognitively appraising them and increasing anticipatory anxiety, avoidance, or other maladaptive patterns.
Mindfulness-based cognitive therapy (MBCT)	In addition to mindfulness meditation, MBCT encourages acceptant nonjudgmental observation of negative thoughts and emotions instead of their cognitive appraisal triggering ruminative negative thoughts and habitual emotional reactivity.
Mindfulness-based relapse prevention	In addition to mindfulness meditation, mindfulness-based relapse prevention teaches relapse prevention skills and nonjudgmental, open, and acceptant observation of cravings. It aims to decouple (1) the negative thoughts and emotions that are associated with cravings and (2) relapse.
Mindfulness training for smoking	In addition to mindfulness meditation, mindfulness training for smoking provides targeted training in how to apply mindfulness to smoking relapse determinants, such as smoking triggers, strong emotions, addictive thoughts, urges, and withdrawal symptoms.
Mind-body bridging and mindfulness-based therapy for insomnia	In addition to mindfulness meditation, mind-body bridging and mindfulness-based therapy for insomnia use behavioral strategies to reduce night wakefulness.
Mindfulness-oriented recovery enhancement (MORE)	In addition to mindfulness meditation, MORE teaches neutral, open, and acceptant observation of painful sensations. It also incorporates positive psychology and behavioral techniques directed toward neuroscientific underpinnings of addiction.

Early studies in pain patients showed promising outcomes on pain symptoms, mood disturbance, anxiety, and depression, as well as pain-related drug utilization (Kabat-Zinn, Lipworth, and Burney, 1985). A 2011 systematic review of ten mindfulness-based interventions for chronic pain patients showed improvements in depressive symptoms and coping, with limited evidence for specific pain effects (Chiesa and Serretti, 2011). That review concluded that further research, using larger, adequately powered studies with robust designs, was warranted. A later review (Lee, Crawford, and Hickey, 2014) funded by the U.S. Army also concluded that additional high-quality research was needed before a recommendation for the use of mindfulness meditation for chronic pain symptoms could be made. Eleven RCTs included in that review investigated the use of mindfulness meditation for chronic pain symptoms, including chronic back pain, fibromyalgia, and musculoskeletal pain. More than half of the studies were poor quality, having high dropout rates, lack of safety reporting, and weak randomization procedures, for example. However, the majority of studies showed promising effects for mindfulness meditation.

The current review was requested by the U.S. Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury. The Centers commissioned the RAND Corporation to develop a series of systematic reviews on complementary and alternative

medicine interventions for conditions such as substance abuse, major depressive disorder, and posttraumatic stress disorder. These reviews may be used by committees charged with updating Department of Veterans Affairs and Department of Defense guidelines for treatment of these conditions.

Key Questions

This systematic review identified randomized controlled trials (RCTs) testing the efficacy and safety of mindfulness meditation to treat individuals with chronic pain. The review aimed to answer the following key questions (KQs):

- KQ 1: What are the efficacy and safety of mindfulness meditation interventions, as an adjunctive or monotherapy, for adults with chronic pain due to migraine, headache, back pain, osteoarthritis, or neuralgic pain compared with treatment as usual, waitlists, no treatment, or other active treatments?
 - KQ 1a: Does the effect vary by the type of mindfulness meditation intervention?
 - KQ 1b: Does the effect vary by medical condition targeted (migraine, headache, back pain, osteoarthritis, or neuralgic pain)?
 - KQ 1c: Does the effect differ when the intervention is offered as an adjunctive therapy rather than as a monotherapy?
 - KQ 1d: Does the effect vary depending on the duration and frequency of mindfulness meditation (i.e., dose effect)?

Chapter Two: Methods

We performed a systematic review to identify RCTs testing the efficacy and safety of mindfulness meditation for chronic pain. The systematic review protocol is registered in PROSPERO, an international registry for systematic reviews.

Sources

We searched the electronic databases PubMed, CINAHL (Cumulative Index to Nursing and Allied Health Literature), PsycINFO, and CENTRAL (Cochrane Central Register of Controlled Trials) for English-language RCTs. In addition to this search and the reference-mining of all included studies identified through it, we reference-mined prior systematic reviews related to this topic and retrieved all studies included therein.

Search Strategy

The search strategy was developed by the chief reference librarian for RAND's Knowledge Services, informed by search results of an environmental scan of the literature at the initiation of this study (as part of unpublished RAND research by Melony Sorbero, Sean Grant, and Susanne Hempel) and existing reviews. The search strings are presented in Appendix A. We searched from the inception of the databases through June 2015.

Eligibility Criteria

The inclusion and exclusion criteria applied to the retrieved publications were developed using the framework of participants, interventions, comparators, outcomes, timing, settings, and study design, or PICOTSS.

- *Participants*: Studies were limited to male and female participants who are 18 years of age or older who report chronic pain. We included studies in which the author defined chronic pain, as well as studies of patients reporting pain for a minimum of three months. Studies not specifying the duration of pain and not referring to chronic pain were excluded.
- *Interventions*: Studies involving mindfulness meditation, either as an adjunctive or monotherapy, were included—for example, MBCT, MBSR, Vipassana, Zazen, Zen, and Shambhala interventions. Studies testing other meditation interventions such as yoga, tai chi, qigong, and transcendental meditation techniques without reference to mindfulness meditation were excluded.
- *Comparators*: Studies that included waitlist control, no treatment, or standard care (e.g., physical activity, pain medications), that compare mindfulness meditation offered as

adjunctive versus monotherapy, and that compare two or more mindfulness meditation interventions were included.

- *Outcomes*: Studies that reported patient pain measures—including pain assessed with a visual analog scale (VAS), the SF-36 pain subscale, the McGill Pain Questionnaire (MPQ), and so on—and studies reporting on change in analgesic use were included.
- *Timing*: Studies could involve any treatment duration and any follow-up time period.
- *Setting*: Studies were not limited by setting.
- *Study design*: Included studies were limited to parallel group, individually-randomized, or cluster-randomized controlled trials.

Inclusion Screening

Two independent reviewers (the project lead, who is an experienced systematic reviewer and former Associate Director of the Southern California Evidence-based Practice Center [EPC], and a RAND research assistant with experience in systematic reviews) independently screened titles and abstracts of retrieved citations following a pilot session to ensure similar interpretation of the inclusion and exclusion criteria.

Citations judged as potentially eligible by one or both reviewers were obtained as full text. The full-text publications were then screened against the specified inclusion criteria by the two independent reviewers; any disagreements were resolved through discussion within the review team. The flow of citations throughout this process was documented in an electronic database, and reasons for exclusion of full-text publications were recorded. A list of excluded publications is shown in Appendix B.

Data Extraction

The two aforementioned reviewers each independently abstracted study-level data in an electronic database. Data collection forms were designed by the project lead, with input from the project team. These two reviewers pilot-tested the data collection forms on a few randomly selected studies, modified the forms, and performed a final pilot of the forms on a random selection of three included studies to ensure agreement of interpretation. EPC biostatisticians abstracted all outcome data to ensure accuracy.

Study-level data were abstracted for the following information:

- *Participants*: gender, age, medical condition(s) and type of pain, baseline pain data, comorbid psychological/behavioral health conditions
- *Interventions*: content of mindfulness meditation sessions, dosage (intensity, frequency, duration), and co-intervention(s)
- *Comparators*: type of comparator
- *Outcomes*: primary endpoint; longest follow-up; measures of pain, use of analgesics, functional status, health-related quality of life, and adverse events for each time point of measurement; domain; method of measurement; metric of data expression (e.g., means, proportions); and corresponding results (e.g., effect estimate, precision)

- *Timing*: time-points of outcome assessment, timing of intervention
- *Setting*: geographic region, clinical setting, interventionist training
- *Study design*: aim of study, definition of chronic pain, inclusion and exclusion criteria, sample size, reported power calculations, items relevant to risk of bias and quality ratings.

If different reports appeared to be from the same study, descriptions of participants were compared to ensure that data from the same study populations entered the analysis only once. For each included study, findings are displayed in an evidence table (see Appendix C) that includes details about the intervention, specific comparisons, and outcomes measured.

Risk of Bias and Study Quality

The two reviewers assessed the risk of bias of included studies using the Cochrane Risk of Bias tool (Higgins and Green, 2011). Specifically, the reviewers assessed risks of bias related to random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and providers (performance bias), blinding of outcome assessors (detection bias), completeness of reporting outcome data (attrition bias), and selective outcome reporting (reporting bias). Involvement of the intervention developers in evaluation of its efficacy was also noted.

Other biases related to the U.S. Preventive Services Task Force’s criteria for internal validity of included studies were assessed, namely those related to: equal distribution among groups of potential confounders at baseline; crossovers or contamination between groups; equal, reliable, and valid outcome measurement; clear definitions of interventions; and intention-to-treat (ITT) analysis (U.S. Preventive Services Task Force, 2008; Lewin Group and ECRI Institute, 2014). These criteria were used to rate the quality of evidence of individual included studies using the following guidelines:

- *Good*: Comparable groups are initially assembled and maintained throughout the study with at least 80-percent follow-up; reliable, valid measurement is used and applied equally to all groups; interventions are clearly described; all important outcomes are considered; appropriate attention is given to confounders in analysis; ITT analysis is used.
- *Fair*: One or more of the following issues is found in the study: some, though not major, differences between groups exist at follow-up; measurement instruments are acceptable but not ideal, though are generally applied equally; some but not all important outcomes are considered; some but not all potential confounders are account for in analyses. ITT analysis must be done.
- *Poor*: One or more of the following “fatal flaws” is found in the study: initially assembled groups are not comparable or maintained throughout the study; unreliable or invalid measurements are used or applied unequally across groups; key confounders are given little to no attention in analyses; ITT analysis is not used.

Data Synthesis

The primary aim of this systematic review was to identify whether mindfulness meditation for chronic pain in adults is effective and safe. As such, when sufficient data were available and statistical heterogeneity was below agreed thresholds (Higgins and Green, 2011), we performed meta-analysis to pool efficacy results across included studies for the outcomes of interest, and we present forest plots for these meta-analyses. We used the Hartung-Knapp-Sidik-Jonkman method for random-effects meta-analysis (Hartung, 1999; Hartung and Knapp, 2001; Sidik and Jonkman, 2006) to estimate the relative risk (RR), standardized mean differences (SMDs), and 95-percent confidence intervals (CIs). This approach may be preferred when the number of studies pooled is small and when there is evidence of heterogeneity (IntHout, Ioannidis, and Borm, 2014), and it has been shown that the error rates are more robust than the previously used DerSimonian and Laird method (Sanchez-Meca and Marin-Martinez, 2008). For studies reporting multiple pain outcomes, we used specific pain measures, such as the MPQ for the main meta-analysis rather than the pain subscale of the SF-36, and average or general pain measures rather than situational measures, such as pain right at the time of assessment. Adverse events were classified and grouped according to the Common Terminology Criteria for Adverse Events system. Due to the small number of adverse events reported, quantitative analysis was not conducted.

In addition, we described results of head-to-head comparisons and conducted subgroup analyses and meta-regressions to address secondary questions of this systematic review. Specifically, we examined whether there were differences in effect sizes between different mindfulness meditation interventions; studies conducted in different population groups (e.g., patients with headache, migraine, back pain, or pain due to osteoarthritis); and mindfulness meditation intervention as monotherapy versus an adjunctive therapy. Given the complexity of the topic, subgroup and sensitivity analysis was performed only for those outcomes with sufficient data. For meta-analysis of data with clear outliers, sensitivity analysis was conducted (excluding the outliers), if appropriate (Hamling et al., 2008). We also conducted sensitivity analyses omitting the lower quality studies for major comparisons.

Quality of Evidence

The quality of the body of evidence was assessed for major outcomes using the Grades of Recommendation, Assessment, Development, and Evaluation (or GRADE) approach (Balshem et al., 2011; Lewin Group and ECRI Institute, 2014) in which the body of evidence is assessed based on the following dimensions: study limitations, directness, consistency, precision, and reporting bias (Egger et al., 1997).

The quality of evidence is graded on a four-item scale:

- *High* indicates that the review authors are very confident that the effect estimate lies close to the true effect for a given outcome, as the body of evidence has few or no deficiencies.

As such, the reviewers believe the findings are stable. That is, further research is very unlikely to change confidence in the effect estimate.

- *Moderate* indicates that the review authors are moderately confident that the effect estimate lies close to the true effect for a given outcome, as the body of evidence has some deficiencies. As such, the reviewers believe that the findings are likely to be stable, but further research may change confidence in the effect estimate and may even change the estimate.
- *Low* indicates that the review authors have limited confidence that the effect estimate lies close to the true effect for a given outcome, as the body of evidence has major or numerous (or both) deficiencies. As such, the reviewers believe that additional evidence is needed before concluding either that the findings are stable or that the effect estimate lies close to the true effect.
- *Very low* indicates that the review authors have very little confidence that the effect estimate lies close to the true effect for a given outcome, as the body of evidence has very major deficiencies. As such, the true effect is likely to be substantially different from the estimated effect; thus, any estimate of effect is very uncertain.

Summary of Findings

Review findings are summarized in a table organized by outcomes that reflect the key questions for this systematic review (Table 4.1). This table lists the intervention and comparators evaluated; the outcomes assessed for each type of comparison; the number of studies and number of participants included for each outcome assessment; the direction and magnitude of the effect for each outcome; and the quality of the evidence for each outcome.

For each outcome, results of pooled analyses are described first, followed by narrative descriptions of individual studies not included in the pooled analyses (if any). Findings are first reported for the broad comparison of mindfulness meditation compared with any comparison group. Findings are then reported separately by intervention (e.g., MBSR), population (e.g., patients with headache, back pain, fibromyalgia), therapy characteristic (i.e., monotherapy, adjunctive therapy), and type of comparator. Meta-analyses results are displayed in figures to allow a transparent overview, and results are described in detail in the text.

Chapter Three: Results

Results of the Search

We identified 639 citations through searches of electronic databases, plus nine citations by reference-mining previous systematic reviews (see Figure 3.1). Full texts were obtained for 88 citations identified as potentially eligible by two independent reviewers. In total, 60 articles were excluded at the full-text stage because they did not meet eligibility criteria. Ten of these studies were excluded because they were off topic, not reporting on mindfulness or chronic pain. Five were excluded due to intervention, as they did not study mindfulness meditation. Thirteen did not report on pain or analgesic use outcomes. Eleven were not RCTs. Five of the publications were dissertations, nine were conference abstracts, and five reported on studies already in the database and did not present new data. One study could not be obtained to be assessed for eligibility, and one publication was retained for background only. Appendix B lists excluded publications, with reasons for exclusion. Twenty-eight RCTs met inclusion criteria. Details of these studies are displayed in the evidence table in Appendix C.

Figure 3.1. Literature Flow Diagram

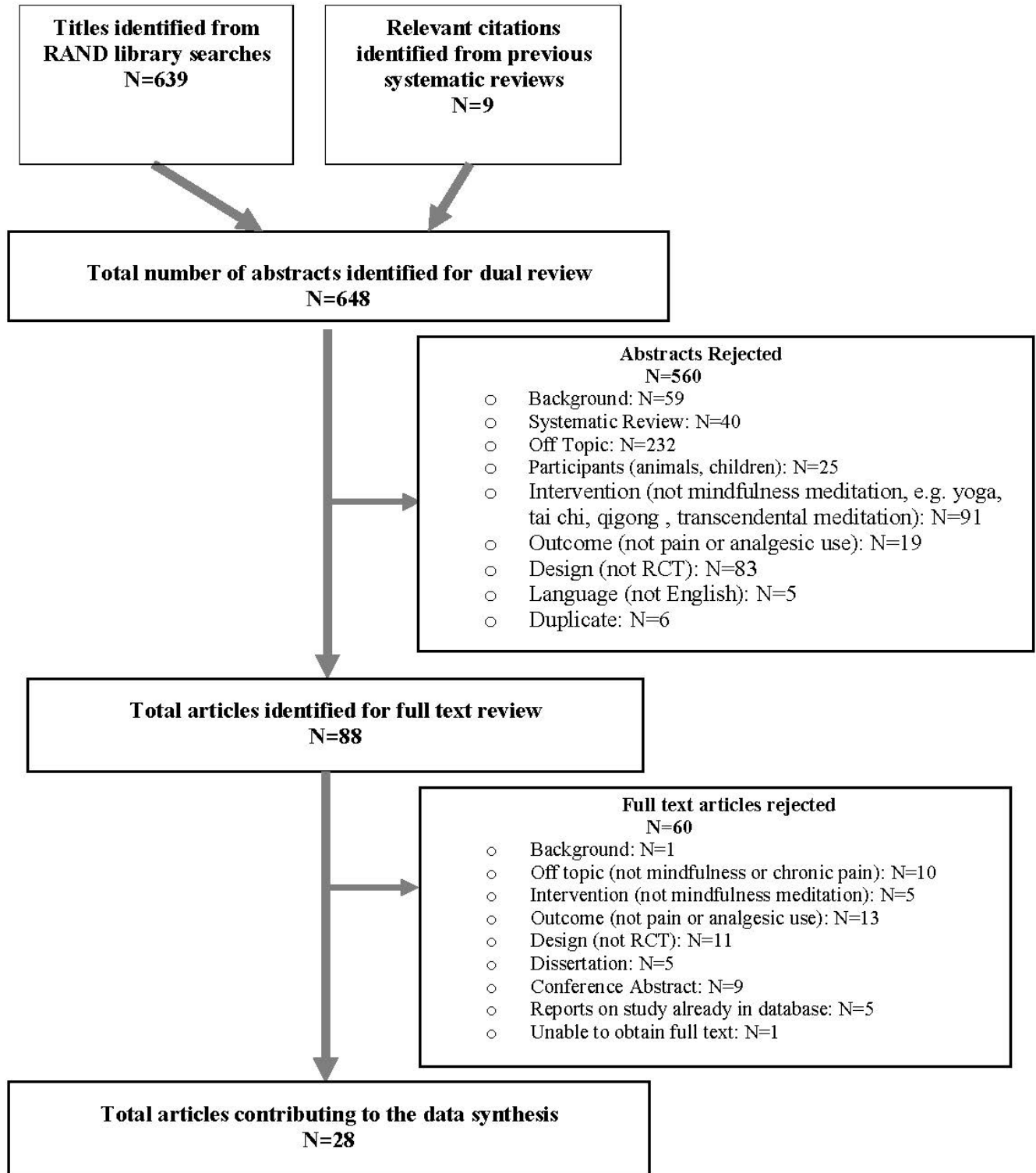


Table 3.1 displays the number of RCTs that address each key question and subquestion. All 28 studies provided data on the efficacy of mindfulness meditation. Only three RCTs addressed the presence or absence of adverse events.

Table 3.1. Evidence Base for Key Questions

Key Question	Number of RCTs
1 What are the efficacy and safety of mindfulness meditation interventions, as an adjunctive or monotherapy, for adults with chronic pain due to migraine, headache, back pain, osteoarthritis, or neuralgic pain compared with treatment as usual, waitlists, no treatment, or other active treatments?	28 RCTs <ul style="list-style-type: none"> • 8 treatment-as-usual comparator • 8 passive comparator • 9 education/support group comparator • 1 stress management comparator • 1 cognitive behavioral therapy comparator • 1 massage comparator • 1 multidisciplinary pain intervention comparator • 1 muscle relaxation/stretching comparator • 1 nutritional information/food diary comparator Note: Some trials have two comparison arms. 3 RCTs report on adverse events.
1a Does the effect vary by the type of mindfulness meditation intervention?	16 MBSR 3 MBCT 1 MORE 1 mindfulness-based pain management 1 mindful socioemotional regulation 6 other mindfulness meditation programs
1b Does the effect vary by medical condition targeted (migraine, headache, back pain, osteoarthritis, or neuralgic pain)?	8 fibromyalgia 6 migraine or other headache 4 back pain 2 osteoarthritis 3 rheumatoid arthritis 1 cancer 3 irritable bowel syndrome 6 other conditions 4 unspecified conditions Note: Categories are not mutually exclusive.
1c Does the effect differ when the intervention is offered as an adjunctive therapy rather than as a monotherapy?	13 monotherapy 13 adjunctive therapy 2 unclear
1d Does the effect vary depending on the duration and frequency of mindfulness meditation (i.e., dose effect)?	2 low frequency (<1 hour per week) 9 medium frequency (1–4 hours per week) 10 high frequency (>4 hours per week) 7 unclear frequency

For KQ 1a on whether the effect of mindfulness meditation varies by intervention type, we identified 16 studies examining MBSR, three studies examining MBCT, one study examining MORE, one study of mindfulness-based pain management, one study of mindful socioemotional regulation, and six studies examining other mindfulness meditation programs.

For KQ 1b on whether the effect of mindfulness meditation varies by type of condition treated, we found eight studies examining fibromyalgia, six studies examining migraine or

headache, four studies examining back pain, two studies examining osteoarthritis, three studies examining rheumatoid arthritis, one study examining cancer, three studies examining irritable bowel syndrome (IBS), six studies examining other conditions, and four studies examining unspecified conditions. (Categories are not mutually exclusive; some studies did not limit enrollment to a particular medical condition or source of pain.)

For KQ 1c on whether mindfulness meditation is more effective as monotherapy than as an adjunctive treatment, we found 13 studies examining meditation as monotherapy, 13 examining it as adjunctive therapy, and two that were unclear.

For KQ 1d on whether the effect of mindfulness meditation varied by the frequency and duration of the intervention, we found that the duration varied from three to 12 weeks (median eight weeks) and that the frequency (defined as the total time spent in group sessions, remote sessions, and “homework”) varied from less than one hour a week in two studies to more than four hours a week in ten studies. Two studies examine programs estimated at less than one hour per week (i.e., low frequency), nine studies examined programs estimated at one to four hours per week (i.e., medium frequency), ten studies examined programs estimated at more than four hours per week (i.e., high frequency), and seven studies were unclear.

Description of Included Studies

Design

One RCT (Zautra et al., 2008) randomized clusters of participants, while the rest randomized individual participants. Overall, studies assigned 2,179 participants; sample sizes ranged from 19 to 195. Eight studies did not report any information about a power calculation, 11 studies reported an a priori power calculation with targeted sample size achieved, and two studies were unclear in the reporting of a power calculation. Seven studies noted there was insufficient power; the authors considered these pilot studies.

Setting

Fourteen studies were conducted in either the United States or Canada, eight took place in Europe, two in Asia, two in the Middle East, one in Australia, and one in New Zealand.

The mindfulness intervention was delivered remotely (e.g., via telephone, Internet, or mobile app) in six of the studies. Two of the studies delivered the mindfulness intervention in an outpatient pain clinic, and three of the studies delivered it in another outpatient setting; in 17 studies, it was unclear where the intervention was delivered.

Participants

The mean age of participants ranged from 34.6 (standard deviation [SD] 9.4) to 74.6 (SD 10.8) years. Twenty-one studies included both male and female participants, five studies

included only female participants, and two studies did not provide information on gender. The proportion of males ranged from 0.7 percent (one patient) to 56 percent.

Medical conditions reported included fibromyalgia in eight studies and back pain in four studies. (Categories are not mutually exclusive; some studies included patients with different conditions.) Osteoarthritis was reported in two studies and rheumatoid arthritis in three. Migraine headache was reported in two studies and another type of headache in four studies. Three studies reported IBS. Six studies reported other causes of pain, and four studies did not specify a medical condition or source of chronic pain.

Interventions

The total length of the intervention program ranged from three to 12 weeks. The majority of intervention programs (21 studies) were eight weeks in length. Sixteen studies utilized MBSR, three used MBCT, and one used MORE. Eight of the studies used another mindfulness intervention, such as a compact disc of guided meditation, daily mindfulness meditation piece from MBSR, and mindful socioemotional regulation.

We identified 13 RCTs that provided the mindfulness intervention as monotherapy and 13 that utilized a mindfulness intervention as adjunctive therapy, specifying that all participants received this in addition to other treatment, such as medication. Two of the studies were unclear about whether the mindfulness intervention was monotherapy or adjunctive therapy.

Comparators

Eight RCTs used treatment as usual as comparators; eight used passive comparators, such as a waitlist; and nine used education or support groups as comparators. Beyond these common comparators, one study each used stress management, cognitive behavioral therapy, massage, a multidisciplinary pain intervention, relaxation/stretching, and nutritional information/food diaries as comparators. (Several studies had two comparison arms, so numbers do not add to 28.)

Study Quality/Risk of Bias for Individual Included Studies

The risk of bias and study quality for each included study is displayed in Table 3.2. Seven studies obtained a “good” quality rating (Fjorback et al., 2013; Fogarty et al., 2015; Ljotsson, Falk, et al., 2010; Ljotsson, Hedman, et al., 2011; Parra-Delgado and Latorre-Postigo, 2013; Wong et al., 2011; Zautra et al., 2008). Ten studies were judged to be of fair quality, primarily due to being unclear in some aspects of the methods (Cash et al., 2015; Davis and Zautra, 2013; Day et al., 2014; Dowd et al., 2015; Garland et al., 2014; Gaylord et al., 2011; la Cour and Petersen, 2015; Morone, Greco, and Weiner, 2008; Schmidt et al., 2011; Wells et al., 2014). Eleven studies were judged to be poor; eight of these were primarily due to issues with completeness of reporting outcome data, such as inadequate or missing ITT analysis or less than 80-percent follow-up (Astin et al., 2003; Brown and Jones, 2013; Cathcart et al., 2014; Esmer et

al., 2010; Meize-Grochowski et al., 2015; Morone et al., 2009; Omid and Zargar, 2014; Plews-Ogan et al., 2005). Three studies were judged poor primarily due to unclear methods (Rahmani and Talepasand, 2015; Teixeira, 2010; Wong, 2009).

Random sequence generation. Ten studies had unclear selection bias because they did not report their random sequence generation method; 18 other studies reported adequate random sequence generation methods (e.g., computerized random generator) so were at low risk for selection bias.

Allocation concealment. Thirteen studies had unclear selection bias because they did not report their allocation concealment method, whereas 14 studies did give a method of allocation concealment, and one other study presented a method of allocation concealment that was at high risk of being inadequate.

Blinding of participants and providers. All but two studies were rated high risk on this domain, as it is almost impossible to blind participants to meditation interventions. One study had low risk of bias because the authors used sham meditation as the control. The remaining study had unclear selection bias because the authors did not report the method of ensuring blinding.

Blinding of outcome assessors. Ten studies had unclear risk of detection bias because they did not report whether outcome assessors were blind to participant intervention conditions. Six studies had low risk of bias, because the authors explicitly indicated that the outcome assessors were blind to intervention assignment, and 12 studies had high risk of bias, indicating assessors were not blinded.

Outcome data. Twenty studies had low risk of attrition bias; seven had high risk due to attrition of more than 20 percent at follow up, and one study was unclear.

Selective outcome reporting. Two of the studies had high risk of reporting bias. Nine studies had low risk of reporting bias because the authors cited a protocol for the study. Seventeen studies had unclear risk of bias because it was not possible to determine whether all outcomes collected were reported.

Other. Four of the studies were identified as having an unequal distribution among groups of potential confounders at baseline, five studies were found to be unclear in this regard, and 19 studies reported no significant differences in baseline characteristics. None of the studies was a crossover trial, and therefore appropriate washout was not applicable. Only one study was judged to have any problems with having equal, reliable, and valid outcome measurement. One study was found to have issues with clear definitions of the interventions. Seven studies were identified as having problems with appropriate ITT analysis for outcomes with missing data, one study was unclear, and the remaining studies had no indication of problems with ITT analysis.

Table 3.2. Quality Ratings

Study ID	Random Sequence Generation (selection bias)	Allocation Concealment (selection bias)	Blinding of Participants and Personnel (performance bias)	Blinding of Outcome Assessors (detection bias)	Completeness of Reporting Outcome Data (attrition bias)	Selective Outcome Reporting (reporting bias)	Other Biases					USPSTF Quality Rating
							Unequal Distribution Among Groups of Potential Confounders at Baseline	Crossovers or Contamination Between Groups	Equal, Reliable, and Valid Outcome Measurement	Clear Definitions of Interventions	ITT Analysis	
Astin et al., 2003	Low risk	Low risk	High risk	Unclear risk	High risk	Unclear risk	No	No	Yes	Yes	No	Poor
Brown and Jones, 2013	Unclear risk	Unclear risk	High risk	Unclear risk	High risk	Unclear risk	Unclear	No	No	Yes	No	Poor
Cash et al., 2015	Low risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	No	No	Yes	Yes	Yes	Fair
Cathcart et al., 2014	Unclear risk	Low risk	High risk	Low risk	Low risk	Low risk	No	No	Yes	Yes	No	Poor
Davis and Zautra, 2013	Low risk	Low risk	High risk	High risk	Low risk	Low risk	No	No	Yes	Yes	Yes	Fair
Day et al., 2014	Low risk	High risk	High risk	High risk	Low risk	Unclear risk	No	No	Yes	Yes	Yes	Fair
Dowd et al., 2015	Low risk	Low risk	High risk	High risk	Low risk	Unclear risk	No	No	Yes	Yes	Yes	Fair
Esmer et al., 2010	Unclear risk	Unclear risk	High risk	High risk	High risk	Unclear risk	No	No	Yes	Yes	Yes	Poor
Fjorback et al., 2013	Low risk	Low risk	High risk	Unclear risk	Low risk	Unclear risk	No	No	Yes	Yes	Yes	Good
Fogarty et al., 2015	Unclear risk	Unclear risk	High risk	Low risk	Low risk	Unclear risk	No	No	Yes	Yes	Yes	Good
Garland et al., 2014	Low risk	Low risk	High risk	Low risk	Low risk	Unclear risk	No	No	Yes	Yes	Yes	Fair
Gaylord et al., 2011	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	No	No	Yes	Yes	Yes	Fair
la Cour and Petersen, 2015	Low risk	Low risk	High risk	High risk	Low risk	Unclear risk	Yes	No	Yes	Yes	Yes	Fair
Ljotsson, Falk, et al., 2010	Low risk	Low risk	High risk	High risk	Low risk	Unclear risk	Unclear	No	Yes	Yes	Yes	Good
Ljotsson, Hedman, et al., 2011	Low risk	Low risk	High risk	High risk	Low risk	High risk	No	No	Yes	Yes	Yes	Good

Study ID	Random Sequence Generation (selection bias)	Allocation Concealment (selection bias)	Blinding of Participants and Personnel (performance bias)	Blinding of Outcome Assessors (detection bias)	Completeness of Reporting Outcome Data (attrition bias)	Selective Outcome Reporting (reporting bias)	Other Biases						USPSTF Quality Rating
							Unequal Distribution Among Groups of Potential Confounders at Baseline	Crossovers or Contamination Between Groups	Equal, Reliable, and Valid Outcome Measurement	Clear Definitions of Interventions	ITT Analysis		
Meize-Grochowski et al., 2015	Unclear risk	Unclear risk	High risk	High risk	High risk	Unclear risk	Unclear	No	Yes	Yes	No	Poor	
Morone, Greco, and Weiner, 2008	Low risk	Low risk	High risk	Unclear risk	Low risk	Unclear risk	No	No	Yes	Yes	Yes	Fair	
Morone et al., 2009	Low risk	Low risk	High risk	Low risk	High risk	Unclear risk	Yes	No	Yes	Yes	No	Poor	
Omidi and Zargar, 2014	Unclear risk	Unclear risk	Unclear risk	Unclear risk	High risk	Low risk	Yes	No	Yes	Yes	No	Poor	
Parra-Delgado and Latorre-Postigo, 2013	Low risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	No	No	Yes	Yes	Yes	Good	
Plews-Ogan et al., 2005	Low risk	Unclear risk	High risk	High risk	High risk	Unclear risk	No	No	Yes	Yes	No	Poor	
Rahmani and Talepasand, 2015	Unclear risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	Yes	No	Yes	Yes	Yes	Poor	
Schmidt et al., 2011	Unclear risk	Unclear risk	Low risk	Low risk	Low risk	High risk	No	No	Yes	Yes	Yes	Fair	
Teixeira, 2010	Unclear risk	Unclear risk	High risk	Unclear risk	Low risk	Low risk	Unclear	No	Yes	Yes	Yes	Poor	
Wells et al., 2014	Low risk	Low risk	High risk	Unclear risk	Low risk	Low risk	Unclear	No	Yes	No	Yes	Fair	
Wong, 2009	Unclear risk	Unclear risk	High risk	High risk	Unclear risk	Unclear risk	No	No	Yes	Yes	Unclear	Poor	
Wong et al., 2011	Low risk	Low risk	High risk	High risk	Low risk	Unclear risk	No	No	Yes	Yes	Yes	Good	
Zautra et al., 2008	Low risk	Unclear risk	High risk	High risk	Low risk	Unclear risk	No	No	Yes	Yes	Yes	Good	

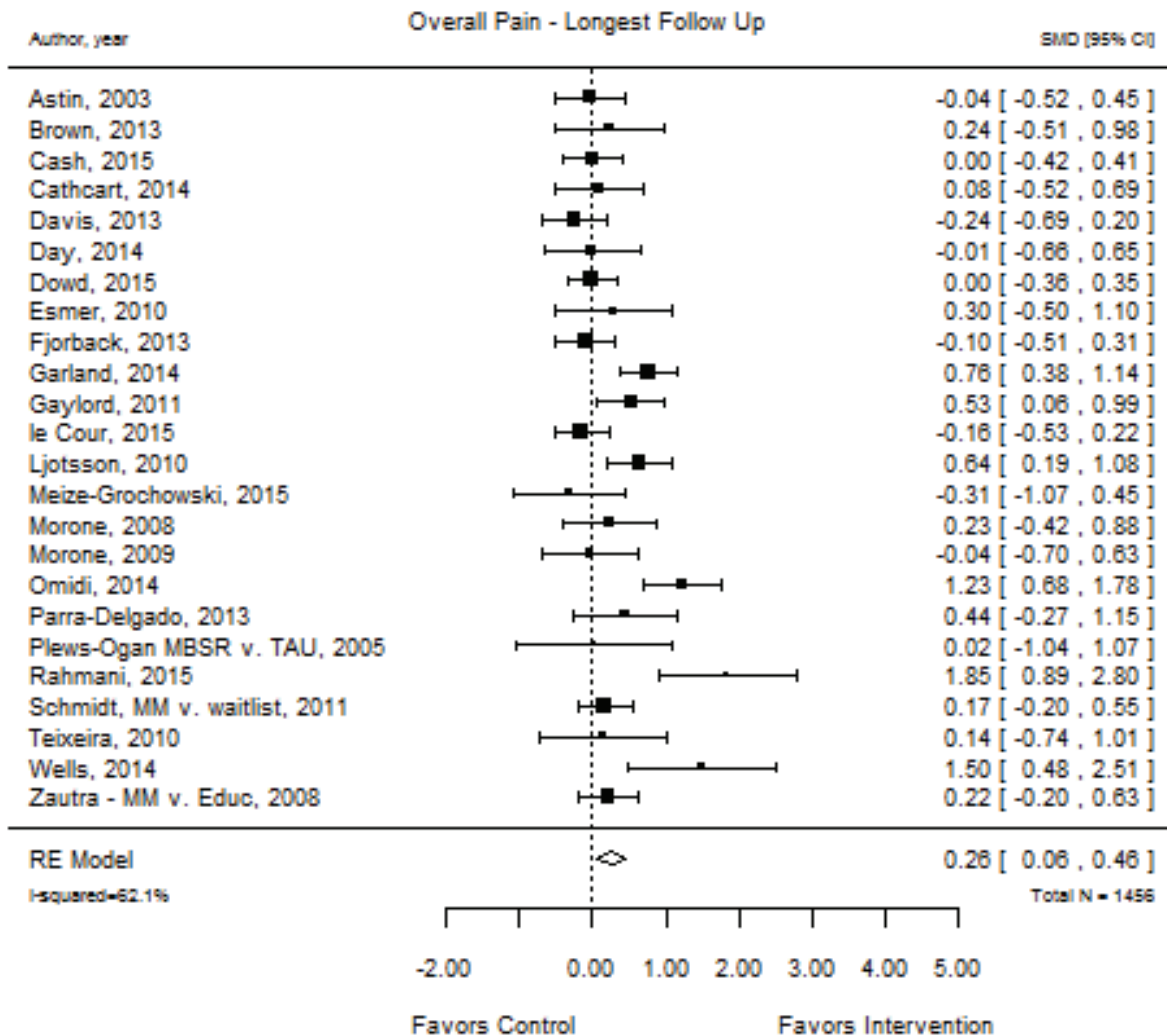
KQ 1: What Are the Efficacy and Safety of Mindfulness Meditation Interventions, as an Adjunctive or Monotherapy, for Adults with Chronic Pain Due to Migraine, Headache, Back Pain, Osteoarthritis, or Neuralgic Pain Compared with Treatment as Usual, Waitlists, No Treatment, or Other Active Treatments?

Chronic Pain Treatment Response Standardized Mean Differences

Twenty-four RCTs reported continuous outcome data on scales assessing chronic pain in each study arm. Pain scales and comparators varied from study to study (Astin et al., 2000; Brown and Jones, 2013; Cash et al., 2015; Cathcart et al., 2014; Davis and Zautra, 2013; Day et al., 2014; Dowd et al., 2015; Esmer et al., 2010; Garland et al., 2014; la Cour and Petersen, 2015; Meize-Grochowski et al., 2015; Morone, Greco, and Weiner, 2008; Morone et al., 2009; Omid and Zargar, 2014; Plews-Ogan et al., 2005; Schmidt et al., 2011; Teixeira, 2010; Wells et al., 2014; Zautra et al., 2008; Parra-Delgado and Latorre-Postigo, 2013; Rahmani and Talepasand, 2015; Fjorback et al., 2013; Gaylord et al., 2011; Ljotsson, Falk, et al., 2010). The median follow-up time was 12 weeks, with a range of four to 60 weeks. Although 15 studies indicated that mindfulness reduced pain, many did not report a statistically significant effect, and confidence intervals varied widely between studies (see Figure 3.2). However, the pooled analysis indicates a statistically significant effect of mindfulness meditation (SMD 0.26; CI 0.06, 0.46; 24 RCTs; I^2 62.1%). Substantial heterogeneity was detected. Begg's and Egger's tests for publication bias were nonsignificant.

The difference in the pooled and individual results could also indicate that the majority of studies were underpowered. This possibility is buttressed by the fact that most of the 24 RCTs either reported being underpowered or did not report power. To investigate the effect of methodological quality on these results, we conducted a sensitivity analysis excluding all poor quality studies (not displayed). The results were very similar to our main pooled analysis (SMD 0.21; CI 0.00, 0.42; 15 RCTs; I^2 57.2%).

Figure 3.2. Mindfulness Meditation Versus Control, Pain Outcome, Longest Follow-Up

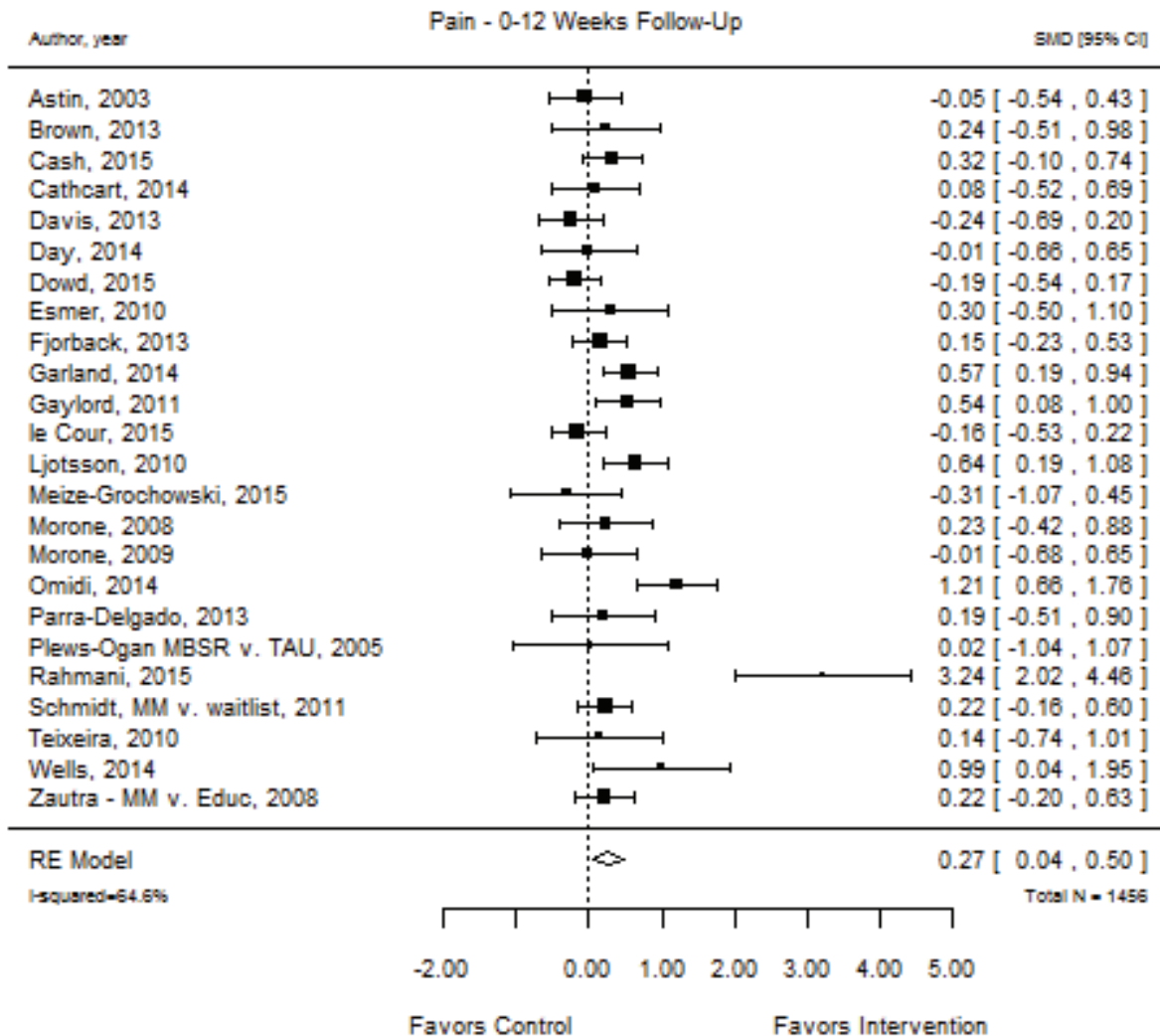


Short Term

To determine the difference between the short- and long-term effects of mindfulness meditation, we split the above analysis into short-term (0–12 weeks) and long-term (>12 weeks) follow-up. The median short-term follow-up time was eight weeks (range 4–12 weeks). Figure 3.3 shows a positive effect of meditation on pain from 0–12 weeks in 17 studies (Brown and Jones, 2013; Cash et al., 2015; Cathcart et al., 2014; Esmer et al., 2010; Garland et al., 2014; Morone, Greco, and Weiner, 2008; Omid and Zargar, 2014; Plews-Ogan et al., 2005; Schmidt et al., 2011; Teixeira, 2010; Wells et al., 2014; Zautra et al., 2008; Parra-Delgado and Latorre-Postigo, 2013; Rahmani and Talepasand, 2015; Fjorback et al., 2013; Gaylord et al., 2011; Ljotsson, Falk, et al., 2010), which was statistically significant in five studies (Garland et al., 2014; Omid and Zargar, 2014; Wells et al., 2014; Rahmani and Talepasand, 2015; Gaylord et al., 2011). The pooled analysis of all 24 RCTs showed a significant positive effect (SMD 0.27;

CI 0.04, 0.50; 24 RCTs; I^2 64.6%). Substantial heterogeneity was detected. Egger's test indicated possible publication bias, while Begg's test did not. However, using the trim and fill method to correct for this bias yielded an estimate identical to the original pooled result. The effect was very similar when nine poor quality studies were excluded from analysis (SMD 0.2; CI 0.03, 0.38; not displayed); heterogeneity was moderate (I^2 43.8%).

Figure 3.3. Mindfulness Meditation Versus Control, Pain Outcome, 0–12 weeks

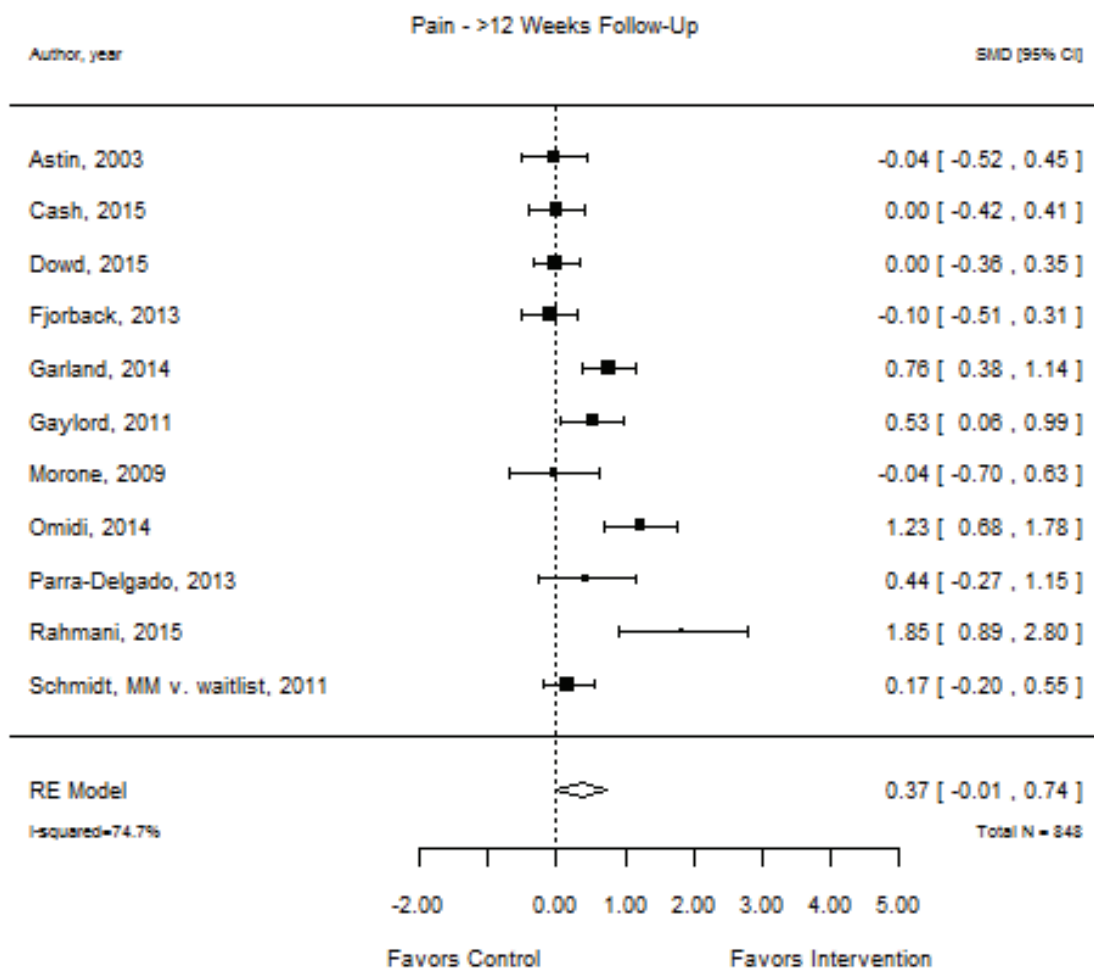


Long Term

Eleven RCTs followed study participants more than 12 weeks (median: 20 weeks; range: 16–60 weeks) (Astin et al., 2003; Cash et al., 2015; Dowd et al., 2015; Garland et al., 2014; Morone et al., 2009; Omid and Zargar, 2014; Schmidt et al., 2011; Parra-Delgado and Latorre-Postigo, 2013; Rahmani and Talepasand, 2015; Fjorback et al., 2013; Gaylord et al., 2011). Figure 3.4 shows that there is an effect of meditation on pain for participants in six of these studies but not

overall (SMD 0.37; CI -0.01, 0.74; 11 RCTs, I^2 74.7%) (Garland et al., 2014; Omid and Zargar, 2014; Schmidt et al., 2011; Parra-Delgado and Latorre-Postigo, 2013; Rahmani and Talepasand, 2015; Gaylord et al., 2011). Substantial heterogeneity was detected. Publication bias was not detected. Removing poor quality studies (not shown) yielded a slightly smaller nonsignificant effect (SMD 0.24; CI -0.07, 0.55; 7 RCTs, I^2 59.8%). It is important to note that no interventions were more than 12 weeks in length, so these findings reflect outcomes collected after the interventions ended. Few studies collected information on continued practice of mindfulness meditation.

Figure 3.4. Mindfulness Meditation Versus Control, Pain Outcome, >12 Weeks

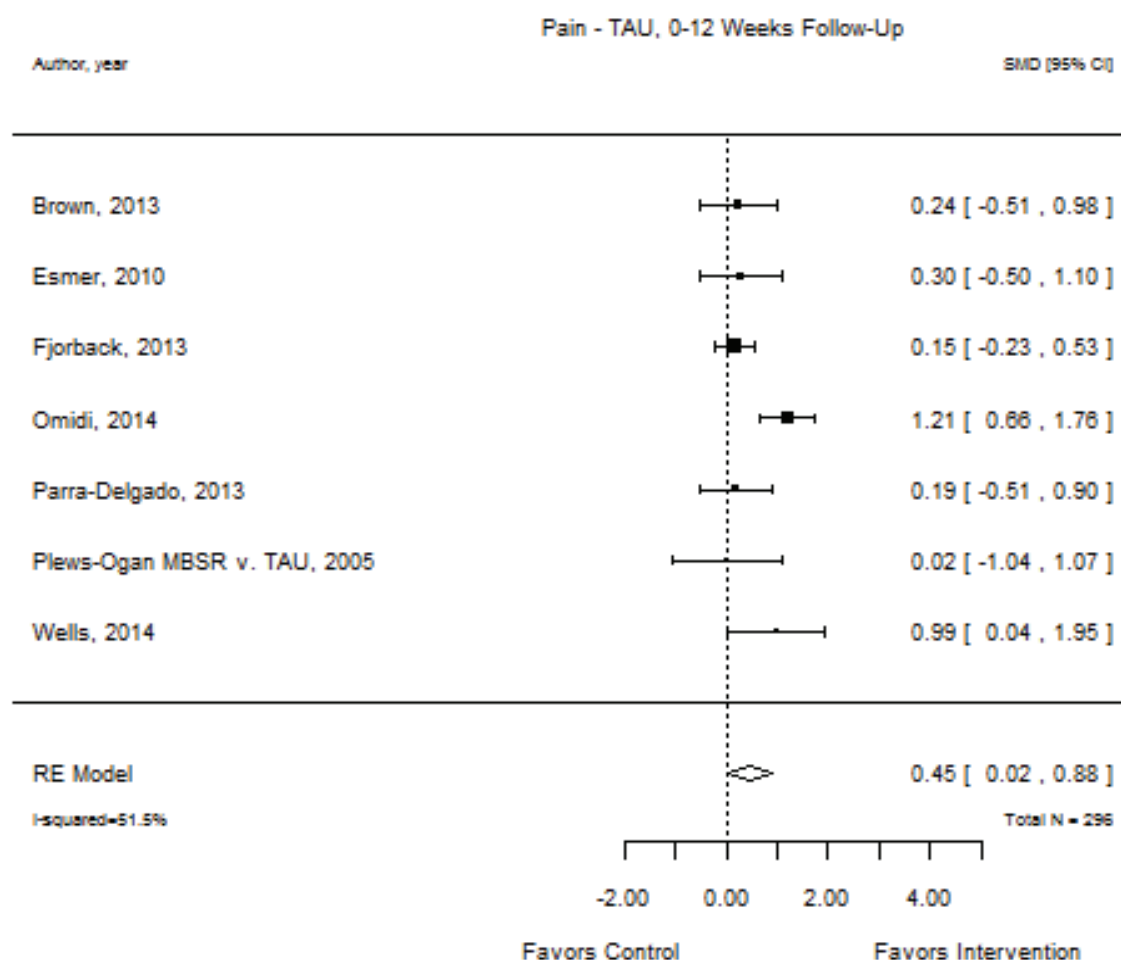


Comparators

Studies examined three major comparators: treatment as usual (TAU), passive control, and education or support groups. Seven RCTs compared the effect of mindfulness meditation to TAU (Brown and Jones, 2013; Esmer et al., 2010; Omid and Zargar, 2014; Plews-Ogan et al., 2005; Wells et al., 2014; Parra-Delgado and Latorre-Postigo, 2013; Fjorback et al., 2013) (see

Figure 3.5). Two of the seven studies reported significant effects and the pooled effect was significant overall (SMD 0.45; CI 0.02, 0.88; 7 RCTs; I^2 51.5%) (Omidi and Zargar, 2014; Wells et al., 2014). Heterogeneity among studies was moderate. Begg's and Egger's tests were nonsignificant for publication bias. The size of the effect decreased and became nonsignificant when poor quality studies were removed from analysis (SMD 0.29; CI -0.62, 1.21; 3 RCTs; I^2 23.1%). A meta-regression found that treatment effects did not differ significantly when TAU was used as a comparator versus all other comparators.

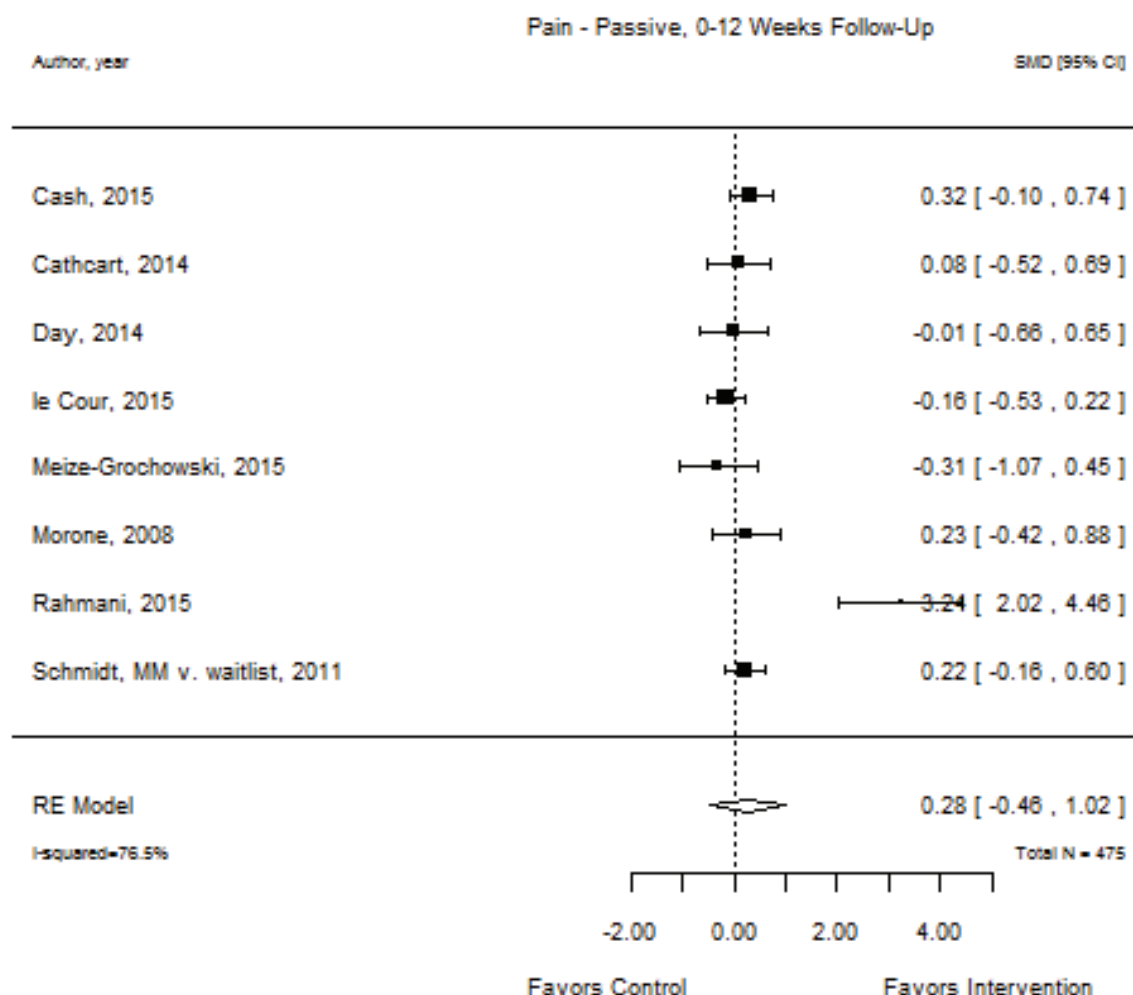
Figure 3.5. Mindfulness Meditation Versus Treatment as Usual



Among the eight RCTs that compared mindfulness meditation to a passive control (either intervention or a waitlist for the primary intervention) (Cash et al., 2015; Cathcart et al., 2014; Day et al., 2014; la Cour and Petersen, 2015; Meize-Grochowski et al., 2015; Morone, Greco, and Weiner, 2008; Schmidt et al., 2011; Rahmani and Talepasand, 2015), one showed a significant effect of meditation on pain (Rahmani and Talepasand, 2015). The pooled effect (displayed in Figure 3.6) was not significant (SMD 0.28; CI -0.46, 1.02; 8 RCTs; I^2 76.5%);

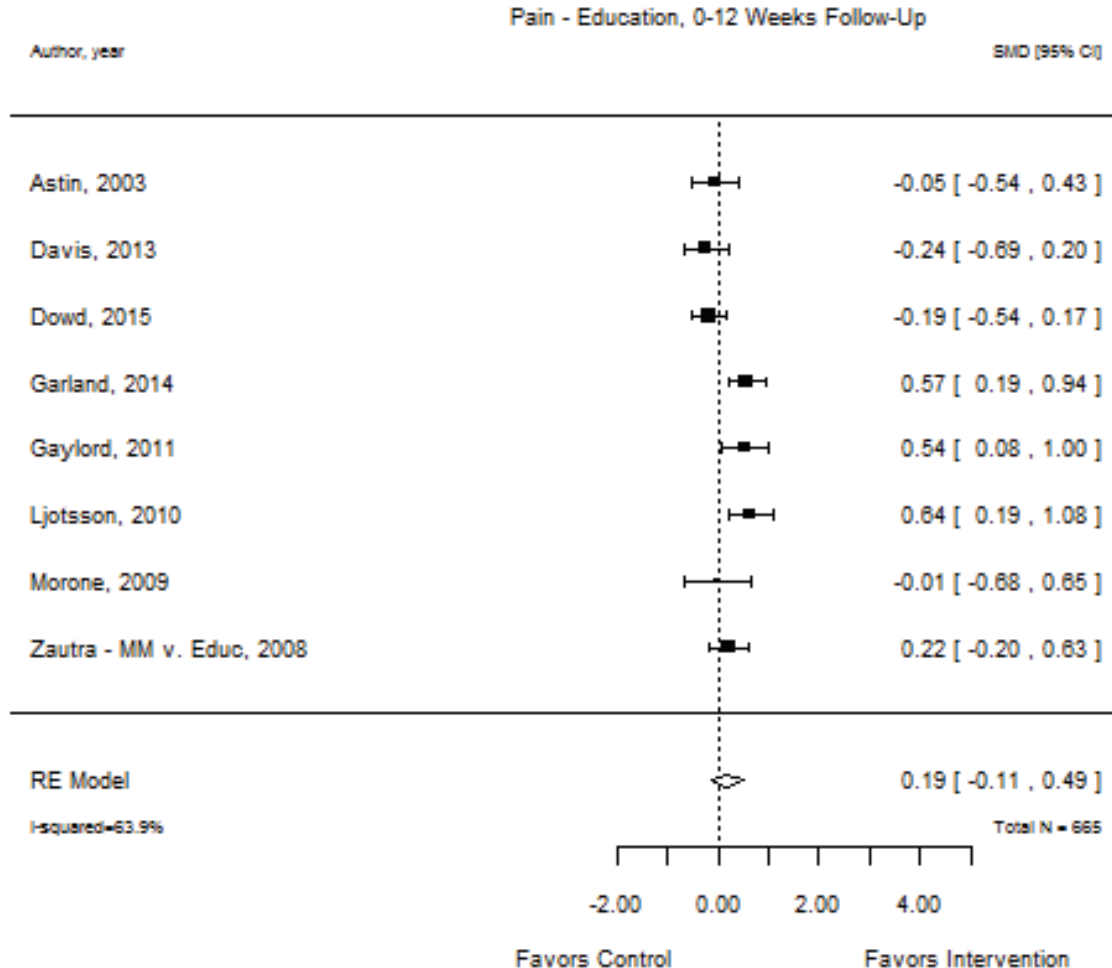
considerable heterogeneity was detected. Nonsignificance persisted when poor quality studies were dropped from analysis (SMD 0.11; CI $-0.10, 0.32$; 6 RCTs; I^2 0%; not displayed).

Figure 3.6. Mindfulness Meditation Versus Passive Control



Eight RCTs examined the effect of mindfulness meditation on pain compared with education or support groups (Astin et al., 2003; Davis and Zautra, 2013; Garland et al., 2014; Dowd et al., 2015; Morone et al., 2009; Gaylord et al., 2011; Ljotsson, Falk, et al., 2010; Zautra et al., 2008) (see Figure 3.7). The effect of meditation was significant in three of these studies, and not significant when studies were pooled (SMD 0.19; CI $-0.11, 0.49$; 8 RCTs; I^2 63.9%) (Garland et al., 2014; Gaylord et al., 2011; Ljotsson, Falk, et al., 2010). Substantial heterogeneity was detected. The nonsignificant effect remained largely unchanged when poor quality studies were removed from analysis (SMD 0.25; CI $-0.16, 0.66$; 6 RCTs; I^2 71.9%; not displayed).

Figure 3.7. Mindfulness Meditation Versus Education or Support Group



Four studies examined the effect of mindfulness meditation on pain versus a comparator other than those listed above. Mindfulness meditation improved self-reported pain more than cognitive behavioral therapy (SMD 0.56; CI 0.16, 0.96) (Zautra et al., 2008) but not more than a nutritional program (SMD 0.08; CI -0.30, 0.45) (Teixeira, 2010). MBSR had no significant effect on pain unpleasantness compared with massage (SMD -0.30; CI -1.34, 0.74) (Plews-Ogan et al., 2005) or on Pain Perception Scale affective component scores compared with relaxation training (SMD 0.08; CI -0.30, .45) (Schmidt et al., 2011).

Effect sizes could not be calculated for four studies because authors reported limited information or nonstandard outcomes. In one study, MBSR had no significant effect on pain intensity versus a multidisciplinary pain intervention at six months postintervention, but in another study, MBSR significantly reduced pain after the same amount of time. In the third, Internet-based cognitive behavioral therapy with a mindfulness component significantly increased relief from IBS-related pain and discomfort at six months. The last study reported a decrease in pain intensity for those participating in MBSR at both eight weeks and six months,

although no numeric data were reported (Wong et al., 2011; Fogarty et al., 2015; Ljotsson, Hedman, et al., 2011; Wong, 2009).

Analgesic Use

Only one study reported use of analgesics as an outcome (Esmer et al., 2010). Esmer and colleagues studied 25 patients with chronic pain due to failed back surgery syndrome. Fifteen of the participants received the MBSR intervention and ten participants were controls, receiving no treatment. Each group kept a log of analgesic medication use, which was scored on a scale of 0 to 4 points (0: no analgesic use; 1: less than daily nonopioid analgesic use; 2: daily nonopioid analgesic use; 3: less than daily opioid analgesic use; and 4: daily opioid medications). At 12-week follow-up, the analgesic medication logs of those in the intervention group documented a decrease in analgesic use compared with those in the control group (−1.5 (SD 1.8) versus 0.4 (SD 1.1), $p < .001$).

Health-Related Quality of Life

Ten RCTs measured depression outcomes (Astin et al., 2003; Gaylord et al., 2011; la Cour and Petersen, 2015; Ljotsson, Falk, et al., 2010; Ljotsson, Hedman, et al., 2011; Meize-Grochowski et al., 2015; Parra-Delgado and Latorre-Postigo, 2013; Schmidt et al., 2011; Wells et al., 2014; Zautra et al., 2008). Overall, meditation significantly reduced depression (SMD 0.17; CI 0.03, 0.31; 10 RCTs; I^2 0%). No heterogeneity was detected. Five (Brown and Jones, 2013; la Cour and Petersen, 2015; Ljotsson, Falk, et al., 2010; Ljotsson, Hedman, et al., 2011; Rahmani and Talepasand, 2015) of the 13 studies reporting mental health-related quality of life reported a significant effect, and this effect is significant in the pooled analysis (SMD 0.44; CI 0.18, 0.69; 13 RCTs; I^2 50.6%) (Brown and Jones, 2013; Fjorback et al., 2013; Gaylord et al., 2011; la Cour and Petersen, 2015; Ljotsson, Falk, et al., 2010; Ljotsson, Hedman, et al., 2011; Meize-Grochowski et al., 2015; Morone, Greco and Weiner, 2008; Plews-Ogan et al., 2005; Rahmani and Talepasand, 2015; Schmidt et al., 2011; Teixeira, 2010; Wells et al., 2014).¹ Twelve studies measured physical health-related quality of life (Brown and Jones, 2013; Fjorback et al., 2013; Gaylord et al., 2011; la Cour and Petersen, 2015; Ljotsson, Falk, et al., 2010; Ljotsson, Hedman, et al., 2011; Meize-Grochowski et al., 2015; Morone, Greco, and Weiner, 2008; Rahmani and Talepasand, 2015; Schmidt et al., 2011; Teixeira, 2010; Wells et al., 2014), and four of these studies used a remote intervention (Ljotsson, Falk, et al., 2010; Ljotsson, Hedman, et al., 2011; Meize-Grochowski et al., 2015; Teixeira, 2010).² Three (Ljotsson, Falk, et

¹ Mental health-related quality of life is assessed by the mental health summary measure of the SF-36 or other instrument that measures such factors as affect, anxiety, vitality, ability to emotionally function in self-identified roles, and social functioning.

² Physical health-related quality of life is assessed by the physical health summary measure of the SF-36, which captures physical functioning, ability to physically function in self-identified roles, general health, and pain.

al., 2010; Ljotsson, Hedman, et al., 2011; Rahmani and Talepasand, 2015) of the 12 and all of those using a remote intervention report a significant positive effect of meditation on physical health-related quality of life. Pooled analyses showed a significant effect for all studies that reported a physical health-related quality of life (SMD 0.3; CI 0.03, 0.57; 12 RCTs; I^2 54.6%) and in those with a remote intervention (SMD 0.61; CI 0.06, 1.15; 4 RCTs; I^2 36.6%). The quality of life analyses detected moderate heterogeneity.

Functional Impairment (Disability Measures)

Three studies reported poolable disability scores. Esmer and colleagues (2010) and Morone, Greco, and Weiner (2008) reported Roland-Morris Disability Questionnaire scores, while Ljotsson, Falk, and colleagues (2010) reported the Sheehan Disability Scale. Improvements in these scores in the mindfulness groups were not significantly different from improvements in the control groups (SMD 0.47; CI -0.18, 1.12; I^2 0%). No heterogeneity was detected.

Adverse Events Reported in RCTs

Only three of the included RCTs reported on adverse events. Of these three, two stated that no adverse events occurred (Morone, Greco, and Weiner, 2008; Morone et al., 2009), and one described that two participants experienced temporary strong feelings of anger toward their pain condition and two of the participants experienced greater anxiety (la Cour and Petersen, 2015).

Study Characteristic Moderators and Risk of Bias

Several meta-regressions were run to determine if changes in pain outcomes systematically differed by several subcategories. Changes in pain outcomes in good ($p=0.72$) and fair ($p=0.32$) quality studies were not significantly different from changes in poor quality studies.

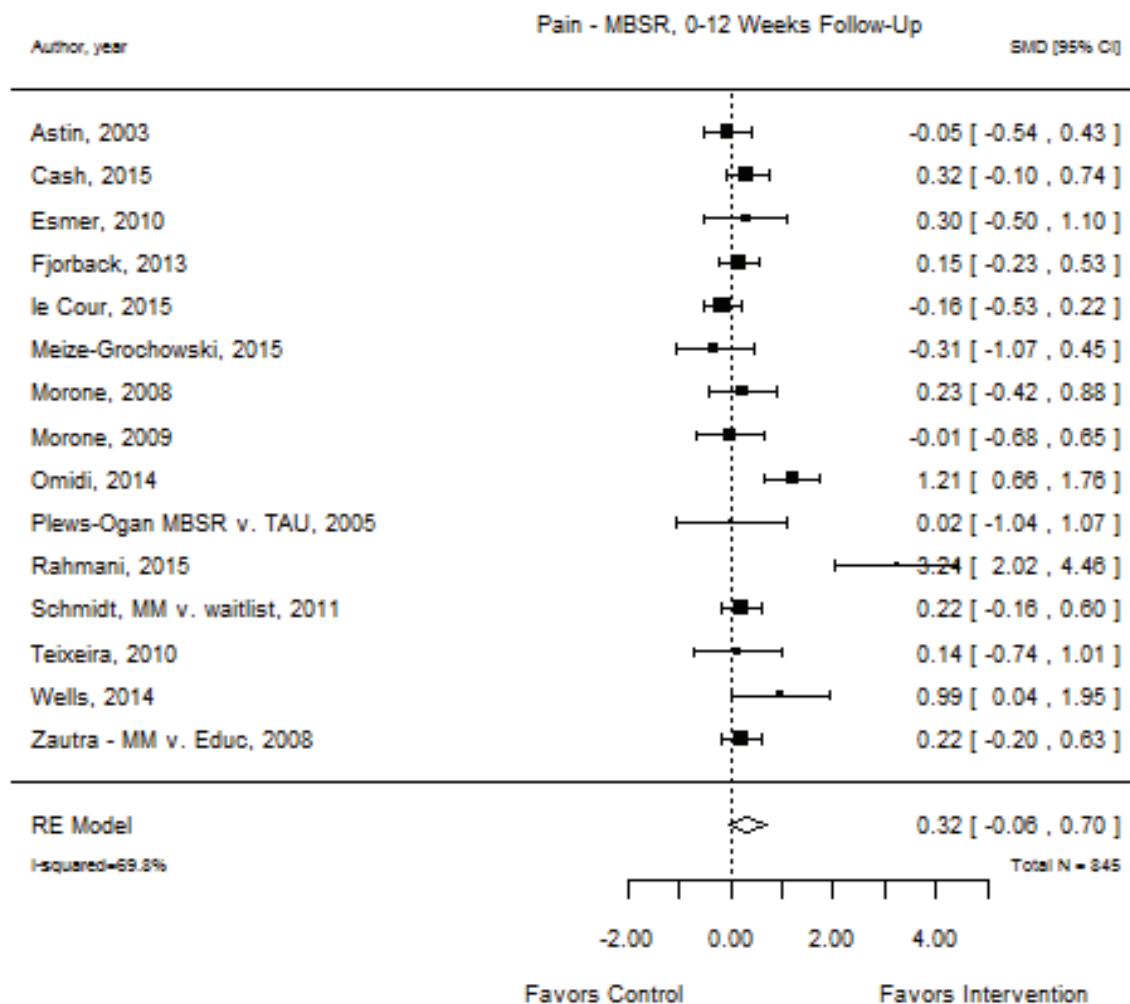
KQ 1a: Does the Effect Vary by the Type of Mindfulness Meditation Intervention?

Mindfulness-Based Stress Reduction

Fifteen RCTs examined the effect of MBSR on a continuous chronic pain measure (Astin et al., 2003; Cash et al., 2015; Esmer et al., 2010; la Cour and Petersen, 2015; Meize-Grochowski et al., 2015; Morone, Greco, and Weiner, 2008; Morone et al., 2009; Omid and Zargar, 2014; Plews-Ogan et al., 2005; Schmidt et al., 2011; Teixeira, 2010; Wells et al., 2014; Zautra et al., 2008; Rahmani and Talepasand, 2015; Fjorback et al., 2013) (see Figure 3.8). Eleven of these studies (Cash et al., 2015; Esmer et al., 2010; Morone, Greco, and Weiner, 2008; Omid and Zargar, 2014; Plews-Ogan et al., 2005; Schmidt et al., 2011; Teixeira, 2010; Wells et al., 2014; Zautra et al., 2008; Rahmani and Talepasand, 2015; Fjorback et al., 2013) reported a positive effect after treatment was applied for up to 12 weeks, three of which were statistically significant

(Omidi and Zargar, 2014; Rahmani and Talepasand, 2015; Wells et al., 2014). This effect was nonsignificant in the pooled analysis (SMD 0.32; CI -0.06, 0.70; 15 RCTs; I^2 69.8%). Substantial heterogeneity was detected. After removing eight poor quality studies from analysis, the effect decreased and remained nonsignificant (SMD 0.18; CI -0.04, 0.39; 7 RCTs; I^2 6%). A meta-regression showed that changes in pain outcomes with MBSR were not significantly different than with other types of mindfulness meditation ($p=0.60$).

Figure 3.8. MBSR Versus Control

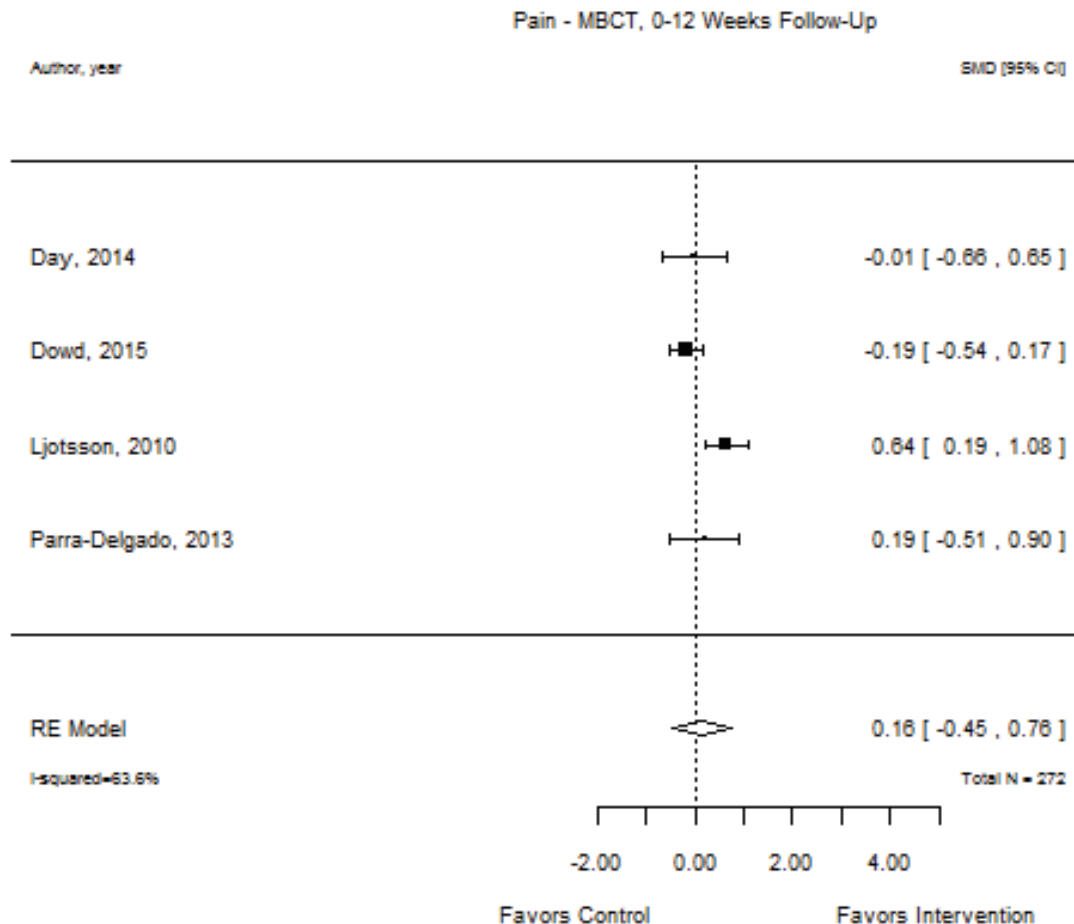


Mindfulness-Based Cognitive Therapy

Only four RCTs explored the relationship between MBCT and chronic pain (Day et al., 2014; Dowd et al., 2015; Parra-Delgado and Latorre-Postigo, 2013; Ljotsson, Falk, et al., 2010) (see Figure 3.9). One of these four (Ljotsson, Falk, et al., 2010) showed that MBCT significantly reduced pain within 12 weeks, but this effect was nonsignificant in the pooled analysis (SMD

0.16; CI $-0.45, 0.76$; 4 RCTs; I^2 63.6%). Substantial heterogeneity was detected. There were no poor quality studies to exclude in this subgroup analysis. A meta-regression did not detect systematic differences between MBSR and other types of mindfulness meditation ($p=0.58$).

Figure 3.9. MBCT Versus Control



Other Interventions

The remaining studies addressed MORE, mindfulness-based pain management, mindful socioemotional regulation, or other unique interventions. Five RCTs delivered mindfulness meditation interventions remotely—via either Internet-based programs or materials instructing participants to conduct mindfulness exercises at home (Davis and Zautra, 2013; Dowd et al., 2015; Meize-Grochowski et al., 2015; Teixeira, 2010; Ljotsson, Falk, et al., 2010). Within 12 weeks, pain was significantly reduced in only one of these five programs, and the effect of the programs in the pooled analysis was close to zero and not statistically significant (SMD 0.01; CI $-0.50, 0.52$; 5 RCTs; I^2 62.9%) (Ljotsson, Falk, et al., 2010). Removing poor quality studies

from analysis increased the estimate of the effect but did not change its nonsignificance (SMD 0.06; CI -1.15, 1.27; 3 RCTs; I^2 80%). A meta-regression showed that changes in pain outcomes with remote treatment did not differ significantly from in-person mindfulness meditation ($p=0.14$).

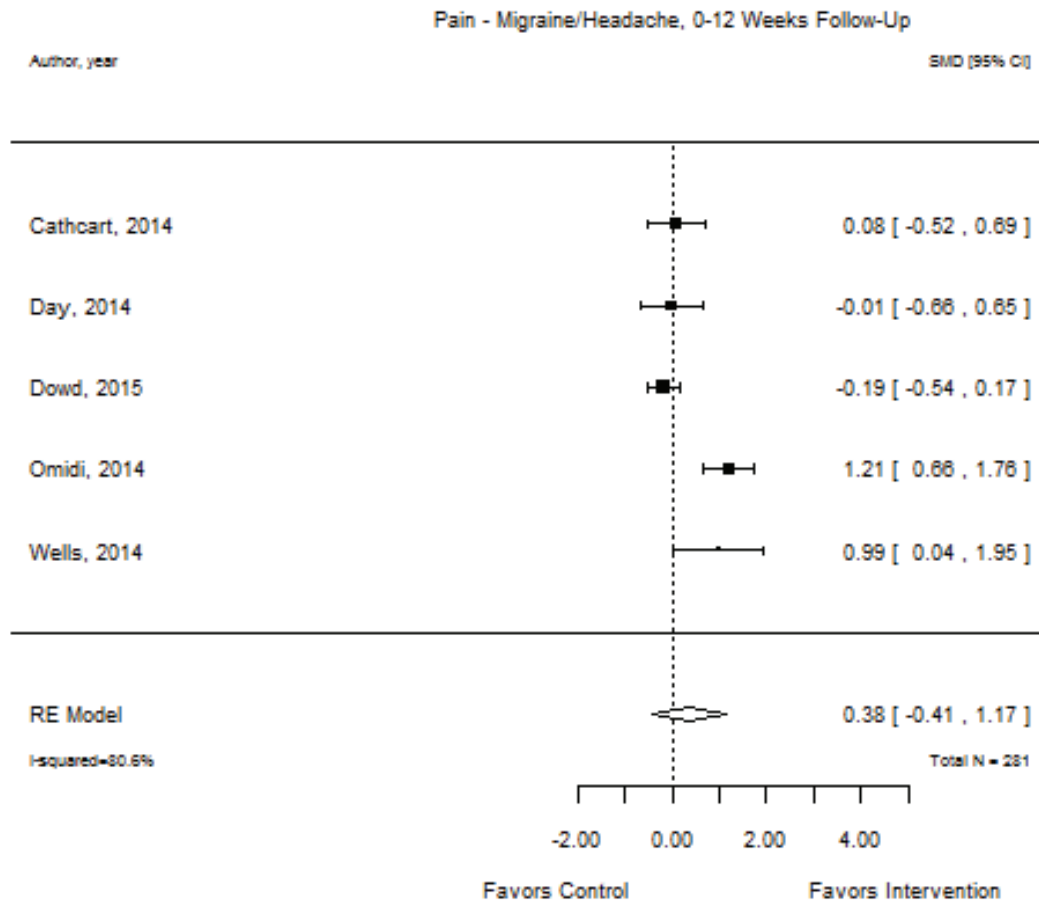
We did not identify any head-to-head trials comparing different meditation interventions.

KQ 1b: Does the Effect Vary by Medical Condition Targeted (Migraine, Headache, Back Pain, Osteoarthritis, or Neuralgic Pain)?

Migraine or Other Headache

Five RCTs reported continuous outcomes measuring the effect of mindfulness meditation on participants with chronic pain from migraine or headache (Cathcart et al., 2014; Day et al., 2014; Dowd et al., 2015; Omid and Zargar, 2014; Wells et al., 2014) (see Figure 3.10). Two of these studies (Omid and Zargar, 2014; Wells et al., 2014) showed a significant positive effect after up to 12 weeks of intervention, but these results were not significant in the pooled analysis (SMD 0.38; CI -0.41, 1.17; 5 RCTs; I^2 80.6%). Considerable heterogeneity was detected. Removing one poor quality study reduced the estimated effect but did not make it significant (SMD 0.08; CI -0.61, 0.77; 4 RCTs; I^2 43.5%). Results from a meta-regression confirmed that participants with chronic migraines or headaches did not benefit from mindfulness meditation more than those with other conditions ($p=0.52$).

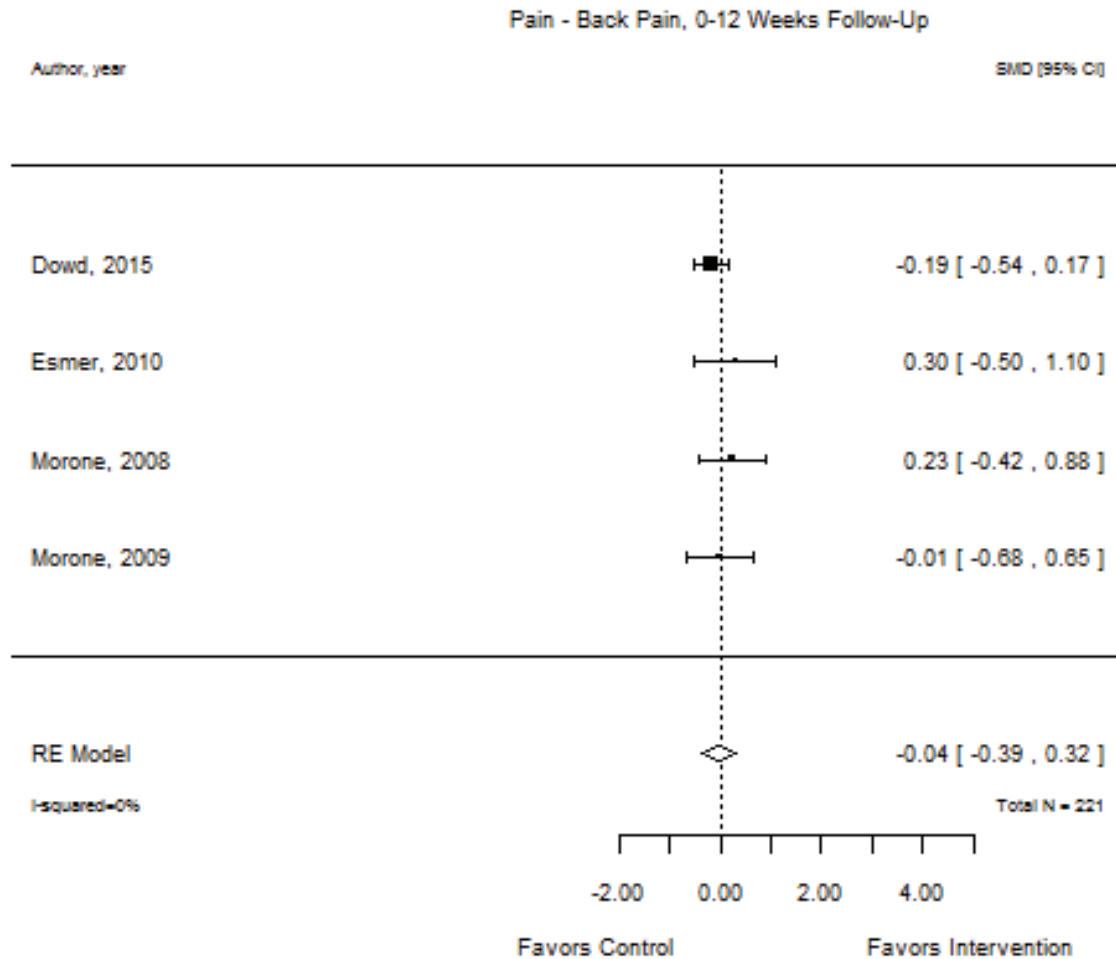
Figure 3.10. Mindfulness Meditation for Migraine or Headache



Back Pain

Four RCTs investigated the effect of mindfulness meditation on participants with chronic back pain (Dowd et al., 2015; Esmer et al., 2010; Morone et al., 2009; Morone, Greco, and Weiner, 2008) (see Figure 3.11). Two of these four studies showed a positive effect after up to 12 weeks of intervention, neither of which was statistically significant (Esmer et al., 2010; Morone, Greco, and Weiner, 2008). The pooled analysis did show a very small effect favoring the comparator, which was not statistically significant (SMD -0.04; CI -0.39, 0.32; 4 RCTs; I^2 0%). No heterogeneity was detected. A pooled analysis without poor quality studies showed roughly the same effect with a larger confidence interval (SMD -0.07; CI -2.46, 2.32; 2 RCTs; I^2 19.1%). Participants suffering from back pain did not differentially benefit from mindfulness meditation, according to results from a meta-regression ($p=0.41$).

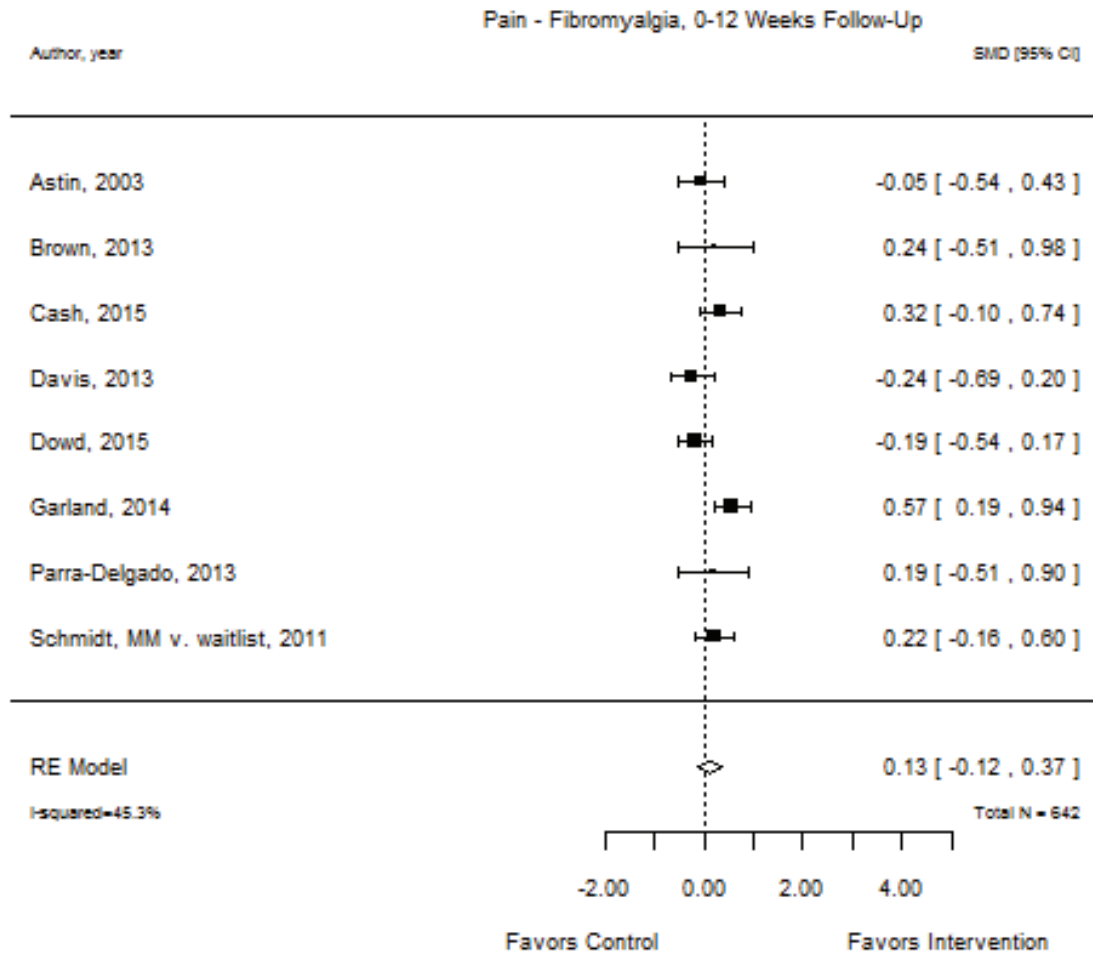
Figure 3.11. Mindfulness Meditation for Back Pain



Fibromyalgia

Eight RCTs examined the effect of mindfulness meditation on chronic pain due to fibromyalgia (Astin et al., 2003; Brown and Jones, 2013; Cash et al., 2015; Davis and Zautra, 2013; Dowd et al., 2015; Garland et al., 2014; Parra-Delgado and Latorre-Postigo, 2013; Schmidt et al., 2011) (see Figure 3.12). In five of these eight, meditation reduced pain (Brown and Jones, 2013; Cash et al., 2015; Garland et al., 2014; Parra-Delgado and Latorre-Postigo, 2013; Schmidt et al., 2011), but the results were statistically significant in one study (Garland et al., 2014). The effect was not significant in the pooled analysis (SMD 0.13; CI -0.12, 0.37; 8 RCTs; I^2 45.3%). Even with the removal of two poor quality studies, this effect remained nonsignificant (SMD 0.14; CI -0.19, 0.48; 6 RCTs; I^2 58.8%). A meta-regression revealed that participants with fibromyalgia did not receive more benefit from mindfulness meditation than participants with other conditions ($p=0.29$).

Figure 3.12. Mindfulness Meditation for Fibromyalgia



KQ 1c: Does the Effect Differ When the Intervention Is Offered as an Adjunctive Therapy Rather Than as a Monotherapy?

Mindfulness meditation was adjunctive to treatment as usual in 13 RCTs (Day et al., 2014; Esmer et al., 2010; Garland et al., 2014; la Cour and Petersen, 2015; Meize-Grochowski et al., 2015; Morone et al., 2009; Wells et al., 2014; Parra-Delgado and Latorre-Postigo, 2013; Rahmani and Talepasand, 2015; Fjorback et al., 2013; Gaylord et al., 2011; Wong et al., 2011; and Fogarty et al., 2015). In one study, meditation was combined with group conscious yoga (Rahmani and Talepasand, 2015). In 13 studies, meditation was given as a monotherapy (Astin et al., 2003; Brown and Jones, 2013; Cash et al., 2015; Cathcart et al., 2014; Dowd et al., 2015; Davis and Zautra, 2013; Morone, Greco, and Weiner, 2008; Omid and Zargar, 2014; Plews-Ogan et al., 2005; Schmidt et al., 2011; Teixeira, 2010; Zautra et al., 2008; Ljotsson, Falk, et al., 2010). In two studies, the treatment status was unclear (Zautra et al., 2008; Ljotsson, Hedman, et al., 2011).

While the efficacy of meditation may vary by its combination with other interventions, no systematic difference in effect between monotherapy and adjunctive therapy was detected in a meta-regression ($p=0.53$).

KQ 1d: Does the Effect Vary Depending on the Duration and Frequency of Mindfulness Meditation (i.e., Dose Effect)?

The efficacy of meditation did not significantly vary by length or frequency of the intervention.

Interventions ranged in length from three to 12 weeks (median eight weeks). In a meta-regression, efficacy did not vary significantly as program duration in weeks increased ($p=0.12$).

In subgroup analyses, the effect was not significant when participation in mindfulness intervention (including homework) was less than one hour per week (SMD -0.18 ; CI $-0.49, 0.10$; 3 RCTs; I^2 0%) (Dowd et al., 2015; Davis and Zautra, 2013; Teixeira, 2010), or one to four hours per week (SMD 0.44 ; CI $-0.16, 1.05$; 10 RCTs; I^2 77.5%) (Astin et al., 2003; Brown and Jones, 2013; Garland et al., 2014; Meize-Grochowski et al., 2015; Omid and Zargar, 2014; Plews-Ogan et al., 2005; Zautra et al., 2008; Parra-Delgado and Latorre-Postigo, 2013; Rahmani and Talepasand, 2015; Fjorback et al., 2013). The effect for programs involving greater than four hours per week (high frequency) bordered on statistical significance (SMD 0.19 ; CI $0.00, 0.39$; 11 RCTs; I^2 4.5%), but the confidence intervals were within those for programs requiring one to four hours (medium frequency) of participation (Cash et al., 2015; Cathcart et al., 2014; Day et al., 2014; Esmer et al., 2010; la Cour and Petersen, 2015; Morone, Greco, and Weiner, 2008; Morone et al., 2009; Schmidt et al., 2011; Wells et al., 2014; Gaylord et al., 2011). In a meta-regression, participation of one to four hours per week ($p=0.32$) or less than one hour per week ($p=0.17$) was not significantly less effective than participation of more than four hours per week.

Chapter Four: Discussion

Summary of Findings

In this chapter, we first summarize the findings in response to each key question and subquestion, along with the quality of the evidence (see Table 4.1). We briefly discuss the findings in the context of prior systematic reviews. We then describe the limitations of the body of literature and provide suggestions for further research based on those limitations.

In total, 28 studies met inclusion criteria. All reported on the efficacy of mindfulness meditation, and three addressed safety. Risk of bias in included studies varied; seven studies obtained a “good” quality rating, ten studies were rated “fair,” and 11 were rated “poor” quality.

KQ 1: What Are the Efficacy and Safety of Mindfulness Meditation Interventions, as an Adjunctive or Monotherapy, for Adults with Chronic Pain Due to Migraine, Headache, Back Pain, Osteoarthritis, or Neuralgic Pain Compared with Treatment as Usual, Waitlists, No Treatment, or Other Active Treatments?

We identified 24 RCTs that met the inclusion criteria and reported continuous pain measures on the efficacy of mindfulness meditation for chronic pain (SMD 0.26; CI 0.06, 0.46; 24 RCTs; I^2 62.1%). (Four studies were excluded from analyses because they did not report appropriate outcome data for meta-analysis.) Study quality was mixed. A sensitivity analysis excluding poor quality studies yielded similar results (SMD 0.21; CI 0.00, 0.42; 15 RCTs; I^2 57.2%). This effect remained up to 12 weeks postintervention (SMD 0.27; CI 0.04, 0.50; 24 RCTs; I^2 64.6%), but dropped out of significance for follow-up periods beyond 12 weeks (SMD 0.37; CI -0.01, 0.74; 11 RCTs, I^2 74.7%). These analyses detected substantial heterogeneity. The quality of evidence that mindfulness meditation is associated with a decrease in chronic pain compared with control is low overall and for short-term follow-up because of the quality of the included studies and heterogeneity. The quality of evidence for long-term follow-up is low because of the quality of the included studies, heterogeneity, and imprecision of results.

In subgroup analyses of comparators, mindfulness meditation significantly reduced pain scale scores compared with TAU (SMD 0.45; CI 0.02, 0.88; 7 RCTs; I^2 51.5%), but not compared with passive controls (SMD 0.28; CI -0.46, 1.02; 8 RCTs; I^2 76.5%) or with education or support groups (SMD 0.19; CI -0.11, 0.49; 8 RCTs; I^2 63.9%). The quality of evidence is low for the first two comparisons and very low for the third because of the quality of the included studies, heterogeneity, and imprecision of results.

A number of the studies reported non-pain outcomes. Ten studies assessed the effect of mindfulness meditation on depression in chronic pain studies; pooled analyses showed that mindfulness meditation significantly reduced depression (SMD 0.17; CI 0.03, 0.31; 10 RCTs; I^2

0%). The quality of evidence is high. Twelve studies assessed physical health-related quality of life (SMD 0.3; CI 0.03, 0.57; 12 RCTs; I^2 54.6%), and 13 assessed mental health-related quality of life (SMD 0.44; CI 0.18, 0.69; 13 RCTs; I^2 50.6%). The quality of evidence regarding the efficacy of mindfulness meditation for quality of life is moderate because of imprecise results. Three studies reported poolable disability measures; improvements in the mindfulness groups were not significantly different from improvements in the control groups (SMD 0.47; CI -0.18, 1.12; I^2 0). Only one study assessed the effect of meditation on the reduction of analgesic use; effects were significant in favor of the mindfulness intervention ($p < 0.001$).

Of the three RCTs reporting adverse events, two stated that participants had no adverse events, and one stated that two participants experienced feelings of anxiety and anger toward their pain. The quality of evidence for adverse events is very low, as the vast majority of the 28 included RCTs did not collect adverse events data.

KQ 1a: Does the Effect Vary by the Type of Mindfulness Meditation Intervention?

The effect of meditation on pain was nonsignificant in pooled analysis of 15 RCTs examining MBSR (SMD 0.32; CI -0.06, 0.70; 15 RCTs; I^2 69.8%); the quality of evidence is low because of the poor quality of the studies and imprecision of the results. Four RCTs examined MBCT (SMD 0.16; CI -0.45, 0.76; 4 RCTs; I^2 63.6%) and five examined remote (e.g., Internet, smart phone) interventions (SMD 0.01; CI -0.50, 0.52; 5 RCTs; I^2 62.9%). The quality of evidence for both comparisons is low because of inconsistency and imprecision of study results. Meta-regression did not indicate that the efficacy of mindfulness meditation differs significantly by type of intervention.

KQ 1b: Does the Effect Vary by Medical Condition Targeted (Migraine, Headache, Back Pain, Osteoarthritis, or Neuralgic Pain)?

Five studies assessed the effect of mindfulness meditation for chronic pain caused by migraine or headache. Pooled analyses showed no significant effect (SMD 0.38; CI -0.41, 1.17; 5 RCTs; I^2 80.6%). The quality of evidence is low because of inconsistent and imprecise results.

Four studies assessed the effect of mindfulness meditation for chronic back pain, and pooled analysis showed no significant effect (SMD -0.04; CI -0.39, 0.32; 4 RCTs; I^2 0%). The quality of evidence is low for no effect because of the quality of the individual studies. Eight studies assessed the effect of mindfulness meditation on chronic pain due to fibromyalgia, and pooled analysis showed no significant effect (SMD 0.13; CI -0.12, 0.37; 8 RCTs; I^2 45.3%). The quality of evidence is moderate because of the heterogeneity of the results. Meta-regressions showed that the effect of mindfulness meditation did not vary by medical condition.

KQ 1c: Does the Effect Differ When the Intervention Is Offered as an Adjunctive Therapy Rather Than as a Monotherapy?

Thirteen studies assessed the effect of mindfulness meditation for chronic pain as monotherapy. The effect was not significant (SMD 0.21; CI -0.02, 0.45; 13 RCTs; I^2 55%) and the quality of evidence is low because of the heterogeneity of the results. Eleven studies assessed the effect of mindfulness meditation as an adjunctive therapy. The effect on chronic pain was not significant (SMD 0.36; CI -0.16, 0.89; 11 RCTs; I^2 73.5%) and the quality of evidence is low because of heterogeneity and imprecision of results. A meta-regression showed that effect of meditation on pain did not differ significantly when offered as a monotherapy compared with as an adjunctive treatment.

KQ 1d: Does the Effect Vary Depending on the Duration and Frequency of Mindfulness Meditation (i.e., Dose Effect)?

Meta-regression indicated that the efficacy of mindfulness meditation did not differ significantly by frequency or duration of the treatment. The effect was not significant at a dose of less than one hour per week (SMD -0.18; CI -0.49, 0.10; 3 RCTs; I^2 0%) or at a dose of one to four hours per week (SMD 0.44; CI -0.16, 1.05; 10 RCTs; I^2 77.5%). The quality of the evidence for these two categories of frequency of practice was low, because of the quality of the individual studies and imprecision. The effect for programs requiring greater than four hours per week bordered on statistical significance (SMD 0.19; CI 0.00, 0.39; 11 RCTs; I^2 4.5%), but the confidence intervals fit within those of the results for programs requiring one to four hours of participation. The quality of the evidence for the effect of the high frequency of participation was moderate because of the quality of the individual studies.

Table 4.1. Summary of Findings and Quality of Evidence Table

Outcome	Study Design (number of RCTs and participants)	Findings (direction and magnitude of effect)	Study Limitations (study quality; risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of Evidence for Outcome
KQ 1							
Longest follow-up	24 RCTs, 1,456 participants	SMD 0.26 (CI 0.06, 0.46), favors mindfulness meditation	Majority good or fair quality; effect similar when poor quality RCTs excluded	Inconsistent; substantial heterogeneity	Direct	Precise	Low
0–12 weeks follow-up	24 RCTs, 1,456 participants	SMD 0.27 (CI 0.04, 0.50), favors mindfulness meditation	Majority good or fair quality; effect similar when poor quality RCTs excluded; possible publication bias	Inconsistent; substantial heterogeneity	Direct	Precise	Low
>12 weeks follow-up	11 RCTs, 848 participants	SMD 0.37 (CI –0.01, 0.74), n.s.	Majority good or fair quality; effect similar when poor quality RCTs excluded	Inconsistent; substantial heterogeneity	Direct	Imprecise	Low
Mindfulness meditation versus TAU, 0–12 weeks	7 RCTs, 296 participants	SMD 0.45 (CI 0.02, 0.88), favors mindfulness meditation	Majority poor quality	Consistent; moderate heterogeneity	Direct	Imprecise	Low
Mindfulness meditation versus passive comparator, 0–12 weeks	8 RCTs, 475 participants	SMD 0.28 (CI –0.46, 1.02), n.s.	Majority fair quality; no good quality; effect similar when poor quality RCTs excluded	Consistent regarding significant no effect; substantial heterogeneity	Direct	Imprecise	Low for no effect
Mindfulness meditation versus education or support groups, 0–12 weeks	8 RCTs, 665 participants	SMD 0.19 (CI –0.11, 0.49), n.s.	Majority good or fair quality; effect similar when poor quality RCTs excluded	Inconsistent; substantial heterogeneity	Direct	Imprecise	Very low for no effect
MBSR versus massage	1 RCT, 23 participants	SMD –0.30 (CI –1.34, 0.74), n.s.	Poor quality	No replication	Direct	Imprecise	Very low for no effect
MBSR versus relaxation training	1 RCT, 168 participants	SMD 0.08 (CI –0.30, 0.45), n.s.	Fair quality	No replication	Direct	Imprecise	Very low for no effect
Mindfulness meditation versus cognitive-based therapy	1 RCT, 137 participants	SMD 0.56 (CI 0.16, 0.96), favors mindfulness meditation	Good quality	No replication	Direct	Imprecise	Very low

Outcome	Study Design (number of RCTs and participants)	Findings (direction and magnitude of effect)	Study Limitations (study quality; risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of Evidence for Outcome
Mindfulness meditation versus nutritional program	1 RCT, 20 participants	SMD 0.08 (CI -0.30, 0.45), n.s.	Poor quality	No replication	Direct	Imprecise	Very low for no effect
Depression	10 RCTs, 801 participants	SMD 0.17 (CI 0.03, 0.31), favors mindfulness meditation	Majority good or fair quality; effect similar when poor quality RCTs excluded	Consistent; no heterogeneity	Direct	Precise	High
Physical health-related quality of life	12 RCTs, 841 participants	SMD 0.30 (CI 0.03, 0.57), favors mindfulness meditation	Majority good or fair quality; effect similar when poor quality RCTs excluded	Consistent; moderate heterogeneity	Direct	Imprecise	Moderate
Mental health-related quality of life	13 RCTs, 855 participants	SMD 0.44 (CI 0.18, 0.69), favors mindfulness meditation	Majority good or fair quality; effect similar when poor quality RCTs excluded	Consistent; moderate heterogeneity	Direct	Imprecise	Moderate
Functional impairment/disability measures	3 RCTs, 143 participants	SMD 0.47 (CI -0.18, 1.12), n.s.	1 poor, 1 fair, 1 good quality RCT	Inconsistent, no heterogeneity	Direct	Imprecise	Very low
KQ 1a							
MBSR, pain 0–12 weeks	15 RCTs, 845 participants	SMD 0.32 (CI -0.06, 0.70), n.s.	Majority poor quality	Consistent; substantial heterogeneity	Direct	Imprecise	Low for no effect
MBCT, pain 0–12 weeks	4 RCTs, 272 participants	SMD 0.16 (CI -0.45, 0.76), n.s.	All good or fair quality	Inconsistent; substantial heterogeneity	Direct	Imprecise	Low for no effect
Meta-regression result, intervention type and pain outcome	24 RCTs, 1,456 participants	Meta-regression did not suggest differences among intervention types (MBSR p=0.60; MBCT p=0.58; remote versus other interventions p=0.14)	Mixed quality	Not applicable	Indirect	Not applicable	Very low
KQ 1b							
Migraine/headache	5 RCTs, 281 participants	SMD 0.38 (CI -0.42, 1.17), n.s.	Majority fair quality; no good quality; effect consistent when poor quality RCTs excluded	Inconsistent; considerable heterogeneity	Direct	Imprecise	Low for no effect

Outcome	Study Design (number of RCTs and participants)	Findings (direction and magnitude of effect)	Study Limitations (study quality; risk of bias)	Inconsistency	Indirectness	Imprecision	GRADE of Evidence for Outcome
Back pain	4 RCTs, 221 participants	SMD -0.04 (CI -0.39, 0.32), n.s. SMD 0.07 (CI -0.15, 0.29), n.s.	Equally fair and poor quality; no good quality; consistent when poor quality RCTs excluded	Consistent; no heterogeneity	Direct	Precise	Low for no effect
Fibromyalgia	8 RCTs, 642 participants	SMD 0.13 (CI -0.12, 0.37), n.s.	Majority good or fair quality; consistent when poor quality RCTs excluded	Consistent; moderate heterogeneity	Direct	Precise	Moderate for no effect
Meta-regression result, source of pain and pain outcome	24 RCTs, 1,456 participants	Meta-regressions did not suggest differences between headache and other conditions (p=0.52), back pain and other conditions (p=0.41), and fibromyalgia and other conditions (p=0.29)	Mixed quality	Not applicable	Indirect	Not applicable	Very low
KQ 1c							
Meta-regression result, monotherapy or adjunctive therapy, pain outcome	24 RCTs, 1,456 participants	Meta-regression did not suggest differences between monotherapy and adjunctive therapy (p=0.53)	Mixed quality	Not applicable	Indirect	Not applicable	Very low
KQ 1d							
Meta-regression result, duration of treatment and pain outcome	24 RCTs, 1,456 participants	Meta-regression did not suggest differences by duration (p=0.12)	Mixed quality	Not applicable	Indirect	Not applicable	Very low
Meta-regression result, frequency of participation and pain outcome	24 RCTs, 1,456 participants	Meta-regression did not suggest differences by frequency (p=0.17)	Mixed quality	Not applicable	Indirect	Not applicable	Very low

NOTE: n.s. = not significant.

Other Reviews in this Area

Numerous systematic reviews on the effects of mindfulness meditation have been published in recent years. Of those that report pain outcomes, several have focused on specific types of pain, such as low back pain (Cramer et al., 2012), fibromyalgia (Lauche et al., 2013), or somatization disorder (Lakhan and Schofield, 2013). Others were not limited to RCTs (Merkes, 2010; Reiner, Tibi, and Lipsitz, 2013). This section focuses on the most recent comprehensive reviews of controlled trials of mindfulness interventions for chronic pain regardless of etiology (Bawa et al., 2015; Chiesa and Serretti, 2011). Despite identifying more than twice as many RCTs as each previous systematic review on this topic, our findings are quite similar.

Chiesa and Serretti (2011) reviewed MBSR and similar mindfulness interventions for chronic pain and depressive symptoms in ten studies (six RCTs, four controlled studies) on fibromyalgia; musculoskeletal pain, such as low back pain; and rheumatoid arthritis. Results demonstrated that interventions could have nonspecific effects related to expectation of a benefit or group support for pain and depressive symptoms, while only limited evidence suggested specific effects of such interventions. Chiesa and Serretti concluded that there is not yet sufficient evidence to determine the magnitude of the effects of mindfulness-based interventions for patients with chronic pain because of methodological issues. In the current review, we included four of the ten studies from Chiesa's review (Astin et al., 2003; Morone, Greco, and Weiner, 2008; Plews-Ogan et al., 2005; Zautra et al., 2008). Four studies were excluded because of no randomization, and two excluded because they did not report pain outcomes.

Lee, Crawford, and Hickey (2014) reviewed MBSR and related mindfulness interventions for back pain, fibromyalgia, musculoskeletal pain, diabetic neuropathy, and unspecified chronic pain in 11 RCTs of mixed methodological quality. The authors report a moderate level of confidence for a small effect of meditation on chronic pain from the five included studies that reported effect sizes. However, they concluded that higher-quality research is necessary to estimate an effect with more confidence. In the current review, we included eight of these 11 studies (Morone, Greco, and Weiner, 2008; Morone et al., 2009; Wong et al., 2011; Wong, 2009; Schmidt et al., 2011; Esmer et al., 2010; Plews-Ogan et al., 2005; Teixeira, 2010). Three studies were excluded for interventions that did not meet our definition of mindfulness meditation; these studied affective self-awareness, the Alexander technique, and loving-kindness meditation.

Bawa and colleagues (Bawa et al., 2015), the most recent review on MBSR and MBCT for chronic pain, included 11 controlled trials of mixed methodological quality on fibromyalgia, rheumatoid arthritis, chronic musculoskeletal pain, failed back surgery syndrome, and mixed etiology. Meta-analysis results yielded small effect sizes for pain, health-related quality of life (physical and mental), and functional status, while affective outcomes, such as pain acceptance, yielded larger effect sizes. The authors concluded that there is limited evidence for efficacy of mindfulness-based interventions for patients with chronic pain and that better-quality studies are required. Of the 11 studies in the Bawa review, we included eight in the current review (Astin et

al., 2003; Brown and Jones, 2013; Esmer et al., 2010; Morone et al., 2009; Plews-Ogan et al., 2005; Schmidt et al., 2011; Wong et al., 2011; Zautra et al., 2008). Two RCTs were excluded because they did not collect outcomes on pain, and another study was excluded due to lack of randomization. Appendix D displays references for the studies included by Bawa, along with their inclusion and exclusion status in the current review.

Two of these prior systematic reviews (Chiesa and Serretti, 2011; Bawa et al., 2015) did not mention adverse events; the third (Lee, Crawford, and Hickey, 2014) noted that two included trials reported that no adverse events occurred.

Our review yielded similar results in that we found low quality evidence that mindfulness meditation is associated with a decrease in chronic pain compared with control. Intervention participants reported significantly lower pain scale scores in the 24 RCTs that reported continuous outcomes; a sensitivity analysis excluding poor quality studies yielded similar results. This effect remained up to 12 weeks postintervention but was no longer statistically significant for follow-up periods beyond 12 weeks. Further, the efficacy of mindfulness meditation did not differ significantly by type of intervention (MBSR, MBCT, other). In subgroup analyses of comparators, mindfulness meditation significantly reduced pain scale scores compared with TAU, but not compared with passive controls or with education or support groups. In terms of non-pain outcomes, mindfulness meditation significantly improved depression, physical health-related quality of life, and mental health-related quality of life.

Strengths and Limitations

This review has several methodological strengths: an a priori research design, duplicate study selection and data abstraction of study information, a comprehensive search of electronic databases, risk of bias assessments, and comprehensive quality of evidence assessments used to formulate review conclusions. One limitation is that we did not contact individual study authors; results reported in the review are based on published data. We excluded the nine conference abstracts identified, because abstracts do not contain enough data to evaluate study quality. In addition, we included only studies published in English.

The included studies had many limitations. Eleven of the 28 studies were rated as poor quality, primarily due to lack of ITT analysis, poor follow-up, or poor reporting of methods. Although mindfulness meditation showed significant improvements in pain compared with control in a meta-analysis of 24 studies, the treatment effect estimate showed significant heterogeneity. In subgroup analyses, mindfulness meditation significantly reduced pain scale scores compared with treatment as usual, but not compared with passive controls or with education or support groups. Additional sensitivity analyses and meta-regression did not identify systematic sources of differences between studies. Because of the small number of trials included in the subgroup analyses, as well as the small sample sizes and heterogeneity of these trials, it is not surprising that the meta-analyses and meta-regressions are often nonsignificant. The authors

of seven studies reported inadequate statistical power to detect differences in pain outcomes between mindfulness meditation and the comparator; those authors considered these pilot studies. Eight other studies did not report a power calculation. Sample sizes were small; 12 studies randomized fewer than 50 participants.

Only one RCT attributed adverse events to mindfulness meditation (two participants experienced greater anxiety, and two experienced strong feelings of anger toward their pain condition). However, only three of the 28 included RCTs mentioned whether adverse event data were collected. Thus, quality of evidence for adverse events reported in RCTs is very low.

Implications for Future Research and Practice

Similar to previous reviews in this area, we conclude that the weaknesses in the body of evidence prevent any strong conclusions about mindfulness meditation for chronic pain. The available evidence did not yield consistent effects for pain outcomes, and few studies were available for many specific causes of pain or forms of mindfulness meditation other than MBSR. Quality of evidence for the efficacy of mindfulness interventions in reducing chronic pain is low. There was higher quality evidence of the efficacy of mindfulness meditation on quality of life outcomes (both physical and mental health, as well as depression). This review is consistent with previous reviews concluding that more well-designed, rigorous, and large RCTs are needed in order to develop an evidence base that can more decisively provide estimates of the efficacy of mindfulness meditation for chronic pain.

Very few RCTs collected information on adverse events. Given published reports of adverse events during meditation, including psychosis (Kuijpers et al., 2007), we strongly suggest that future trials actively collect adverse event data. In addition, a systematic review of observational studies and case reports would shed additional light on adverse events during mindfulness meditation.

Committees charged with updating the Department of Veterans Affairs and Department of Defense clinical practice guidelines for treating chronic pain may use this report as a source of evidence on mindfulness meditation. Unfortunately, we identified no RCTs that focused on active military or veteran populations; future RCTs incorporating military-related eligibility criteria could provide evidence more applicable to pain resulting from military service and evidence for use by decisionmakers in military and veteran health systems.

Further research examining the effect of mindfulness meditation on chronic pain also should focus on better understanding whether there is a minimum frequency or duration of meditation practice for it to be effective. Future trials should monitor adherence (meditation practice) both during the intervention program and after the program ends if long-term results are to be assessed.

Appendix A: Search Strategy

TIME PERIOD COVERED:

Since inception to June 2015

SEARCH STRATEGY:

“Mindfulness”[Mesh]) OR “Meditation”[Mesh] OR mindfulness* or mindfulness-based or mbsr or mbct or m-bct or meditation or meditat* OR Vipassana or satipaṭṭhāna OR anapanasati OR Zen OR Pranayama OR Sudarshan OR Kriya OR zazen OR shambhala OR buddhis*

AND

Pain[MH] OR pain*[tiab] OR headache disorders[mh] OR headache* or head ache* or head-ache* or migraine* OR cephalalgia* OR neuralgia* OR osteoarthritis OR arthrosis OR backache* OR back ache* OR back-ache* OR Neuralgia OR neuropathic pain OR neuropathy OR radiculopathy OR, complex regional pain syndrome* OR CPRS OR causalgia OR herpetic neuralgia OR sciatic* OR cervicalgia*

AND

systematic[sb] OR systematic review* OR random* OR rct* OR randomized controlled trial*[pt] OR “Randomized Controlled Trial” [Publication Type] OR “Randomized Controlled Trials as Topic”[Mesh] OR meta-analy* OR metaanaly* OR meta analy*

LANGUAGE:

English

Appendix B: Excluded Full-Text Articles

Reason Excluded: Background

Blodt, S., D. Pach, S. Roll, and C. M. Witt, “Effectiveness of App-Based Relaxation for Patients with Chronic Low Back Pain (Relaxback) and Chronic Neck Pain (Relaxneck): Study Protocol for Two Randomized Pragmatic Trials,” *Trials*, Vol. 15, 2014, p. 490.

Reason Excluded: Off Topic (Not Mindfulness or Chronic Pain)

Arefnasab, Z., M. Ghanei, A. A. Noorbala, A. Alipour, F. Babamahmoodi, A. Babamahmoodi, and M. Salehi, “Effect of Mindfulness Based Stress Reduction on Quality of Life (SF-36) and Spirometry Parameters, in Chemically Pulmonary Injured Veterans,” *Iranian Journal of Public Health*, Vol. 42, No. 9, September 2013, pp. 1026–1033.

Dion, L. J., D. J. Engen, V. Lemaine, D. K. Lawson, C. G. Brock, B. S. Thomley, S. S. Cha, A. Sood, B. A. Bauer, and D. L. Wahner-Roedler, “Massage Therapy Alone and in Combination with Meditation for Breast Cancer Patients Undergoing Autologous Tissue Reconstruction: A Randomized Pilot Study,” *Complementary Therapies in Clinical Practice*, May 12, 2015.

Fernros, Lotta, Anna-Karin Furhoff, and Per E. Wändell, “Improving Quality of Life Using Compound Mind-Body Therapies: Evaluation of a Course Intervention with Body Movement and Breath Therapy, Guided Imagery, Chakra Experiencing and Mindfulness Meditation,” *Quality of Life Research: An International Journal of Quality of Life Aspects of Treatment, Care & Rehabilitation*, Vol. 17, No. 3, April 2008, pp. 367–376.

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Lengacher, C. A., V. Johnson-Mallard, J. Post-White, M. S. Moscoso, P. B. Jacobsen, T. W. Klein, R. H. Widen, S. G. Fitzgerald, M. M. Shelton, M. Barta, M. Goodman, C. E. Cox, and K. E. Kip, “Randomized Controlled Trial of Mindfulness-Based Stress Reduction (MBSR)

for Survivors of Breast Cancer,” *Psycho-Oncology*, Vol. 18, No. 12, December 2009, pp. 1261–1272.

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Pickut, B., and S. Vanneste, “Mindfulness Training Among Individuals with Parkinson’s Disease: Neurobehavioral Effects,” Vol. 2015, 2015, p. 816404.

Price, C. J., B. McBride, L. Hyerle, and D. R. Kivlahan, “Mindful Awareness in Body-Oriented Therapy for Female Veterans with Post-Traumatic Stress Disorder Taking Prescription Analgesics for Chronic Pain: A Feasibility Study,” *Alternative Therapies in Health and Medicine*, Vol. 13, No. 6, November–December 2007, pp. 32–40.

Reason Excluded: Outcome (Not Pain or Analgesic Use)

Astin, J. A., “Stress Reduction Through Mindfulness Meditation: Effects on Psychological Symptomatology, Sense of Control, and Spiritual Experiences,” *Psychotherapy and Psychosomatics*, Vol. 66, No. 2, 1997, pp. 97–106.

Berrill, J. W., M. Sadlier, K. Hood, and J. T. Green, “Mindfulness-Based Therapy for Inflammatory Bowel Disease Patients with Functional Abdominal Symptoms or High Perceived Stress Levels,” *Journal of Crohn’s and Colitis*, Vol. 8, No. 9, September 2014, pp. 945–955.

Bogosian, A., P. Chadwick, S. Windgassen, S. Norton, P. McCrone, I. Mosweu, E. Silber, and R. Moss-Morris, “Distress Improves After Mindfulness Training for Progressive MS: A Pilot Randomised Trial,” *Multiple Sclerosis*, March 12, 2015.

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Feuille, M., and K. Pargament, “Pain, Mindfulness, and Spirituality: A Randomized Controlled Trial Comparing Effects of Mindfulness and Relaxation on Pain-Related Outcomes in Migraineurs,” *Journal of Health Psychology*, November 7, 2013.

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Garland, E. L., and M. O. Howard, “Mindfulness-Oriented Recovery Enhancement Reduces Pain Attentional Bias in Chronic Pain Patients,” *Psychotherapy and Psychosomatics*, Vol. 82, No. 5, 2013, pp. 311–318.

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Zernicke, K. A., T. S. Campbell, P. K. Blustein, T. S. Fung, J. A. Johnson, S. L. Bacon, and L. E. Carlson, “Mindfulness-Based Stress Reduction for the Treatment of Irritable Bowel Syndrome Symptoms: A Randomized Wait-List Controlled Trial,” *International Journal of Behavioral Medicine*, Vol. 20, No. 3, September 2013, pp. 385–396.

Reason Excluded: Design (Not RCT)

Brotto, Lori A., Rosemary Basson, Kelly B. Smith, Miriam Driscoll, and Leslie Sadownik, “Mindfulness-Based Group Therapy for Women with Provoked Vestibulodynia,” *Mindfulness*, Vol. 6, No. 3, June 2015, pp. 417–432.

Cusens, Bryany, Geoffrey B. Duggan, Kirsty Thorne, and Vidyamala Burch, “Evaluation of the Breathworks Mindfulness-Based Pain Management Programme: Effects on Well-Being and Multiple Measures of Mindfulness,” *Clinical Psychology & Psychotherapy*, Vol. 17, No. 1, January–February 2010, pp. 63–78.

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Reason Excluded: Reports on Study Already in Database

- Cathcart, Stuart, Vanessa Barone, Maarten Immink, and Michael Proeve, "Mindfulness Training Does Not Reduce Generalized Hyperalgesia in Chronic Tension-Type Headache," *Journal of Pain Management*, Vol. 6, No. 3, July–September 2013, pp. 217–221.

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Garland, Eric L., Brett Froeliger, and Matthew O. Howard, “Effects of Mindfulness-Oriented Recovery Enhancement on Reward Responsiveness and Opioid Cue-Reactivity,” *Psychopharmacology*, Vol. 231, No. 16, August 2014, pp. 3229–3238.

Reason Excluded: Conference Abstract

Cour, P., M. C. Pedersen, and J. Hojsted, “Mindfulness and Chronic Pain: A Randomized, Controlled Study of Effect and Feasibility,” *European Journal of Pain Supplements*, Vol. 5, No. 1, 2011.

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Meize-Grochowski, R., A. Prasad, C. Murray-Krezan, R. Schrader, M. DuVal, B. Smith, and C. Herman, “Mindfulness Meditation in Community Dwelling Older Adults with Postherpetic Neuralgia,” *BMC Complementary and Alternative Medicine*, Vol. 12, 2012.

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Reason Excluded: Dissertation

- Day, Melissa A., "Mindfulness-Based Cognitive Therapy for the Treatment of Chronic Headache Pain," *Dissertation Abstracts International: Section B: The Sciences and Engineering*, Vol. 75, No. 1-B(E), 2014.
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- Wong, Chi Ming, "Four-Step Mindfulness-Based Therapy for Chronic Pain: A Pilot Randomized Controlled Trial," *Dissertation Abstracts International: Section B: The Sciences and Engineering*, Vol. 72, No. 1-B, 2011, p. 562.

Reason Excluded: Intervention (Not Mindfulness Meditation)

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Appendix C: Evidence Table of Included Studies

Study Details	Participants	Intervention	Outcomes
<p>Reference: Astin et al., 2003</p> <p>Location: United States or Canada</p> <p>Purpose: To test the short- and long-term benefits of an 8-week mind-body intervention that combined training in mindfulness meditation with Qigong movement therapy for individuals with fibromyalgia syndrome</p> <p>Quality Rating: Poor</p>	<p>Number of Patients: 128</p> <p>Medical Condition/Type of Pain: Fibromyalgia</p> <p>Definition of Chronic Pain: 3 months minimum or “past normal time for tissue healing”</p> <p>Baseline Pain Score: SF-36 pain score Intervention Group: 32.3 (SD 14.4); Control Group: 31.4 (SD 16.7)</p> <p>Mean Age: 47.7 (SD 10.6)</p> <p>Gender (% Male): 0.7</p> <p>Inclusion Criteria: Clinical diagnosis of fibromyalgia syndrome by patient’s own health care provider; fulfillment of American College of Rheumatology classification criteria for fibromyalgia syndrome verified by rheumatologic examination—widespread pain (axial plus upper and lower segment plus left and right side pain for 3 months, and tenderness at 11 of the 18 specific tender point sites; age between 18 and 70 years; able to read and speak English fluently; able to attend group intervention session if assigned to that group; and able to give informed consent.</p> <p>Exclusion Criteria: Pregnancy, substance abuse, major psychiatric disorder (that would prevent compliance), involvement in impending litigation or judgment for disability workers’ compensation, or uncontrolled hypertension, diabetes, congestive heart failure, or other severe chronic medical conditions judged by the clinician to place the patient at risk of possible severe consequences of his or her disease.</p>	<p>Content of Intervention: Treatment was a combination of MBSR and Qigong. Each session focused first on the mindfulness meditation aspects of MBSR and then the physical postures, breathing techniques, and focused attention aspects of Qigong.</p> <p>Setting: Unclear</p> <p>Dosage, Duration: 1–4 hours spent in session, homework, and other each week, for 8 weeks</p> <p>Co-interventions: NA</p> <p>Comparator: Education or support group</p> <p>Primary Endpoint: SF-36 pain score</p> <p>Power Calculation: Power insufficient (post hoc test by authors)</p> <p>Follow-Up Time: 24 weeks</p>	<p>Pain Measures: SF-36 pain score, 14 weeks: SMD 0.02 (CI –0.47, 0.5) SF-36 pain score, 24 weeks: SMD –0.04 (CI –0.52, 0.45) SF-36 pain score, 8 weeks: SMD –0.05 (CI –0.54, 0.43)</p> <p>Depression Measures: BDI: SMD 0.15 (CI –0.35, 0.64)</p> <p>Analgesic Use: No</p> <p>Adverse Events: No mention</p>

Study Details	Participants	Intervention	Outcomes
<p>Reference: Brown and Jones, 2013</p> <p>Location: Europe</p> <p>Purpose: To investigate whether improvement in mental health might require (1) reduction in the sensory pain experience and brain correlates of that experience, and/or (2) improved perceptions of the controllability of pain and corresponding brain activity related to cognitive control and emotional regulation</p> <p>Quality Rating: Poor</p>	<p>Number of Patients: 40</p> <p>Medical Condition/Type of Pain: Fibromyalgia, rheumatoid arthritis, other musculoskeletal</p> <p>Definition of Chronic Pain: No definition</p> <p>Baseline Pain Score: Laser Pain Unpleasantness Intervention Group: 5.4 (SD 2); Control Group: 5.9 (SD 1.3)</p> <p>Mean Age Intervention: 48 (SD 10); Control: 45 (SD 12)</p> <p>Gender (% Male): 25.5</p> <p>Inclusion Criteria: Right-handed patients with any type of musculoskeletal pain.</p> <p>Exclusion Criteria: History of neurological, psychiatric, or cardiovascular disease.</p>	<p>Content of Intervention: The program teaches not to try to do anything about the underlying unpleasant sensation of pain, but to train in mindfulness to lessen the reactive cycle that leads to physical and emotional stress. This is done by teaching breath awareness, body awareness, gentle movement, and how to manage pain, illness, and fatigue in daily life, as well as cultivating kindness and compassion toward oneself and others.</p> <p>Setting: Unclear</p> <p>Dosage, Duration: 1–4 hours spent in session, homework, and other each week, for 8 weeks</p> <p>Co-interventions: NA</p> <p>Comparator: TAU or standard of care</p> <p>Primary Endpoint: Laser Pain Unpleasantness</p> <p>Power Calculation: Power insufficient (post hoc test by authors)</p> <p>Follow-Up Time: 24 weeks</p>	<p>Pain Measures: Laser Pain Unpleasantness: SMD 0.24 (CI -0.51, 0.98)</p> <p>Analgesic Use: No</p> <p>Mental Health-Related Quality of Life (QoL) Measure: SF-36 Mental Health: SMD 1.16 (CI 0.36, 1.96)</p> <p>Physical Health-Related QoL Measure: SF-36 Physical Health: SMD -0.42 (CI -1.17, 0.33)</p> <p>Adverse Events: No mention</p>

Study Details	Participants	Intervention	Outcomes
<p>Reference: Cash et al., 2015</p> <p>Location: United States or Canada</p> <p>Purpose: Randomized prospective trial of MBSR among female fibromyalgia patients</p> <p>Quality Rating: Fair</p>	<p>Number of Patients: 91</p> <p>Medical Condition/Type of Pain: Fibromyalgia</p> <p>Definition of Chronic Pain: 3 months minimum or "past normal time for tissue healing"</p> <p>Baseline Pain Score: VAS Intervention Group: 68.1 (SD 25.4); Control Group: 69.2 (SD 19.6)</p> <p>Mean Age: Not reported</p> <p>Gender (% Male): 0</p> <p>Inclusion Criteria: Female fibromyalgia sufferers aged 18 years and older who were able to attend a weekly group and had a physician-verified diagnosis.</p> <p>Exclusion Criteria: Severe mental illness.</p>	<p>Content of Intervention: Both formal and informal mindfulness practices were introduced, including instruction/discussion, an attention-focusing technique (body scan, directing attention throughout the body in a relaxed, supine state), sitting meditation (systematically directing attention to breath and immediate sensory and cognitive experiences), and a series of simple yoga positions taught as a means of encouraging relaxed and focused movement</p> <p>Setting: Unclear</p> <p>Dosage, Duration: >4 hours spent in session, homework, and other each week, for 8 weeks</p> <p>Co-interventions: NA</p> <p>Comparator: Passive (e.g., waitlist, no treatment)</p> <p>Primary Endpoint: VAS</p> <p>Power Calculation: Yes (sufficient power)</p> <p>Follow-Up Time: 8 weeks</p>	<p>Pain Measures: VAS, 16 weeks: SMD 0 (CI -0.42, 0.41) VAS, 8 weeks: SMD 0.32 (CI -0.1, 0.74)</p> <p>Analgesic Use: No</p> <p>Adverse Events: No mention</p>

Study Details	Participants	Intervention	Outcomes
<p>Reference: Cathcart et al., 2014</p> <p>Location: Australia</p> <p>Purpose: To conduct a pilot study into the efficacy of brief mindfulness-based therapy for chronic tension-type headache</p> <p>Quality Rating: Fair</p>	<p>Number of Patients: 58</p> <p>Medical Condition/Type of Pain: Other headache</p> <p>Definition of Chronic Pain: Other definition</p> <p>Baseline Pain Score: Headache Intensity Intervention Group: 2.26 (SD 0.62); Control Group: 2.51 (SD 0.82)</p> <p>Mean Age: Intervention: 45.78 (SD 13.10); Control: 45.26 (SD 14.18)</p> <p>Gender (% Male): 37.25</p> <p>Inclusion Criteria: Satisfying International Headache Society-II criteria for chronic tension-type headache, aged 18–65 years, not currently receiving (or having received in the past 12 months) intervention for headache, no psychiatric or major medical condition currently or in the past 12 months, and no other headache, pain symptoms, or diagnoses in addition to chronic tension-type headache, including suspected or probable medication overuse headache (i.e., medication use ten or more days per month, for three or more months).</p> <p>Exclusion Criteria: NA</p>	<p>Content of Intervention: The mindfulness-based therapy intervention, based on MBSR and MBCT, was conducted over a 3-week period involving twice-weekly group classes and daily practice. The program, which included a particular focus on management of headache pain and related psychosocial sequelae and of stress as a contributing factor to headache, was developed by some of the authors, who are psychologists with formal training in mindfulness therapy (e.g., completion of MBSR and MBCT training courses, and clinical experience in the delivery of these), and extensive teaching, practice, and research experience in mindfulness-based meditation (e.g., university lecturing and research, clinical practice instruction).</p> <p>Setting: Unclear</p> <p>Dosage, Duration: >4 hours spent in session, homework, and other each week, for 3 weeks</p> <p>Co-interventions: NA</p> <p>Comparator: Passive (e.g., waitlist, no treatment)</p> <p>Primary Endpoint: Headache Intensity</p> <p>Power Calculation: No</p> <p>Follow-Up Time: 8 weeks</p>	<p>Pain Measures: Headache Intensity: SMD 0.08 (CI -0.52, 0.69)</p> <p>Analgesic Use: No</p> <p>Adverse Events: No mention</p>

Study Details	Participants	Intervention	Outcomes
<p>Reference: Davis and Zautra, 2013</p> <p>Location: United States or Canada</p> <p>Purpose: To compare the effects of a 12-module online intervention targeting socioemotional regulation via mindful awareness/acceptance (mindful socioemotional regulation) with those of an attention-control treatment and healthy lifestyle tips</p> <p>Quality Rating: Fair</p>	<p>Number of Patients: 79</p> <p>Medical Condition/Type of Pain: Fibromyalgia</p> <p>Definition of Chronic Pain: No definition</p> <p>Baseline Pain Score: Pain Intervention Group: 59.89 (SD 22.11); Control Group: 55.03 (SD 24.65)</p> <p>Mean Age: 46.14; range: 22–81</p> <p>Gender (% Male): 2</p> <p>Inclusion Criteria: Being over 18 years of age, being able to understand written and spoken English, reporting having received a diagnosis of fibromyalgia syndrome from a physician, and having daily access to the Internet.</p> <p>Exclusion Criteria: History of more than five past episodes of depression.</p>	<p>Content of Intervention: Mindful socioemotional regulation. Training focused on (1) the regulation of emotions via enhancing awareness and acceptance of the full range of emotion experiences via mindfulness meditation, and (2) the use of mindful awareness skills to make choices that build stronger social bonds, enhancing a sense of belonging and increasing enjoyment of social relations.</p> <p>Setting: Remote (e.g., telephone Internet app)</p> <p>Dosage, Duration: 1 hour or less spent in session, homework, and other each week, for 6 weeks</p> <p>Co-interventions: NA</p> <p>Comparator: Health tips via the Internet</p> <p>Primary Endpoint: Pain</p> <p>Power Calculation: Yes (sufficient power)</p> <p>Follow-Up Time: 6 weeks</p>	<p>Pain Measures: Pain: SMD -0.24 (CI -0.69, 0.2)</p> <p>Analgesic Use: No</p> <p>Adverse Events: No mention</p>

Study Details	Participants	Intervention	Outcomes
<p>Reference: Day et al., 2014</p> <p>Location: United States or Canada</p> <p>Purpose: To investigate the feasibility, tolerability, acceptability, and initial estimates of efficacy of MBCT compared with a delayed treatment control for headache pain</p> <p>Quality Rating: Fair</p>	<p>Number of Patients: 36</p> <p>Medical Condition/Type of Pain: Migraine, other headache</p> <p>Definition of Chronic Pain: 3 months minimum or "past normal time for tissue healing"</p> <p>Baseline Pain Score: Brief Pain Index (BPI) Intensity Intervention Group: 3.59 (SD 1.74); Control Group: 3.37 (SD 2.03)</p> <p>Mean Age: 41.7 (SD 12.0)</p> <p>Gender (% Male): 11.1</p> <p>Inclusion Criteria: 19 years of age or older; at least three pain days per month (for the past 3 months or longer) due to a primary headache pain type (i.e., migraine, tension-type headache, cluster, or other) as defined by the International Headache Society; headache pain was the primary source of pain; if currently using psychotropic or headache medications, use of these medications must have begun at least 4 weeks before baseline assessment; and reading ability was sufficient to comprehend self-monitoring forms.</p> <p>Exclusion Criteria: Human immunodeficiency virus–related pain and cancer pain, because these are associated with malignant disease; history of seizure or facial neuralgia, as these conditions might preclude the accurate diagnosis of headache; significant cognitive impairment, evidenced by a positive screen on the Mini-cog21; current participation in other psychological treatments for any pain condition; and schizophrenia, bipolar affective disorder, seizure disorder not adequately controlled by medication, or current substance abuse.</p>	<p>Content of Intervention: The 8-week MBCT for headache pain manual was adapted from an existing 8-week MBCT for depression protocol. The adapted manual, developed by Day and Thorn, incorporated knowledge about the specific issues of relevance and importance to a headache pain population. The treatment development phase included piloting the manual and treatment approach within a group of patients with heterogeneous chronic pain conditions.</p> <p>Setting: Outpatient pain clinic</p> <p>Dosage, Duration: >4 hours spent in session, homework, and other each week, for 8 weeks</p> <p>Co-interventions: TAU or standard of care</p> <p>Comparator: Passive (e.g., waitlist, no treatment)</p> <p>Primary Endpoint: BPI Intensity</p> <p>Power Calculation: Power insufficient (post hoc test by authors)</p> <p>Follow-Up Time: 8 weeks</p>	<p>Pain Measures: BPI Intensity: SMD -0.01 (CI -0.66, 0.65)</p> <p>Analgesic Use: No</p> <p>Adverse Events: No mention</p>

Study Details	Participants	Intervention	Outcomes
<p>Reference: Dowd et al., 2015</p> <p>Location: Europe</p> <p>Purpose: To test the effectiveness of a computerized MBCT intervention compared with computerized pain management psychoeducation in a randomized study</p> <p>Quality Rating: Fair</p>	<p>Number of Patients: 124</p> <p>Medical Condition/Type of Pain: Other headache, back pain, osteoarthritis, fibromyalgia, unspecified, nerve damage/pain, neuropathy</p> <p>Definition of Chronic Pain: Other definition</p> <p>Baseline Pain Score: Average Pain Intervention Group: 5.57 (SD 1.89); Control Group: 5.86 (SD 1.89)</p> <p>Mean Age: 44.53 (SD 12.25)</p> <p>Gender (% Male): 9.7</p> <p>Inclusion Criteria: Self-reported chronic pain</p> <p>Exclusion Criteria: Had <6 months of pain; reported experiencing chronic pain due to cancer; reported possible symptoms of psychosis (Health Problems Questionnaire); were under the age of 18 years; and were unable to complete the required questionnaires due to insufficient English language or cognitive ability.</p>	<p>Content of Intervention: Computerized MBCT intervention included audio-recorded meditation, psychoeducation component, a mindfulness practice focus, and a cognitive and behavioral change component</p> <p>Setting: Remote (e.g., telephone internet app)</p> <p>Dosage, Duration: 1 hour or less spent in session, homework, and other each week, for 6 weeks</p> <p>Co-interventions: NA</p> <p>Comparator: Psychoeducation program</p> <p>Primary Endpoint: Average Pain</p> <p>Power Calculation: Yes (sufficient power)</p> <p>Follow-Up Time: 30 weeks</p>	<p>Pain Measures:</p> <p>Average Pain, 6 weeks: SMD 0 (CI -0.36, 0.35)</p> <p>Average Pain, 30 weeks: SMD -0.19 (CI -0.54, 0.17)</p> <p>Analgesic Use: No</p> <p>Adverse Events: No mention</p>

Study Details	Participants	Intervention	Outcomes
<p>Reference: Esmer et al., 2010</p> <p>Location: United States or Canada</p> <p>Purpose: To evaluate short-term efficacy of MBSR therapy for improving quality of life in adults with failed back surgery syndrome</p> <p>Quality Rating: Poor</p>	<p>Number of Patients: 40</p> <p>Medical Condition/Type of Pain: Back pain, leg pain</p> <p>Definition of Chronic Pain: No definition</p> <p>Baseline Pain Score: VAS Intervention Group: 23.2 (SD 5); Control Group: 24.3 (SD 7.8)</p> <p>Mean Age: Intervention: 55.2 (SD 11.2); Control: 54.9 (SD 9.5)</p> <p>Gender (% Male): 56</p> <p>Inclusion Criteria: Persistent leg pain, back pain, or both despite a history of lumbosacral spinal surgery within the previous 2 years.</p> <p>Exclusion Criteria: Pregnancy, cognitive impairment, relapsed chemical dependency, and lack of effective transportation.</p>	<p>Content of Intervention: MBSR course educated participants on the physiology of stress and stress hardness, and provided participants with coping strategies for pain by developing and refining the capacity to be mindful. Participants were encouraged to be present with their experience of pain and stress, in particular. The intervention helped students to resist their experience of pain less and thereby reduce the suffering caused by their resistance. Participants were taught to perform daily mindfulness practices: gentle yoga, walking, and seated meditation.</p> <p>Setting: Unclear</p> <p>Dosage, Duration: >4 hours spent in session, homework, and other each week, for 8 weeks</p> <p>Co-interventions: Traditional care as prescribed by their medical care providers</p> <p>Comparator: Traditional care as prescribed by their medical care providers</p> <p>Primary Endpoint: VAS</p> <p>Power Calculation: No</p> <p>Follow-Up Time: 12 weeks</p>	<p>Pain Measures: VAS: SMD 0.3 (CI -0.5, 1.1)</p> <p>Analgesic Use: Yes: analgesic medication log on a 4-point scale: 0=no meds, 4=daily narcotic meds; statistically significant reduction in analgesic use at 12-week follow up</p> <p>Adverse Events: No mention</p>

Study Details	Participants	Intervention	Outcomes
<p>Reference: Fjorback et al., 2013</p> <p>Location: Europe</p> <p>Purpose: To conduct a feasibility and efficacy trial of mindfulness therapy in somatization disorder and functional somatic syndromes, such as fibromyalgia, IBS, and chronic fatigue syndrome, defined as bodily distress syndrome</p> <p>Quality Rating: Good</p>	<p>Number of Patients: 120</p> <p>Medical Condition/Type of Pain: Bodily distress syndrome, a somatization disorder</p> <p>Definition of Chronic Pain: No definition</p> <p>Baseline Pain Score: SF-36 Bodily Pain</p> <p>Intervention Group: 27.2 (SD 23.1); Control Group: 29.8 (SD 21.3)</p> <p>Mean Age: Mindfulness: 38 (SD 9); Enhanced TAU: 40 (SD 8)</p> <p>Gender (% Male): 20</p> <p>Inclusion Criteria: Chronic (i.e., at least 2 years) of the multi-organ type bodily distress syndrome, which requires functional somatic symptoms from at least three out of four bodily systems—the cardiopulmonary, gastrointestinal, musculoskeletal, or general symptoms; moderate to severe impairment in daily living; age 20 to 50 years; absence of severe psychiatric morbidity (i.e., psychotic and bipolar disorders). The patients with comorbid depression and anxiety, and with comorbid medical conditions (e.g., asthma, diabetes) were included if symptoms attributed to these conditions could be clearly differentiated from symptoms due to bodily distress syndrome.</p> <p>Exclusion Criteria: Current alcohol or drug abuse; pregnancy; not fluent in the Danish language (operationalized as non-Scandinavian origin); no informed consent.</p>	<p>Content of Intervention: Based on Kabat-Zinn (2005) MBSR manual. The intervention included psychoeducation, symptom registration, and a model for graded exercise from the STreSS-1 manual.</p> <p>Setting: Other outpatient</p> <p>Dosage, Duration: 1–4 hours spent in session, homework, and other each week, for 8 weeks</p> <p>Co-interventions: TAU or standard of care; patients received proper diagnoses, psychoeducation, and treatment advice on medicine and graded exercise</p> <p>Comparator: “Enhanced TAU,” enhanced by a face-to-face meeting with a psychiatrist</p> <p>Primary Endpoint: SF-36 Bodily Pain</p> <p>Power Calculation: Yes (sufficient power)</p> <p>Follow-Up Time: 60 weeks</p>	<p>Pain Measures:</p> <p>SF-36 Bodily Pain, 12 weeks: SMD 0.15 (CI –0.23, 0.53)</p> <p>SF-36 Bodily Pain, 36 weeks: SMD 0.23 (CI –0.18, 0.63)</p> <p>SF-36 Bodily Pain, 60 weeks: SMD –0.1 (CI –0.51, 0.31)</p> <p>Analgesic Use: No</p> <p>Mental Health-Related QoL Measure:</p> <p>SF-36 Mental Composite: SMD –0.04 (CI –0.42, 0.34)</p> <p>Physical Health-Related QoL Measure:</p> <p>SF-36 Physical Composite: SMD 0.22 (CI –0.16, 0.61)</p> <p>Adverse Events: No mention</p>

Study Details	Participants	Intervention	Outcomes
Reference: Fogarty et al., 2015	Number of Patients: 51	Content of Intervention: Standardized 8-week program developed by the University of Massachusetts Medical School	Pain: Significant reduction reported; no usable data
Location: New Zealand	Medical Condition/Type of Pain: Rheumatoid arthritis	Setting: Unclear	Analgesic Use: No
Purpose: To examine the effects of a standardized MBSR intervention on rheumatoid arthritis disease activity	Definition of Chronic Pain: No definition	Dosage, Duration: Dosage is unclear, for 8 weeks	Adverse Events: No mention
Quality Rating: Good	Mean Age: Intervention: 52 (SD 12); Control: 55 (SD 13)	Co-interventions: TAU or standard of care: acetaminophen, rheumatic painkiller, and opioids	
	Gender (% Male): 12	Comparator: Passive (e.g., waitlist, no treatment), TAU or standard of care: acetaminophen, rheumatic painkiller, and opioids	
	Inclusion Criteria: Rheumatoid arthritis, according to the 1987 American College of Rheumatology classification criteria.	Primary Endpoint: Arthritis activity	
	Exclusion Criteria: Prior meditation experience.	Power Calculation: No	

Study Details	Participants	Intervention	Outcomes
<p>Reference: Garland et al., 2014</p> <p>Location: United States or Canada</p> <p>Purpose: To conduct an early-stage RCT of MORE, a multimodal intervention designed to simultaneously target mechanisms underpinning chronic pain and opioid misuse</p> <p>Quality Rating: Fair</p>	<p>Number of Patients: 115</p> <p>Medical Condition/Type of Pain: Osteoarthritis, fibromyalgia</p> <p>Definition of Chronic Pain: Other definition</p> <p>Baseline Pain Score: BPI Severity Intervention Group: 5.44 (SD 1.4); Control Group: 5.49 (SD 1.54)</p> <p>Mean Age: 48 (SD 14)</p> <p>Gender (% Male): 32</p> <p>Inclusion Criteria: Reported recurrent pain (i.e., pain on more days than not) stemming from chronic benign (i.e., non-cancer-related) pain conditions, arthritis or fibromyalgia and had been prescribed and taken opioids for analgesia daily or nearly every day (≥ 5 days per week) for at least the past 90 days.</p> <p>Exclusion Criteria: Actively suicidal or psychotic via assessment on Mini-International Neuropsychiatric Interview 6.0.</p>	<p>Content of Intervention: MORE unites complementary aspects of mindfulness training, third-wave cognitive-behavioral therapy, and principles from positive psychology into an integrative intervention strategy. Techniques drawn from these therapeutic approaches were integrated into a manualized 8-session group intervention designed to address the multiplicity of pathogenic factors involved in chronic pain and long-term opioid use. MORE sessions involved mindfulness training to target automatic habit behavior and foster nonreactivity, positive reappraisal training to regulate negative emotions and foster a sense of meaningfulness in life, and training in savoring pleasant events and emotions to ameliorate deficits in natural reward processing and positive affectivity.</p> <p>Setting: Unclear</p> <p>Dosage, Duration: 1–4 hours spent in session, homework, and other each week, for 8 weeks</p> <p>Co-interventions: TAU or standard of care: medical care, prescription pain medications</p> <p>Comparator: Support groups</p> <p>Primary Endpoint: BPI Severity</p> <p>Power Calculation: Yes (sufficient power)</p> <p>Follow-Up Time: 20 weeks</p>	<p>Pain Measures: BPI Severity, 20 weeks: SMD 0.76 (CI 0.38, 1.14) BPI Severity, 8 weeks: SMD 0.57 (CI 0.19, 0.94)</p> <p>Analgesic Use: No; reports on prescription opioid misuse post-treatment</p> <p>Adverse Events: No mention</p>

Study Details	Participants	Intervention	Outcomes
Reference: Gaylord et al., 2011	Number of Patients: 75	Content of Intervention: The mindfulness-based stress and pain management program was based on the MBSR program developed by Jon Kabat-Zinn and Saki Santorelli at the University of Massachusetts. The basic course was adapted to an IBS population by emphasizing the relevance of mindfulness in coping with IBS-related symptoms and perceptions.	Pain Measures: Pain Severity, 20 weeks: SMD 0.53 (CI 0.06, 0.99) Pain Severity, 8 weeks: SMD 0.54 (CI 0.08, 1)
Location: United States or Canada	Medical Condition/Type of Pain: IBS	Setting: Unclear	Depression Measures: Brief Symptom Inventory-18 depression: SMD 0.03 (CI -0.42, 0.49)
Purpose: To explore the feasibility and efficacy of a group program of mindfulness training, a cognitive-behavioral technique, for women with irritable bowel syndrome	Definition of Chronic Pain: No definition Baseline Pain Score: Pain Severity Intervention Group: 54.54 (SD 22.82); Control Group: 53.35 (SD 28.12)	Dosage, Duration: >4 hours spent in session, homework, and other each week, for 8 weeks	Analgesic Use: No
Quality Rating: Fair	Mean Age: Mindfulness Group: 44.72 (SD 12.55); Control Group: 40.89 (SD 14.68) Gender (% Male): 0 Inclusion Criteria: IBS diagnosis according to Rome II criteria and physician diagnosis; female; age 18–75 years; ability to understand English; willingness to document bowel symptoms and medication use regularly and complete the assessments; and willingness to attend eight weekly sessions, plus one additional half-day session of either mindfulness training or support group. Exclusion Criteria: Diagnosis of mental illness with psychosis; a history of inpatient admission for psychiatric disorder within the past 2 years; a history or current diagnosis of inflammatory bowel disease or gastrointestinal malignancy; active liver or pancreatic disease; uncontrolled lactose intolerance; celiac disease; a history of abdominal trauma or surgery involving gastrointestinal resection; or pregnancy.	Co-interventions: TAU or standard of care; subjects continued with their usual medical care throughout the study Comparator: TAU or standard of care (subjects continued with their usual medical care throughout the study); social-support group intervention Primary Endpoint: Pain Severity Power Calculation: No Follow-Up Time: 20 weeks	General QoL Measure: IBS Quality of Life: SMD 0.25 (CI -0.21, 0.7) Adverse Events: No mention

Study Details	Participants	Intervention	Outcomes
<p>Reference: la Cour and Petersen, 2015</p> <p>Location: Europe</p> <p>Purpose: To investigate the effects on pain, physical function, mental function, pain acceptance, and health-related quality of life of mindfulness meditation via MBSR on nonspecific chronic pain as compared with a waitlist control group</p> <p>Quality Rating: Fair</p>	<p>Number of Patients: 109</p> <p>Medical Condition/Type of Pain: Unspecified, varied</p> <p>Definition of Chronic Pain: No definition</p> <p>Baseline Pain Score: BPI average score Intervention Group: 19 (SD 6.6); Control Group: 19.2 (SD 5.2)</p> <p>Mean Age: Intervention: 46.52 (SD 12.42); Control: 48.84 (SD 12.20)</p> <p>Gender (% Male): 15</p> <p>Inclusion Criteria: Chronic pain diagnosis by trained physicians who specialized in treating pain; all pain conditions and physical abilities were included.</p> <p>Exclusion Criteria: Unstable clinical situations, such as pharmaceutical treatments that continued to change, and patients with obvious mental disabilities, such as severe cognitive problems or emotional turmoil; very poor Danish language skills.</p>	<p>Content of Intervention: MBSR standard program modified for chronic pain patients</p> <p>Setting: Outpatient pain clinic</p> <p>Dosage, Duration: >4 hours spent in session, homework, and other each week, for 8 weeks</p> <p>Co-interventions: TAU or standard of care</p> <p>Comparator: Passive (e.g., waitlist, no treatment), TAU or standard of care</p> <p>Primary Endpoint: BPI</p> <p>Power Calculation: Yes (sufficient power)</p> <p>Follow-Up Time: 8 weeks</p>	<p>Pain Measures: BPI average score: SMD -0.16 (CI -0.53, 0.22)</p> <p>Depression Measures: Hospital Anxiety and Depression Scale, depression: SMD 0.37 (CI -0.01, 0.75)</p> <p>Analgesic Use: No</p> <p>Mental Health-Related QoL Measure: SF36 Mental Composite: SMD 0.53 (CI 0.15, 0.91)</p> <p>Physical Health-Related QoL Measure: SF-36 Physical Composite: SMD 0 (CI -0.38, 0.38)</p> <p>Adverse Events: Yes; two participants experienced temporary strong feelings of anger toward their pain condition, and two patients experienced greater anxiety</p>

Study Details	Participants	Intervention	Outcomes
<p>Reference: Ljotsson, Falk, et al., 2010</p> <p>Location: Europe</p> <p>Purpose: To investigate if cognitive behavior therapy based on exposure and mindfulness exercises delivered via the Internet would be effective in treating participants with IBS</p> <p>Quality Rating: Good</p>	<p>Number of Patients: 85</p> <p>Medical Condition/Type of Pain: IBS</p> <p>Definition of Chronic Pain: No definition</p> <p>Baseline Pain Score: Total Pain Intervention Group: 2.6 (SD 1.7); Control Group: 2.4 (SD 1.5)</p> <p>Mean Age: 34.6 (SD 9.4)</p> <p>Gender (% Male): 15</p> <p>Inclusion Criteria: A previous diagnosis of IBS given by a physician, and currently fulfilling the Rome III criteria for IBS.</p> <p>Exclusion Criteria: Patients with symptoms that in a live care setting would have rendered a somatic investigation to rule out organic disease; symptom debut after age 50; blood in stool without satisfactory medical explanation (such as known hemorrhoids); diarrhea predominant IBS with no colonoscopy performed; rapid weight loss that could not be linked to change in diet; night symptoms that persistently caused sleeplessness; less than 2 years of IBS-symptoms; any presence of current or previous inflammatory bowel disease; lactose or gluten intolerance where proper adjustments in diet had not been made; suicide ideation based on Montgomery Åsberg Depression Rating Scale Self-report; severe depressive symptoms (total score 30) based on Montgomery Åsberg Depression Rating Scale Self-report; substance dependence according to Alcohol Use Disorders Identification Test or Drug Use Disorders Identification Test; psychosis; manic episode; or anorexia according to the Mini-International Neuropsychiatric Interview.</p>	<p>Content of Intervention: Text-based (online) self-help manual divided into five steps: Step 1. A rationale for the treatment and instructions on mindfulness. The mindfulness instructions included exercises to be practiced daily, aimed at bringing the participant into immediate awareness of current gastrointestinal symptoms, thoughts, feelings, and behavioral impulses. Steps 2–4. A presentation of a psychological model of IBS and continued mindfulness exercises. Step 5. Three categories of exposure exercises: (a) exercises that provoke symptoms, such as certain foods, physical activity, and stressful situations; (b) abolishment of behaviors that serve to control symptoms, such as distraction, excessive toilet visits, eating certain foods, resting, and taking unprescribed medications; (c) exposure to situations where symptoms were unwanted, such as attending a meeting when experiencing abdominal pain or riding the bus with fear of losing control of the bowels. The steps were to be done in order, about one per week, and homework exercises and a symptom diary were to be completed. Participants were also encouraged to contact a therapy student, online.</p> <p>Setting: Remote (e.g., telephone Internet app)</p> <p>Dosage, Duration: Dosage is unclear, for 10 weeks</p> <p>Co-interventions: NA</p> <p>Comparator: Passive (e.g., waitlist, no treatment); also, participants randomized to waiting list were therefore given access to an online discussion forum (separate from the one used by the treatment intervention) where suggestions about general discussions regarding IBS were given each week</p> <p>Primary Endpoint: Total Pain</p> <p>Power Calculation: Yes (sufficient power)</p> <p>Follow-Up Time: 10 weeks</p>	<p>Pain Measures: Total Pain: SMD 0.64 (CI 0.19, 1.08)</p> <p>Depression Measures: Montgomery–Åsberg Depression Rating Scale–Self-Report: SMD 0.43 (CI –0.02, 0.87)</p> <p>Analgesic Use: No</p> <p>General QoL Measure: IBS Quality of Life: SMD 0.95 (CI 0.49, 1.41)</p> <p>Adverse Events: No mention</p>

Study Details	Participants	Intervention	Outcomes
<p>Reference: Ljotsson, Hedman, et al., 2011</p> <p>Location: Europe</p> <p>Purpose: To compare Internet-based cognitive behavioral therapy with Internet-delivered stress management for IBS to assess whether the effects of such therapy are specific and not attributable to credibility or expectation of improvement</p> <p>Quality Rating: Good</p>	<p>Number of Patients: 195</p> <p>Medical Condition/Type of Pain: IBS</p> <p>Definition of Chronic Pain: No definition</p> <p>Mean Age: 38.9 (SD 11.1)</p> <p>Gender (% Male): 21</p> <p>Inclusion Criteria: A previous diagnosis of IBS given by a physician; fulfillment of the Rome III criteria for IBS; symptom history of at least 2 years.</p> <p>Exclusion Criteria: Symptom onset after age 50, blood in stool without satisfactory medical explanation (such as known hemorrhoids); diarrhea predominant IBS with no colonoscopy performed, rapid weight loss that could not be linked to change in diet, and nocturnal symptoms that persistently caused sleeplessness. In addition to the alarm symptoms, the following criteria were cause for exclusion: <2 years of IBS symptoms (regardless of when diagnosis had been given), any presence of current or previous inflammatory bowel disease, lactose or gluten intolerance where proper dietary changes had not been made, and severe alcohol dependence, depression, or suicidal ideation.</p>	<p>Content of Intervention: Text-based (online) self-help manual divided into five steps. Step 1. A rationale for the treatment and instructions on mindfulness. The mindfulness instructions included exercises to be practiced daily, aimed at bringing the participant into immediate awareness of current gastrointestinal symptoms, thoughts, feelings, and behavioral impulses. Steps 2–4. A presentation of a psychological model of IBS and continued mindfulness exercises. Step 5. Three categories of exposure exercises: (a) exercises that provoke symptoms, such as certain foods, physical activity, and stressful situations; (b) abolishment of behaviors that serve to control symptoms, such as distraction, excessive toilet visits, eating certain foods, resting, and taking unprescribed medications; (c) exposure to situations where symptoms were unwanted, such as attending a meeting when experiencing abdominal pain or riding the bus with fear of losing control of the bowels. The steps were to be done in order, about one per week, and homework exercises and a symptom diary were to be completed. Participants were also encouraged to contact a therapy student, online.</p> <p>Setting: Remote (e.g., telephone Internet app)</p> <p>Dosage, Duration: Dosage is unclear, for 10 weeks</p> <p>Co-interventions: NA</p> <p>Comparator: Internet stress management</p> <p>Primary Endpoint: Relief from IBS symptoms</p> <p>Power Calculation: Yes (sufficient power)</p> <p>Follow-Up Time: 24 weeks</p>	<p>Pain: Increased relief from IBS pain and discomfort significant</p> <p>Depression Measures: HADS depression: SMD 0 (CI -0.28, 0.28)</p> <p>Analgesic Use: No</p> <p>General QoL Measure: IBS Quality of Life: SMD 0.51 (CI 0.22, 0.8)</p> <p>Adverse Events: No mention</p>

Study Details	Participants	Intervention	Outcomes
<p>Reference: Meize-Grochowski et al., 2015</p> <p>Location: United States or Canada</p> <p>Purpose: To examine daily meditation versus usual care in a diverse sample of older adults with postherpetic neuralgia</p> <p>Quality Rating: Poor</p>	<p>Number of Patients: 31</p> <p>Medical Condition/Type of Pain: Postherpetic neuralgia</p> <p>Definition of Chronic Pain: No definition</p> <p>Baseline Pain Score: Short-Form MPQ – total pain score</p> <p>Intervention Group: 3.5 (SD 2.2); Control Group: 2.4 (SD 1.5)</p> <p>Mean Age: 72 (SD 9.6)</p> <p>Gender (% Male): 44.4</p> <p>Inclusion Criteria: 50 years of age or older, able to read and write English, and self-reported persistent pain after the shingles rash had resolved.</p> <p>Exclusion Criteria: Consistent use of meditation in the previous year; medical instability from severe heart disease, lung disease, or diabetes mellitus; multiple recent falls; pain caused by an acute injury in the previous month; unable to stand independently; and underlying serious illness, such as unexplained weight loss, fever, or pain from cancer.</p>	<p>Content of Intervention: MBSR: 1 hour instruction focusing breathing while seated comfortably, daily meditation using a compact disc, phone call reminders, and daily journal</p> <p>Setting: Remote (e.g., telephone Internet app)</p> <p>Dosage, Duration: 1–4 hours spent in session, homework, and other each week, for 6 weeks</p> <p>Co-interventions: TAU or standard of care</p> <p>Comparator: TAU or standard of care</p> <p>Primary Endpoint: SF MPQ</p> <p>Power Calculation: Power insufficient (post hoc test by authors)</p> <p>Follow-Up Time: 8 weeks</p>	<p>Pain Measures: Short-Form MPQ – total pain score, 2 weeks: SMD -0.48 (CI -1.25, 0.28) Short-Form MPQ – total pain score, 8 weeks: SMD -0.31 (CI -1.07, 0.45)</p> <p>Depression Measures: Center for Epidemiologic Studies Depression Scale score: SMD -0.32 (CI -1.08, 0.44)</p> <p>Analgesic Use: No</p> <p>Mental Health-Related QoL Measure: Emotional Well-Being: SMD 0.07 (CI -0.69, 0.82)</p> <p>Physical Health-Related QoL Measure: Average Physical Subscales: SMD -0.02 (CI -0.77, 0.74)</p> <p>Adverse Events: No mention</p>

Study Details	Participants	Intervention	Outcomes
<p>Reference: Morone et al., 2009</p> <p>Location: United States or Canada</p> <p>Purpose: To determine the impact of an 8-week mindfulness meditation program on disability, psychological function, and pain severity in community-dwelling older adults with chronic low back pain, and test the education control program for feasibility</p> <p>Quality Rating: Poor</p>	<p>Number of Patients: 40</p> <p>Medical Condition/Type of Pain: Back pain</p> <p>Definition of Chronic Pain: 3 months minimum or "past normal time for tissue healing"</p> <p>Baseline Pain Score: Short-Form MPQ – total pain score</p> <p>Intervention Group: 15.6 (SD 7.52); Control Group: 16.1 (SD 7.52)</p> <p>Mean Age: Intervention: 78 (SD 7.1); Control: 73 (SD 6.2)</p> <p>Gender (% Male): 37</p> <p>Inclusion Criteria: Chronic lower back pain of at least 3 months' duration and of at least moderate intensity according to a vertical verbal descriptor scale (pain thermometer), age ≥ 65 years, and intact cognition (Mini-Mental Status Exam ≥ 24).</p> <p>Exclusion Criteria: Non-English speaking, previous participation in a mindfulness meditation program, serious hearing or vision impairment that would preclude responding to questionnaires or participating in the meditation program, medical instability from heart or lung disease, multiple recent falls or inability to stand independently, pain caused by an acute injury in the previous 3 months, and underlying red flags of serious underlying illness, such as recent unexplained weight loss, fever, or sudden worsening of back pain.</p>	<p>Content of Intervention: Partial MBSR: The methods used were (1) the body scan, where in a lying position, the participant is guided to place attention nonjudgmentally on each area of the body, from the toes to the top of the head; (2) sitting practice, where the participant is guided to focus attention on breathing while sitting on a chair; and (3) walking meditation, where the participant is guided in mindful slow walking with focused attention on body sensation and/or breathing</p> <p>Setting: Unclear</p> <p>Dosage, Duration: >4 hours spent in session, homework, and other each week, for 8 weeks</p> <p>Co-interventions: Over the counter medication (ibuprofen, Tylenol, acetaminophen, etc.), opioids, other prescription medications</p> <p>Comparator: Over the counter medication (ibuprofen, Tylenol, acetaminophen, etc.), opioids, other prescription medications, health education program</p> <p>Primary Endpoint: SF MPQ – total pain score</p> <p>Power Calculation: Unclear (cannot tell for outcomes of interest)</p> <p>Follow-Up Time: 24 weeks</p>	<p>Pain Measures:</p> <p>Short-Form MPQ – total pain score, 24 weeks: SMD -0.04 (CI -0.7, 0.63)</p> <p>Short-Form MPQ – total pain score, 8 weeks: SMD -0.01 (CI -0.68, 0.65)</p> <p>Analgesic Use: No</p> <p>Adverse Events: None reported</p>

Study Details	Participants	Intervention	Outcomes
<p>Reference: Morone, Greco, and Weiner, 2008</p> <p>Location: United States or Canada</p> <p>Purpose: To assess the feasibility of recruitment and adherence to an eight-session mindfulness meditation program for community-dwelling older adults with chronic low back pain, and develop initial estimates of treatment effects</p> <p>Quality Rating: Fair</p>	<p>Number of Patients: 37</p> <p>Medical Condition/Type of Pain: Back pain</p> <p>Definition of Chronic Pain: 3 months minimum or "past normal time for tissue healing"</p> <p>Baseline Pain Score: Short-Form MPQ Intervention Group: 15.5 (SD 10); Control Group: 15.2 (SD 7)</p> <p>Mean Age: Intervention: 74.1(SD 6.1); Controls: 75.6 (SD 5.0)</p> <p>Gender (% Male): 43</p> <p>Inclusion Criteria: (1) Were 65 years of age or older; (2) had intact cognition (Mini-Mental Status Exam P23); (3) had chronic low back pain, defined as moderate pain occurring daily or almost every day for at least the previous three months; and (4) spoke English.</p> <p>Exclusion Criteria: Had previously participated in a mindfulness meditation program and had "red flags" suggestive of serious underlying illness (e.g. malignancy, infection, unexplained fever, weight loss, or recent trauma) causing their pain.</p>	<p>Content of Intervention: Partial MBSR: The techniques used were: (1) the body scan, where in a lying position, the participant is guided to place attention nonjudgmentally on each area of the body, from the toes to the top of the head; (2) sitting practice, which is focused attention on breathing while sitting on a chair or on a meditation cushion on the floor; and (3) walking meditation, which is mindful slow walking with focused attention on body sensation and/or breathing</p> <p>Setting: Unclear</p> <p>Dosage, Duration: >4 hours spent in session, homework, and other each week, for 8 weeks</p> <p>Co-interventions: NA</p> <p>Comparator: Passive (e.g., waitlist, no treatment)</p> <p>Primary Endpoint: Adherence</p> <p>Power Calculation: Power insufficient (post hoc test by authors)</p> <p>Follow-Up Time: 8 weeks</p>	<p>Pain Measures: Short-Form MPQ: SMD 0.23 (CI -0.42, 0.88)</p> <p>Analgesic Use: No</p> <p>Mental Health-Related QoL Measure: SF-36 Mental Composite: SMD 0.22 (CI -0.43, 0.86)</p> <p>Physical Health-Related QoL Measure: SF-36 Physical Composite: SMD 0.11 (CI -0.53, 0.76)</p> <p>Adverse Events: None reported</p>

Study Details	Participants	Intervention	Outcomes
Reference: Omid and Zargar, 2014 Location: Middle East Purpose: Evaluating the efficacy of MBSR in improving pain severity and mindful awareness in patients with tension headache Quality Rating: Poor	Number of Patients: 66 Medical Condition/Type of Pain: Other headache Definition of Chronic Pain: Other definition Baseline Pain Score: Pain Severity Intervention Group: 7.36 (SD 1.25); Control Group: 7.5 (SD 1.35) Mean Age: Intervention: 34.5 (SD 2.41); Control: 32 (SD 3.2) Gender (% Male): 20 Inclusion Criteria: Having a tension headache according to the International Headache Classification Subcommittee, and tending to participate in the study. Exclusion Criteria: A medical diagnosis of organic brain disorder or psychotic disorder, and a history of psychologic treatment during the preceding six months.	Content of Intervention: Standard MBSR Setting: Unclear Dosage, Duration: 1–4 hours spent in session, homework, and other each week, for 8 weeks Co-interventions: NA Comparator: TAU or standard of care Primary Endpoint: Pain Severity Power Calculation: No Follow-Up Time: 20 weeks	Pain Measures: Pain Severity, 20 weeks: SMD 1.23 (CI 0.68, 1.78) Pain Severity, 8 weeks: SMD 1.21 (CI 0.66, 1.76) Analgesic Use: No Adverse Events: No mention

Study Details	Participants	Intervention	Outcomes
<p>Reference: Parra-Delgado and Latorre-Postigo, 2013</p> <p>Location: Europe</p> <p>Purpose: To examine whether MBCT is successful in reducing the impact of the illness, as well as the depressive symptoms and the pain perceived in different parts of the body in fibromyalgia patients</p> <p>Quality Rating: Good</p>	<p>Number of Patients: 33</p> <p>Medical Condition/Type of Pain: Fibromyalgia</p> <p>Definition of Chronic Pain: No definition</p> <p>Baseline Pain Score: VAS average score Intervention Group: 1.88 (SD 0.55); Control Group: 1.83 (SD 0.47)</p> <p>Mean Age: 52.67 (SD 10.08)</p> <p>Gender (% Male): 0</p> <p>Inclusion Criteria: Being diagnosed with fibromyalgia syndrome in accordance with the diagnostic criteria proposed by the American College of Rheumatology, and committing to the daily practice of mindfulness.</p> <p>Exclusion Criteria: Being diagnosed with alcohol or substance dependence or abuse, and receiving psychological therapy from the Castillo-La Mancha Health Service fibromyalgia team.</p>	<p>Content of Intervention: MBCT: Different practical mindfulness exercises were conducted at each of the sessions, with special focus on pain-related stimuli. The main aim was for patients to learn mindfulness techniques in order to relate to their experience of pain and the thoughts and feelings it provokes in a different way, responding in a compassionate and nonjudgmental way. The participants were invited to reflect on the transitory nature of the different painful stimuli and were invited to experience their thoughts as passing events of the mind rather than absolute truths. The modifications to the MBCT for the women with fibromyalgia were taking a closer look at the acceptance of the experience of pain in the different meditation practices of mindfulness, encouraging participants to be aware of the automatic thoughts related to the response to pain and their relationship to the feelings and behaviors it caused, providing information on anxiety and its causes (requested by the patients), and explaining the importance of not forcing their body into yoga postures and of feeling comfortable by using appropriate clothes and postures during the practice of mindfulness.</p> <p>Setting: Unclear</p> <p>Dosage, Duration: Dosage is unclear, for 12 weeks</p> <p>Co-interventions: TAU or standard of care</p> <p>Comparator: TAU or standard of care; all participants continued with their usual medication treatment, medical visits, rehabilitation sessions, and activities proposed by the Fibromyalgia Association</p> <p>Primary Endpoint: VAS</p> <p>Power Calculation: No</p> <p>Follow-Up Time: 24 weeks</p>	<p>Pain Measures: VAS average score, 12 weeks: SMD 0.19 (CI -0.51, 0.9) VAS average score, 24 weeks: SMD 0.44 (CI -0.27, 1.15)</p> <p>Depression Measures: BDI: SMD 0.36 (CI -0.35, 1.07)</p> <p>Analgesic Use: No</p> <p>Adverse Events: No mention</p>

Study Details	Participants	Intervention	Outcomes
<p>Reference: Plews-Ogan et al., 2005</p> <p>Location: United States or Canada</p> <p>Purpose: To evaluate the feasibility of studying MBSR and massage for the management of chronic pain, and estimate their effects on pain and mood</p> <p>Quality Rating: Poor</p>	<p>Number of Patients: 30</p> <p>Medical Condition/Type of Pain: Musculoskeletal pain</p> <p>Definition of Chronic Pain: Musculoskeletal pain for greater than 3 months</p> <p>Baseline Pain Score: Pain Unpleasantness Intervention Group: 6.7 (SD 2.69); Control Group: 6.9 (SD 2.55)</p> <p>Mean Age: 46.5</p> <p>Gender (% Male): 23</p> <p>Inclusion Criteria: Musculoskeletal pain for greater than 3 months.</p> <p>Exclusion Criteria: Prisoner status, cognitive impairment, lack of reliable transportation, or being pregnant.</p>	<p>Content of Intervention: Standard MBSR: Meditation and yoga techniques were practiced to foster mindfulness (present moment, nonjudgmental awareness)</p> <p>Setting: Unclear</p> <p>Dosage, Duration: Dosage is unclear, for 8 weeks</p> <p>Co-interventions: NA</p> <p>Comparator: Massage, TAU</p> <p>Primary Endpoint: Pain unpleasantness</p> <p>Power Calculation: No</p> <p>Follow-Up Time: 12 weeks</p>	<p>Pain Measures:</p> <p>Pain Unpleasantness vs. TAU, 12 weeks: SMD 0.02 (CI -1.04, 1.07)</p> <p>Pain Unpleasantness vs. Massage, 12 weeks: SMD -0.16 (CI -1.19, 0.88)</p> <p>Pain Unpleasantness, vs TAU, 4 weeks: SMD 0.07 (CI -0.99, 1.13)</p> <p>Pain Unpleasantness vs. Massage, 4 weeks: SMD 0.11 (CI -0.92, 1.14)</p> <p>Pain Unpleasantness vs. TAU, 8 weeks: SMD 0.17 (CI -0.89, 1.23)</p> <p>Pain Unpleasantness vs. Massage, 8 weeks: SMD -0.3 (CI -1.34, 0.74)</p> <p>Analgesic Use: No</p> <p>Mental Health-Related QoL Measure: SF-12 Mental Health: SMD 0.67 (CI -0.42, 1.75)</p> <p>Adverse Events: No mention</p>

Study Details	Participants	Intervention	Outcomes
<p>Reference: Rahmani and Talepasand, 2015</p> <p>Location: Middle East</p> <p>Purpose: To examine the effectiveness of the MBSR program and conscious yoga on the mental fatigue severity and life quality of women with breast cancer</p> <p>Quality Rating: Poor</p>	<p>Number of Patients: 24</p> <p>Medical Condition/Type of Pain: Cancer</p> <p>Definition of Chronic Pain: No definition</p> <p>Baseline Pain Score: Global Quality Symptoms – Pain</p> <p>Intervention Group: 68.05 (SD 4.81); Control Group: 75 (SD 15.08)</p> <p>Mean Age: Treatment: 43.25 (SD 3.07); Control: 44.8 (SD 3.28)</p> <p>Gender (% Male): 0</p> <p>Inclusion Criteria: Diagnosis of stages I, II, or III of breast cancer based on the clinical findings, cytological studies, and diagnosis of a physician; fatigue severity score higher than 4; duration of breast cancer greater than a month; no anemia; no other cancer diagnosis; age between 30 and 55 years; no other psychological treatment from the time of diagnosis; minimum of secondary school education; consent to participate; and ability to take part in the desired courses.</p> <p>Exclusion Criteria: Absence of more than two intervention sessions, not wanting to continue to participate in the intervention, and disease recurrence or development of metastasis elsewhere in the body during the study.</p>	<p>Content of Intervention: MBSR with group conscious yoga; MBSR was based on Kabat-Zinn (2005)</p> <p>Setting: Other outpatient</p> <p>Dosage, Duration: 1–4 hours spent in session, homework, and other each week, for 8 weeks</p> <p>Co-interventions: Group conscious yoga</p> <p>Comparator: Passive (e.g., waitlist, no treatment)</p> <p>Primary Endpoint: Global Quality</p> <p>Power Calculation: Unclear (cannot tell for outcomes of interest)</p> <p>Follow-Up Time: 16 weeks</p>	<p>Pain Measures:</p> <p>Global Quality Symptoms – Pain, 16 weeks: SMD 1.85 (CI 0.89, 2.8)</p> <p>Global Quality Symptoms – Pain, 8 weeks: SMD 3.24 (CI 2.02, 4.46)</p> <p>Analgesic Use: No</p> <p>General QoL Measure:</p> <p>Global Quality Total Score: SMD 1.18 (CI 0.32, 2.05)</p> <p>Adverse Events: No mention</p>

Study Details	Participants	Intervention	Outcomes
<p>Reference: Schmidt et al., 2011</p> <p>Location: Europe</p> <p>Purpose: To investigate the efficacy of MBSR for enhanced well-being of fibromyalgia patients in a three-armed trial, which was a follow-up to an earlier quasi-randomized investigation</p> <p>Quality Rating: Fair</p>	<p>Number of Patients: 177</p> <p>Medical Condition/Type of Pain: Fibromyalgia</p> <p>Definition of Chronic Pain: No definition</p> <p>Baseline Pain Score: Pain Perception Scale – affective</p> <p>Intervention Group: 35.47 (SD 9.38); Control Group: 34.78 (SD 7.66)</p> <p>Mean Age: 52.5 (SD 9.6)</p> <p>Gender (% Male): 0</p> <p>Inclusion Criteria: Women 18–70 years of age who currently had fibromyalgia, as defined by the American College of Rheumatology criteria; command of the German language and motivation to participate.</p> <p>Exclusion Criteria: Life-threatening diseases, evidence of suppressed immune functioning, or participation in other clinical trials.</p>	<p>Content of Intervention: Modified MBSR: Each session covered specific exercises and topics within the context of mindfulness practice and training. These included various types of formal mindfulness practice, mindful awareness of dynamic yoga postures, and mindfulness during stressful situations and social interactions. The all-day retreat included a combination of previously used and newly introduced mindfulness exercises.</p> <p>Setting: Unclear</p> <p>Dosage, Duration: >4 hours spent in session, homework, and other each week, for 8 weeks</p> <p>Co-interventions: NA</p> <p>Comparator: Passive (e.g., waitlist, no treatment); Active control: muscle relaxation and stretching</p> <p>Primary Endpoint: Pain Perception Scale</p> <p>Power Calculation: Yes (sufficient power)</p> <p>Follow-Up Time: 16 weeks</p>	<p>Pain Measures:</p> <p>Pain Perception Scale – affective vs. waitlist, 16 weeks: SMD 0.17 (CI –0.2, 0.55)</p> <p>Pain Perception Scale – affective vs. active, 16 weeks: SMD 0.15 (CI –0.22, 0.53)</p> <p>Pain Perception Scale – affective vs. waitlist, 8 weeks : SMD 0.08 (CI –0.3, 0.45)</p> <p>Pain Perception Scale – affective vs. active, 8 weeks: SMD 0.22 (CI –0.16, 0.6)</p> <p>Depression Measures:</p> <p>Center for Epidemiologic Studies Depression Scale score: SMD 0.1 (CI –0.27, 0.48)</p> <p>Analgesic Use: No</p> <p>General QoL Measure:</p> <p>QoL Profile for Chronically Ill: SMD 0.26 (CI –0.12, 0.63)</p> <p>Adverse Events: No mention</p>

Study Details	Participants	Intervention	Outcomes
Reference: Teixeira, 2010 Location: United States or Canada Purpose: To explore the effect of mindfulness meditation on quality of life for adults with diabetic neuropathy Quality Rating: Poor	Number of Patients: 22 Medical Condition/Type of Pain: Diabetic peripheral neuropathy Definition of Chronic Pain: No definition Mean Age: 74.6 (SD 10.8) Gender (% Male): 25 Inclusion Criteria: Type 1 or Type 2 diabetes for at least 1 year, diabetic neuropathy symptoms of pain and/or numbness for at least 6 months, male or female between the ages of 50 and 92 years, able to provide informed consent, and not currently practicing formal meditation. Exclusion Criteria: NA	Content of Intervention: Received instruction in mindfulness meditation and was instructed to listen to a guided compact disc 5 days per week over a 4-week period Setting: Remote (e.g., telephone Internet app) Dosage, Duration: Dosage is unclear, for 4 weeks Co-interventions: NA Comparator: Nutritional information and food diary Primary Endpoint: EuroQol Pain Power Calculation: Power insufficient (post hoc test by authors) Follow-Up Time: 4 weeks	Pain Measures: Neuro QoL Pain: SMD 0.14 (CI -0.74, 1.01) Analgesic Use: No General QoL Measure: Neuro QoL Overall: SMD 0.79 (CI -0.12, 1.7) Adverse Events: No mention

Study Details	Participants	Intervention	Outcomes
<p>Reference: Wells et al., 2014</p> <p>Location: United States or Canada</p> <p>Purpose: To assess the safety, feasibility, and effects of the standardized 8-week MBSR course in adults with migraines</p> <p>Quality Rating: Fair</p>	<p>Number of Patients: 19</p> <p>Medical Condition/Type of Pain: Migraine</p> <p>Definition of Chronic Pain: Other definition</p> <p>Baseline Pain Score: Headache severity Intervention Group: 4.4 (SD 1.11); Control Group: 4.8 (SD 1.33)</p> <p>Mean Age: Intervention: 45.9 (SD 17); Control: 45.2 (SD 12)</p> <p>Gender (% Male): 10.5</p> <p>Inclusion Criteria: Diagnosis of migraine with or without aura (according to the International Classification of Headache Disorders-II); 4–14 migraine days per month; one-year history of migraines; at least 18 years old; able and willing to attend weekly sessions and willing to participate in daily mindfulness assignments of up to 30–45 minutes per day; agreeable to participate and to be randomized to either group; fluent in English; and in good general health with no additional diseases expected to interfere with the study.</p> <p>Exclusion Criteria: Current regular meditation/yoga practice; major systemic illness or unstable medical/psychiatric condition (e.g., suicide risk) requiring immediate treatment or that could compromise protocol adherence; medication overuse headache (according to the International Classification of Headache Disorders-II); current or planned pregnancy or breastfeeding; new prophylactic migraine medicine started within 4 weeks of the screening visit; unwilling to maintain stable migraine medication dosages; and failure to complete baseline headache logs.</p>	<p>Content of Intervention: Standard MBSR</p> <p>Setting: Other outpatient</p> <p>Dosage, Duration: >4 hours spent in session, homework, and other each week, for 8 weeks</p> <p>Co-interventions: TAU or standard of care; participants were allowed to continue taking their prophylactic and abortive medications as usual</p> <p>Comparator: Passive (e.g., waitlist, no treatment), TAU or standard of care; participants were allowed to continue taking their prophylactic and abortive medications as usual</p> <p>Primary Endpoint: Headache severity</p> <p>Power Calculation: Power insufficient (post hoc test by authors)</p> <p>Follow-Up Time: 8 weeks</p>	<p>Pain Measures: Headache severity, 12 weeks: SMD 0.99 (CI 0.04, 1.95) Headache severity, 8 weeks: SMD 1.5 (CI 0.48, 2.51)</p> <p>Depression Measures: Patient Health Questionnaire Depression: SMD 0.59 (CI –0.33, 1.51)</p> <p>Analgesic Use: No</p> <p>General QoL Measure: Migraine-Specific QoL: SMD –0.43 (CI –1.34, 0.48)</p> <p>Adverse Events: No mention</p>

Study Details	Participants	Intervention	Outcomes
<p>Reference: Wong et al., 2011</p> <p>Location: Asia</p> <p>Purpose: To compare the clinical effectiveness of the MBSR program with a multidisciplinary pain intervention program in terms of pain intensity, pain-related distress, quality of life, and mood in patients with chronic pain</p> <p>Quality Rating: Good</p>	<p>Number of Patients: 100</p> <p>Medical Condition/Type of Pain: Unspecified</p> <p>Definition of Chronic Pain: 3 months minimum or "past normal time for tissue healing"</p> <p>Mean Age: 47.9 (SD 7.84)</p> <p>Gender (% Male): Not Reported</p> <p>Inclusion Criteria: Age between 18 and 65 years; the presence of chronic pain, which had persisted for at least 3 months at the moderate-to-severe level (i.e., at least 4 of 10 on an 11-point Numerical Rating Scale pain score); agreement by the participant not to receive other new treatments during the intervention, including the use of new medication, topical treatment, medication or other over-the-counter medication, or other nonpharmacological treatment; ability to give a written consent.</p> <p>Exclusion Criteria: Receiving concurrent treatment with therapies other than medications for pain or psychological symptoms; having a known, concurrent doctor-diagnosed Diagnostic and Statistical Manual of Mental Disorders-IV Axis I disorder; having previously participated in an MBSR program; having been engaged, currently or previously, in the practice of meditation or relaxation techniques, including an MBSR program; being illiterate, as the participant would not be able to complete the meditation diary.</p>	<p>Content of Intervention: Standard MBSR: Included three primary elements: (1) theoretical material related to mindfulness, relaxation, meditation, yoga, and the body-mind connection; (2) experimental practice of meditation and yoga; and (3) group activities that focused on removing impediments to effective practice, practical day-to-day applications of mindfulness, and supportive intervention between group members</p> <p>Setting: Unclear</p> <p>Dosage, Duration: 1–4 hours spent in session, homework, and other each week, for 8 weeks</p> <p>Co-interventions: TAU or standard of care: acetaminophen, rheumatic painkiller, and opioids</p> <p>Comparator: Multidisciplinary pain intervention</p> <p>Primary Endpoint: Pain Intensity</p> <p>Power Calculation: Yes (sufficient power)</p>	<p>Pain: No significant effect, data not usable</p> <p>Analgesic Use: No</p> <p>Adverse Events: No mention</p>

Study Details	Participants	Intervention	Outcomes
<p>Reference: Wong, 2009</p> <p>Location: Asia</p> <p>Purpose: To compare the effectiveness of MBSR with an education program in terms of reduction of pain and improvement in quality of life for chronic pain patients</p> <p>Quality Rating: Poor</p>	<p>Number of Patients: 100</p> <p>Medical Condition/Type of Pain: Unspecified</p> <p>Definition of Chronic Pain: 3 months minimum or "past normal time for tissue healing"</p> <p>Mean Age: Not reported</p> <p>Gender (% Male): Not Reported</p> <p>Inclusion Criteria: Aged 18 to 65 years, with any chronic pain for at least 3 months. The pain had to be moderate to severe (scoring at least 4 out of 10 in an 11-point Numeric Rating Scale) verified by a trained research assistant and confirmed by a family physician.</p> <p>Exclusion Criteria: Received concurrent treatment other than medications for pain or psychological symptoms; had a concurrent Diagnostic and Statistical Manual of Mental Disorders Axis-I diagnosis; participated in an MBSR group, engaged in current or prior practice of meditation or relaxation techniques, including MBSR; were illiterate and unable to complete the meditation diary.</p>	<p>Content of Intervention: Standard MBSR</p> <p>Setting: Unclear</p> <p>Dosage, Duration: Dosage is unclear, for 8 weeks</p> <p>Co-interventions: NA</p> <p>Comparator: Multidisciplinary education program</p> <p>Primary Endpoint: Pain reduction</p> <p>Power Calculation: No</p>	<p>Pain: Decrease in pain intensity significant (no usable data)</p> <p>Analgesic Use: No</p> <p>Adverse Events: No mention</p>

Study Details	Participants	Intervention	Outcomes
<p>Reference: Zautra et al., 2008</p> <p>Location: United States or Canada</p> <p>Purpose: To investigate whether cognitive behavioral therapy and mindfulness interventions that target responses to chronic stress, pain, and depression reduce pain and improve the quality of everyday life for adults with rheumatoid arthritis</p> <p>Quality Rating: Good</p>	<p>Number of Patients: 144</p> <p>Medical Condition/Type of Pain: Rheumatoid arthritis</p> <p>Definition of Chronic Pain: No definition</p> <p>Baseline Pain Score: Pain Intervention Group: 28.19 (SD 19.43); Control Group: 34.31 (SD 18.07)</p> <p>Mean Age: Men: 62.11; Women: 50.62</p> <p>Gender (% Male): 32</p> <p>Inclusion Criteria: Described themselves as having rheumatoid arthritis at screening and could obtain a written confirmation of rheumatoid arthritis from their rheumatologist.</p> <p>Exclusion Criteria: Taking any cyclical estrogen replacement therapies; have Lupus.</p>	<p>Content of Intervention: Mindfulness meditation and emotion regulation therapy: Designed to develop two distinct sets of skills—one to reduce the negative impact of stressful life events and illness burdens, and the other to enhance the ability to sustain positive social engagements despite pain and stress. The treatment modules included (1) mindfulness and the bidimensional model of emotion; (2) mindfulness and awareness; (3) emotional clarity and well-being; (4) acceptance, negative thoughts, and reframing; (5) positive emotions and pleasant event scheduling; (6) enhanced social relations; (7) intimacy, stress, and mindfulness; and (8) maintenance and generalization.</p> <p>Setting: Unclear</p> <p>Dosage, Duration: 1–4 hours spent in session, homework, and other each week, for 8 weeks</p> <p>Co-interventions: NA</p> <p>Comparator: Cognitive behavioral therapy for pain, education</p> <p>Primary Endpoint: Pain</p> <p>Power Calculation: Yes (sufficient power)</p> <p>Follow-Up Time: 8 weeks</p>	<p>Pain Measures:</p> <p>Pain vs. Education, 8 weeks: SMD 0.22 (CI -0.2, 0.63)</p> <p>Pain vs. Cognitive Behavior Therapy, 8 weeks: SMD 0.56 (CI 0.16, 0.96)</p> <p>Depression Measures:</p> <p>Depressive Symptoms: SMD 0.28 (CI -0.13, 0.7)</p> <p>Analgesic Use: No</p> <p>Adverse Events: No mention</p>

NOTE: NA = not applicable.

Appendix D: Studies Included in the Most Recent Systematic Review

The studies listed in Table D.1 were included in the most recent systematic review on mindfulness meditation for chronic pain (Bawa et al., 2015). We note whether each study was included in the present review, and if not, the reason for exclusion.

Table D.1. Studies Included in the Most Recent Systematic Review

Reference	Status in Current Report	If Excluded, Reason
Astin, J. A., B. M. Berman, B. Bausell, W. L. Lee, M. Hochberg, and K. L. Forys, "The Efficacy of Mindfulness Meditation Plus Qigong Movement Therapy in the Treatment of Fibromyalgia: A Randomized Controlled Trial," <i>Journal of Rheumatology</i> , Vol. 30, No. 10, October 2003, pp. 2257–2262.	Included	
Brown, C. A., and A. K. Jones, "Psychobiological Correlates of Improved Mental Health in Patients with Musculoskeletal Pain After a Mindfulness-Based Pain Management Program," <i>Clinical Journal of Pain</i> , Vol. 29, No. 3, March 2013, pp. 233–244.	Included	
Esmer, G., J. Blum, J. Rulf, and J. Pier, "Mindfulness-Based Stress Reduction for Failed Back Surgery Syndrome: A Randomized Controlled Trial," <i>Journal of the American Osteopathic Association</i> , Vol. 110, No. 11, November 2010, pp. 646–652.	Included	
Morone, N. E., B. L. Rollman, C. G. Moore, Q. Li, and D. K. Weiner, "A Mind-Body Program for Older Adults with Chronic Low Back Pain: Results of a Pilot Study," <i>Pain Medicine</i> , Vol. 10, No. 8, November 2009, pp. 1395–1407.	Included	
Plews-Ogan, M., J. E. Owens, M. Goodman, P. Wolfe, and J. Schorling, "A Pilot Study Evaluating Mindfulness-Based Stress Reduction and Massage for the Management of Chronic Pain," <i>Journal of General Internal Medicine</i> , Vol. 20, No. 12, December 2005, pp. 1136–1138.	Included	
Pradhan, E. K., M. Baumgarten, P. Langenberg, B. Handwerker, A. K. Gilpin, T. Magyari, M. C. Hochberg, and B. M. Berman, "Effect of Mindfulness-Based Stress Reduction in Rheumatoid Arthritis Patients," <i>Arthritis and Rheumatism</i> , Vol. 57, 2007, pp. 1134–1142.	Excluded	Our review required pain outcome. This study focuses on depressive symptoms, psychological distress, well-being, and mindfulness.
Schmidt, S., P. Grossman, B. Schwarzer, S. Jena, J. Naumann, and H. Walach, "Treating Fibromyalgia with Mindfulness-Based Stress Reduction: Results from a 3-Armed Randomized Controlled Trial," <i>Pain</i> , Vol. 152, No. 2, February 2011, pp. 361–369.	Included	
Sephton, S. E., P. Salmon, I. "Weissbecker, C. Ulmer, A. Floyd, K. Hoover, and J. L. Studts, "Mindfulness Meditation Alleviates Depressive Symptoms in Women with Fibromyalgia: Results of a Randomized Clinical Trial," <i>Arthritis and Rheumatism</i> , Vol. 57, 2007, pp. 77–85.	Excluded	Our review required pain outcome. This study reported depressive symptoms.

Reference	Status in Current Report	If Excluded, Reason
Weissbecker, I., P. Salmon, J. L. Studts, A. R. Floyd, E. A. Dedert, and S. E. Sephton, "Mindfulness-Based Stress Reduction and Sense of Coherence Among Women with Fibromyalgia," <i>Journal of Clinical Psychology in Medical Settings</i> , Vol. 9, No. 4, 2002, pp. 297–307.	Excluded	Design was not randomized.
Wong, S. Y., F. W. Chan, R. L. Wong, M. C. Chu, Y. Y. Kitty Lam, S. W. Mercer, and S. H. Ma, "Comparing the Effectiveness of Mindfulness-Based Stress Reduction and Multidisciplinary Intervention Programs for Chronic Pain: A Randomized Comparative Trial," <i>Clinical Journal of Pain</i> , Vol. 27, No. 8, October 2011, pp. 724–734.	Included	
Zautra, A. J., M. C. Davis, J. W. Reich, P. Nicassario, H. Tennen, P. Finan, A. Kratz, B. Parrish, and M. R. Irwin, "Comparison of Cognitive Behavioral and Mindfulness Meditation Interventions on Adaptation to Rheumatoid Arthritis for Patients With and Without History of Recurrent Depression," <i>Journal of Consulting and Clinical Psychology</i> , Vol. 76, No. 3, June 2008, pp. 408–421.	Included	

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