

Draft Comparative Effectiveness Review

Number XX

Meditation Programs for Stress and Well-being

Prepared for:

Agency for Healthcare Research and Quality
U.S. Department of Health and Human Services
540 Gaither Road
Rockville, MD 20850
www.ahrq.gov

Contract No. xxx-xx-xxxx

Prepared by:

<Name> Evidence-based Practice Center
<City, State>

Investigators:

First and Last Names, X.X.
First and Last Names, X.X.

AHRQ Publication No. xx-EHCxxx

<Month Year>

Statement of Funding and Purpose

This report is based on research conducted by an Evidence-based Practice Center (EPC) under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. xxx-xx-xxxx). The findings and conclusions in this document are those of the authors, who are responsible for its contents; the findings and conclusions do not necessarily represent the views of AHRQ. Therefore, no statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

The information in this report is intended to help health care decisionmakers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of health care services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

This report may be used, in whole or in part, as the basis for development of clinical practice guidelines and other quality enhancement tools, or as a basis for reimbursement and coverage policies. AHRQ or U.S. Department of Health and Human Services endorsement of such derivative products may not be stated or implied.

Public Domain Notice

This document is in the public domain and may be used and reprinted without special permission. Citation of the source is appreciated.

Disclaimer Regarding 508-Compliance

Persons using assistive technology may not be able to fully access information in this report. For assistance contact EffectiveHealthCare@ahrq.hhs.gov.

Financial Disclosure Statement

None of the investigators has any affiliations or financial involvement that conflicts with the material presented in this report.

Suggested citation: <Authors>. Meditation Programs for Stress and Well-being. Evidence Report/Technology Assessment. No. <#>. (Prepared by .) Rockville, MD: Agency for Healthcare Research and Quality. <Month, Year>. <http://www.ahrq.gov/clinic/epcix.htm>. Accessed: <Date>. <URL>.

Preface

The Agency for Healthcare Research and Quality (AHRQ) conducts the Effective Health Care Program as part of its mission to organize knowledge and make it available to inform decisions about health care. As part of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Congress directed AHRQ to conduct and support research on the comparative outcomes, clinical effectiveness, and appropriateness of pharmaceuticals, devices, and health care services to meet the needs of Medicare, Medicaid, and the Children's Health Insurance Program (CHIP).

AHRQ has an established network of Evidence-based Practice Centers (EPCs) that produce Evidence Reports/Technology Assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care. The EPCs now lend their expertise to the Effective Health Care Program by conducting comparative effectiveness reviews (CERs) of medications, devices, and other relevant interventions, including strategies for how these items and services can best be organized, managed, and delivered.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews are useful because they define the strengths and limits of the evidence, clarifying whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about systematic reviews, see

<http://www.effectivehealthcare.ahrq.gov/reference/purpose.cfm>

AHRQ expects that CERs will be helpful to health plans, providers, purchasers, government programs, and the health care system as a whole. In addition, AHRQ is committed to presenting information in different formats so that consumers who make decisions about their own and their family's health can benefit from the evidence.

Transparency and stakeholder input from are essential to the Effective Health Care Program. Please visit the Web site (<http://www.effectivehealthcare.ahrq.gov>) to see draft research questions and reports or to join an e-mail list to learn about new program products and opportunities for input. Comparative Effectiveness Reviews will be updated regularly.

We welcome comments on this CER. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by e-mail to epc@ahrq.hhs.gov.

Carolyn M. Clancy, M.D.
Director
Agency for Healthcare Research and Quality

Stephanie Chang, M.D., M.P.H.
Director
Evidence-based Practice Program
Center for Outcomes and Evidence
Agency for Healthcare Research and Quality

Jean Slutsky, P.A., M.S.P.H.
Director, Center for Outcomes and Evidence
Agency for Healthcare Research and Quality

Shilpa H. Amin, M.D., MBsc, FAAFP
Task Order Officer
Center for Outcomes and Evidence
Agency for Healthcare Research and Quality

Acknowledgments

The authors gratefully acknowledge the continuing support of our AHRQ Task Order Officer, Shilpa H. Amin, M.D. We extend our appreciation to our Key Informants and members of our Technical Expert Panel (listed below), all of whom provided thoughtful advice and input during our research process.

The investigators deeply appreciate the considerable support, commitment, and contributions of the EPC team staff at <NAME>. We express our gratitude to the following individuals for their contributions to this project: <NAME, degrees>

Key Informants

<Name>

<Place>

<City>, <ST>

Technical Expert Panel

<Name>

<Place>

<City>, <ST>

<Name>

<Place>

<City>, <ST>

Peer Reviewers

<Name>

<Place>

<City>, <ST>

<Name>

<Place>

<City>, <ST>

Structured Abstract

Objectives: Meditation, a mind-body method, employs a variety of techniques designed to facilitate the mind's capacity to affect bodily function and symptoms. An increasing number of patients are using meditation programs, but the effect of meditation on stress outcomes is unknown. We aimed to determine the comparative effectiveness and safety of mindfulness- and concentration-based meditation programs on stress-related outcomes (e.g., anxiety, depression, stress, distress, well-being, positive mood, quality of life, attention, health-related behaviors affected by stress, pain, and weight).

Data Sources: We searched MEDLINE®, PsycINFO, EMBASE®, PsycArticles, SCOPUS, CINAHL, AMED, and the Cochrane Library in October 2011. We also performed hand searches from the reference lists.

Review Methods: We included randomized controlled trials with an active control that reported on the stress outcomes of interest. Two reviewers independently screened titles to find trials that reported on outcomes and then extracted data on trial characteristics and effect modifiers (amount of training or teacher qualifications). Using a deliberative process, we prioritized scales to measure outcomes of interest. We assessed the risk of bias of the trials, and we graded the strength of evidence using four domains (risk of bias, precision, directness, and consistency). We assessed applicability by using tools adapted from the Agency for Healthcare Research and Quality methods guide. To assess the direction and magnitude of reported effects of the interventions, we calculated the relative difference between groups in how each outcome measure changed from baseline. We conducted meta-analysis using standardized mean differences to obtain aggregate estimates of effects with 95 percent confidence intervals.

Results: After a review of 14,788 citations, we included 34 randomized controlled trials with 2,954 participants. Most trials were short-term but ranged from four weeks to three years in duration. Trials conducted against non-specific active controls provided the most useful evidence of an effect. Among trials using a non-specific active control in a variety of clinical populations, moderate grade evidence indicated that mindfulness-based stress reduction reduced pain severity to a small degree (4 trials, n=341), and low grade evidence indicated that mindfulness meditation programs reduced dimensions of negative affect including anxiety, depressive symptoms, and stress/distress, as well as negative affect overall (9 trials, n=600). Low grade evidence also indicated that mantra meditation programs improved anxiety (6 trials, n=342). We found insufficient strength of evidence for most other outcomes. Only seven trials had a low risk of bias. Limitations include clinical heterogeneity, variability in the types of controls, and heterogeneity of the interventions (e.g., dosing, frequency, duration, technique).

Conclusions: Evidence indicates that meditation programs, mindfulness in particular, reduce negative affect, and may help to reduce pain. We need more research using adequately powered high-quality randomized controlled trials that address the effects of meditation programs on stress and its correlates.

Contents

Executive Summary	ES-1
Introduction	1
Background.....	1
Definition of Meditation.....	1
Current Practice and Prevalence of Use.....	1
Forms of Meditation.....	1
Stress Outcomes.....	2
Evidence to Date.....	2
Clinical and Policy Relevance.....	3
Objective.....	3
Scope and Key Questions.....	3
Framework.....	5
Methods	6
Topic Development.....	6
Search Strategy.....	6
Study Selection.....	6
Data Abstraction and Data Management.....	9
Data Synthesis.....	12
Assessment of Methodological Quality of Individual Studies.....	13
Assessment of Potential Publication Bias.....	14
Strength of the Body of Evidence.....	15
Applicability.....	18
Results	19
Results of the Search.....	19
Description of Type of Trials Retrieved.....	21
Key Question 1. What are the efficacy and harms of meditation programs on negative affect (e.g. anxiety, stress) and positive affect (e.g. well-being) among those with a clinical condition (medical or psychiatric)?.....	34
Key Points and Evidence Grades.....	34
Trial Characteristics.....	36
Population Characteristics.....	37
Intervention Characteristics.....	37
Outcomes.....	38
Key Question 2. What are the efficacy and harms of meditation programs on attention among those with a clinical condition (medical or psychiatric)?.....	91
Key Points and Evidence Grades.....	91
Trial Characteristics.....	92
Population Characteristics.....	92
Intervention Characteristics.....	92
Outcomes.....	92

Key Question 3. What are the efficacy and harms of meditation programs on health-related behaviors affected by stress, specifically substance use, sleep, and eating, among those with a clinical condition (medical or psychiatric)?.....	95
Key Points and Evidence Grades	95
Trial Characteristics	95
Population Characteristics	96
Intervention Characteristics.....	96
Outcomes	97
 Key Question 4. What are the efficacy and harms of meditation programs on pain and weight among those with a clinical condition (medical or psychiatric)?	105
Key Points and Evidence Grades	105
Trial Characteristics	105
Population Characteristics	106
Intervention Characteristics.....	106
Outcomes	107
 Discussion	117
Key Question 1. What are the efficacy and harms of meditation programs on negative affect (e.g. anxiety, stress) and positive affect (e.g. well-being) among those with a clinical condition (medical or psychiatric)?.....	117
Key Question 2. What are the efficacy and harms of meditation programs on attention among those with a clinical condition (medical or psychiatric)?	119
Key Question 3. What are the efficacy and harms of meditation programs on health-related behaviors affected by stress, specifically substance use, sleep, and eating, among those with a clinical condition (medical or psychiatric)?.....	120
Key Question 4. What are the efficacy and harms of meditation programs on pain and weight among those with a clinical condition (medical or psychiatric)?.....	120
Limitations of the Primary Studies	121
Limitations of the Review.....	122
Future Directions	123
Conclusion	124
 References	126
Tables	
Table 1. Study inclusion and exclusion criteria	8
Table 2. Organization of various scales (instruments or measurement tools) for each Key Question.....	10
Table 3. List of major and minor criteria in assessing risk of bias.....	14
Table 4. Characteristics of included trials.....	22
Table 5. Training dose for included trials over duration of training period (numbers are calculated from information provided in trials).....	30
Table 6. Teacher qualifications for included trials	31
Table 7. Risk of bias for included trials	32
Table 8. Grade of trials addressing the efficacy of mindfulness meditation program on anxiety compared with non-specific active controls among various populations	40

Table 9. Grade of trials addressing the efficacy of mantra meditation programs on anxiety compared with non-specific active controls among various populations.	45
Table 10. Grade of trials addressing the efficacy of mindfulness meditation programs on symptoms of depression compared with non-specific active controls among clinical populations.	48
Table 11. Grade of trials addressing the efficacy of mantra meditation program on symptoms of depression compared with Non-specific active controls among clinical populations.....	53
Table 12. Grade of trials assessing the efficacy of mindfulness programs on stress and distress compared with Non-specific active controls among various populations.....	56
Table 13. Grade of trials addressing the efficacy of mantra meditation programs on stress compared with Non-specific active controls among cardiac and HIV patients.....	59
Table 14. Grade of trials addressing the efficacy of mindfulness meditation programs on the mental component of health-related quality of life compared with non-specific active controls among organ transplant/chronic obstructive pulmonary disease patients.....	61
Table 15. Grade of trials addressing the efficacy of mindfulness meditation programs on positive affect compared with non-specific active controls among organ transplant recipients and breast cancer patients.....	66
Table 16. Grade of trials addressing the efficacy of transcendental meditation on positive affect compared with non-specific active controls among cardiac patients.	70
Table 17. Grade of trials addressing the efficacy of mindfulness meditation programs on negative affect compared with non-specific active controls among diverse populations	73
Table 18. Grade of trials addressing the efficacy of mantra meditation programs on negative affect compared with non-specific active controls among diverse populations	75
Table 19. Grade of trials addressing the efficacy of mindfulness meditation programs on anxiety compared with specific active controls among diverse populations	78
Table 20. Grade of trials addressing the efficacy of clinically standardized meditation programs on anxiety compared with progressive muscle relaxation among anxious participants.....	80
Table 21. Grade of trials addressing the efficacy of mindfulness meditation programs on depressive symptoms compared with specific active controls among diverse populations	82
Table 22. Grade of trials addressing the efficacy of clinically standardized meditation programs on depression compared with progressive muscle relaxation among anxious participants.....	84
Table 23. Grade of trials addressing the efficacy of mindfulness meditation programs on distress compared with specific active controls among populations with emotional distress.....	85
Table 24. Grade of trials addressing the efficacy of mindfulness meditation programs on the mental component of health-related quality of life compared with specific active controls among various populations.....	87
Table 25. Grade of trials addressing the efficacy of mindfulness meditation programs on positive affect compared with progressive muscle relaxation or spirituality among patients with worry or mood disorders.....	89
Table 26. Grade of trials addressing the efficacy of meditation programs on measures of attention compared with a non-specific active control among elderly individuals.....	94
Table 27. Grade of trials addressing the efficacy of mindfulness meditation program on sleep quality among various populations compared with a non-specific active control.....	97
Table 28. Grade of trials addressing the efficacy of mindfulness meditation programs on health-related behaviors affected by stress (substance use, sleep, eating) compared with specific active controls in various populations	101

Table 29. Grade of trials addressing the efficacy and harms of mantra meditation programs on alcohol use among heavy alcohol drinkers compared with intensive running program or biofeedback	103
Table 30. Grade of trials addressing the efficacy of mindfulness-based stress reduction on pain severity compared with non-specific active controls among visceral pain, musculoskeletal pain, and organ transplant patients.....	108
Table 31. Grade of trials addressing the efficacy of transcendental meditation on pain severity compared with non-specific active controls among cardiac patients	111
Table 32. Grade of trials addressing the efficacy of mindfulness-based stress reduction on pain severity compared with specific active controls among chronic pain and mood disturbance patients.....	112
Table 33. Grade of trials addressing the efficacy of mindfulness-based stress reduction on weight among breast cancer patients compared with a specific active control	114
Table 34. Grade of trials addressing the efficacy of meditation programs on weight among those with a clinical condition	115

Figures

Figure 1. Analytic framework for meditation programs conducted in clinical and psychiatric populations	5
Figure 2. Algorithm for rating the strength of evidence.....	17
Figure 3. Summary of the literature search	20
Figure 4. Relative difference between groups in the changes in measures of general anxiety, in the mindfulness versus non-specific active control studies	41
Figure 5. Meta-analysis of the effects of meditation programs on anxiety with up to 8 weeks of followup.....	42
Figure 6. Meta-analysis of the effects of meditation programs on anxiety after 3-6 months of followup.....	43
Figure 7. Relative difference between groups in the changes in measures of general anxiety, in the mantra versus non-specific active control/ specific active control studies	46
Figure 8. Relative difference between groups in the changes in measures of depression, in the mindfulness versus non-specific active control studies	49
Figure 9. Meta-analysis of the effects of meditation programs on depression with up to 3 months of followup	50
Figure 10. Meta-analysis of the effects of meditation programs on depression after 3-6 months of followup.....	51
Figure 11. Relative difference between groups in the changes in measures of depression, in the mantra versus non-specific active control / specific active control studies	54
Figure 12. Relative difference between groups in the changes in measures of stress/distress, in the mindfulness versus non-specific active control studies	57
Figure 13. Meta-analysis of the effects of meditation programs on stress/distress with up to 14 weeks of followup.....	58
Figure 14. Relative difference between groups in the changes in measures of stress, in the mantra versus non-specific active control studies.....	60
Figure 15. Relative difference between groups in the changes in measures of negative affect, in the mindfulness versus non-specific active control studies	62
Figure 16. Meta-analysis of the effects of meditation programs on negative affect	63

Figure 17. Relative difference between groups in the changes in measures of negative affect, in the mindfulness versus non-specific active control studies (sensitivity analysis	64
Figure 18. Meta-analysis of the effects of meditation programs on negative affect - sensitivity analysis (Mindfulness meditation versus non-specific active control interventions).....	65
Figure 19. Relative difference between groups in the changes in measures of negative affect, in the mantra versus non-specific active control studies	67
Figure 20. Relative difference between groups in the changes in measures of negative affect, in the mantra versus non-specific active control studies (sensitivity analysis).....	68
Figure 21. Meta-analysis of the effects of mantra meditation programs on negative affect - sensitivity analysis (mantra versus non-specific active control interventions).....	69
Figure 22. Relative difference between groups in the changes in measures of positive affect, in the mindfulness versus non-specific active control / specific active control studies).....	71
Figure 23. Meta-analysis of the effects of meditation programs on positive affect with up to 4 months of followup.....	72
Figure 24. Relative difference between groups in the changes in measures of positive affect, in the mantra versus non-specific active control studies	74
Figure 25. Relative difference between groups in the changes in measures of studies mental component of health-related quality of life, in the mindfulness versus non-specific active control / specific active control studies	76
Figure 26. Relative difference between groups in the changes in measures of general anxiety, in the mindfulness versus specific active control studies	79
Figure 27. Relative difference between groups in the changes in measures of depression, in the mindfulness versus specific active control studies	83
Figure 28. Relative difference between groups in the changes in measures of distress, in the mindfulness versus specific active control studies	86
Figure 29: Meta-analysis of the effects of meditation programs on the mental health component of health-related quality of life with up to 3 months of followup	90
Figure 30. Relative difference between groups in the changes in measures of sleep, in the mindfulness versus non-specific active control studies	98
Figure 31: Meta-analysis of the effects of meditation programs on sleep with up to 3 months of followup.....	99
Figure 32. Relative difference between groups in the changes in measures of sleep/substance use/ eating, in the mindfulness versus specific active control studies	102
Figure 33. Relative difference between groups in the changes in measures of substance use, in the mantra versus specific active control studies.....	104
Figure 34. Relative difference between groups in the changes in measures of pain, in the mindfulness versus non-specific active control studies	109
Figure 35: Meta-analysis of the effects of meditation programs on pain severity with 8 to 10 weeks of followup.....	110
Figure 36. Relative difference between groups in the changes in measures of pain, in the mindfulness versus specific active control studies	113
Figure 37. Relative difference between groups in the changes in measures of weight, in the mindfulness /mantra versus specific active control studies	116

Appendixes

Appendix A. Abbreviations and Acronyms

Appendix B. Search String

Appendix C. Screening and Data Abstraction Forms
Appendix D. Excluded Articles
Appendix E. Evidence Tables

Executive Summary

Background

Definition of Meditation

The National Center for Complementary and Alternative Medicine considers meditation to be a “mind-body” method. This category of complementary and alternative medicine includes interventions that employ a variety of techniques designed to facilitate the mind’s capacity to affect bodily function and symptoms. In meditation, a person learns to focus attention. Some forms of meditation instruct the practitioner to become mindful of thoughts, feelings, and sensations, and to observe them in a nonjudgmental way. This practice is believed to result in a state of greater calmness, physical relaxation, and psychological balance.¹

Current Practice and Prevalence of Use

Many people use meditation to treat stress and stress-related conditions, as well as to promote general health.^{2,3} A national survey in 2008 found that the number of people meditating has been increasing over the years, with approximately ten percent of the population having some experience with meditation.² A number of hospitals and programs offer courses in meditation to patients seeking alternative or additional methods to relieve ailments or to promote health.

Forms of Meditation

Meditation training programs vary in several ways, including the emphasis on religion or spirituality, the type of mental activity promoted, the nature and amount of training, the use of an instructor, and the qualifications of an instructor, which may all affect the level and nature of the meditative skills learned. Some meditative techniques are integrated into a broader alternative approach that includes dietary and/or movement therapies (e.g., Ayurveda or yoga).

Researchers have categorized meditative techniques as emphasizing “mindfulness” or “concentration.” Popular techniques like Transcendental Meditation (TM), which emphasize attentional focus on the repetition of a mantra, are classified as “concentration” focused; whereas other popular techniques, like mindfulness-based stress reduction (MBSR), are classified as “mindfulness” and emphasize training in present-focused awareness. There remains uncertainty about the extent to which these distinctions actually influence outcomes.

Stress Outcomes

Researchers have postulated that meditation programs may affect a range of outcomes related to stress and well-being.⁴ The research ranges from the rare examination of positive outcomes, such as increased well-being, to the more common approach of examining reductions in negative outcomes, such as anxiety or sleep disturbance. Some studies address symptoms related to the primary condition (e.g., pain in patients with low back pain, or anxiety in patients with social phobia) whereas others address similar emotional symptoms in clinical groups who may or may not present with clinically significant symptoms (e.g., anxiety or depression in individuals with cancer).

Evidence to Date

Reviews to date have demonstrated that both “mindfulness” and “concentration” meditation techniques reduce emotional symptoms (e.g., anxiety and depression, stress) and improve physical symptoms (e.g., pain) from a small to moderate degree.^{5-16 17-25} These reviews, have largely included uncontrolled studies, or studies that used control groups that did not receive additional treatment (i.e., usual care or “waiting list”). In wait-list controlled studies, the control group receives usual care while “waiting” to receive the intervention at some time in the future, providing a usual-care control for the purposes of the study. Thus, it is unclear whether the apparently beneficial effects of meditation training are a result of the expectations for improvement that participants naturally form when obtaining this type of treatment. Additionally, many programs involve lengthy and sustained efforts on the part of participants and trainers, possibly yielding beneficial effects from the added attention, group participation, and support participants receive, as well as the suggestion that symptoms are expected to improve with these efforts.^{26 27}

The meditation literature has significant limitations related to inadequate control comparisons. An informative analogy is the use of placebos in pharmaceutical trials. The placebo is typically designed to match to the “active intervention” in order to elicit the same expectations of benefit on the part of both provider and patient, but not contain the “active” ingredient. Additionally, placebo treatment includes all components of care received by the “active” group, including office visits and patient-provider interactions in which the provider engages with the patient in the same way irrespective of which group the patient is randomized to. These nonspecific factors are particularly important to control when the evaluation of outcome relies on patient reporting. In this situation where double blinding is not feasible, the challenge to execute studies that are not biased by these nonspecific factors is more pressing.²⁷ Thus, there is a clear need to examine the specific effects of meditation in randomized trials in which expectations for outcome and attentional support are controlled.

Clinical and Policy Relevance

Much uncertainty exists about the differences and similarities between the effects of different types of meditation.^{28 29} Given the increasing use of meditation across a large number of conditions, it is important for patients, clinicians, and policymakers to understand the effects of meditation, types and duration of meditation, settings and conditions for which meditation is efficacious. While some reviews have focused on randomized controlled trials (RCTs), many, if not most, of the included studies involved wait-list or usual-care controls. Thus, there is a need to examine the specific effects of meditation interventions relative to control conditions in which expectations for outcome and attentional support are controlled.

Objectives

The objectives of this systematic review are to evaluate the effects of meditation programs on affect, attention, and health-related behaviors affected by stress, pain, and weight, among those with a medical or psychiatric condition in randomized controlled trials with appropriate comparators.

Scope and Key Questions

This report reviews the efficacy of meditation programs on stress-related outcomes among those with a clinical condition. Affect refers to emotion or mood. It can be positive, such as the feeling of well-being, or negative, such as anxiousness, depression, or stress. Studies usually measure affect through self-reported questionnaires designed to gauge how much someone experiences a particular affect. Attention refers to our ability to maintain focus on particular stimuli; clinicians measure this directly. Studies measure substance use as the amount consumed or smoked over a period of time, and include alcohol consumption, cigarette smoking, or other drugs such as cocaine. They measure sleep as the amount of time spent sleeping versus awake or as overall sleep quality. Studies measure sleep time through either polysomnography or actigraphy, and sleep quality through self-reported questionnaires. They measure eating using eating diaries to calculate how much energy or fat a person has consumed over a particular period of time. They measure pain, similar to affect, by a self-reported questionnaire to assess how much pain an individual is experiencing. Studies measure pain severity on a numerical rating scale from 0-10 or by using other self-reported questionnaires. The studies measure weight in pounds or kilograms.

The Key Questions (KQs) are as follows.

Key Question 1. What are the efficacy and harms of meditation programs on negative affect (e.g. anxiety, stress) and positive affect (e.g. well-being) among those with a clinical condition (medical or psychiatric)?

Key Question 2. What are the efficacy and harms of meditation programs on attention among those with a clinical condition (medical or psychiatric)?

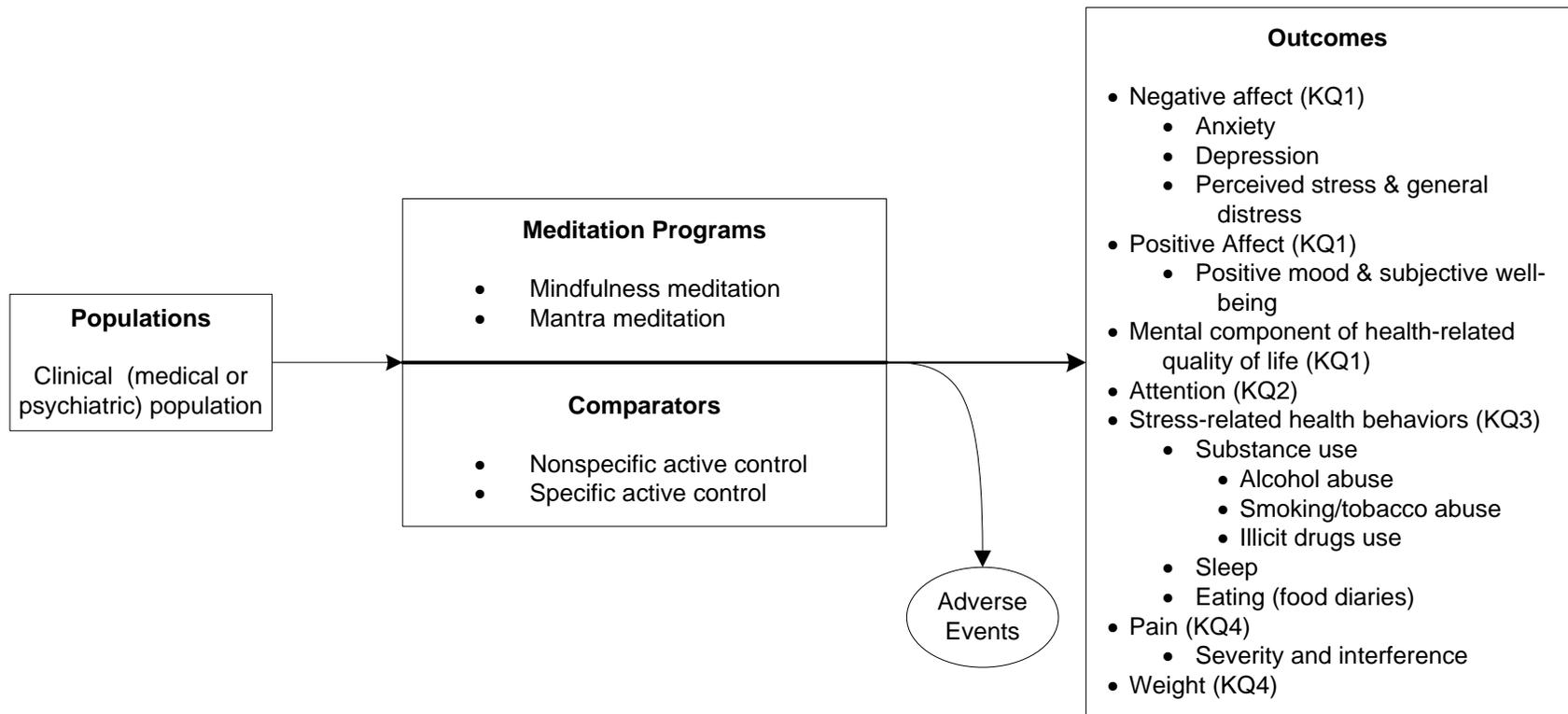
Key Question 3. What are the efficacy and harms of meditation programs on health-related behaviors affected by stress, specifically substance use, sleep, and eating, among those with a clinical condition (medical or psychiatric)?

Key Question 4. What are the efficacy and harms of meditation programs on pain and weight among those with a clinical condition (medical or psychiatric)?

Analytic Framework

Our analytic framework for the systematic review is presented in Figure A. The figure illustrates the populations of interest, the meditation programs, and the outcomes that we reviewed. This figure depicts the key questions within the context of the PICOTS (Population, Intervention, Comparator, Outcomes, Timing, and Setting) framework described in Table A. Adverse events may occur at any point after the meditation program.

Figure A. Analytic framework for meditation programs conducted in clinical and psychiatric populations



Methods

Literature Search Strategy

We searched the following databases for primary studies: MEDLINE®, PsycINFO, EMBASE®, PsycArticles, SCOPUS, CINAHL, AMED, and the Cochrane Library through October 11, 2011. We developed a search strategy for MEDLINE, accessed via PubMed®, based on medical subject headings (MeSH®) terms and text words of key articles that we identified a priori. We used a similar strategy in the other electronic sources. We reviewed the reference lists of included articles, relevant review articles, and related systematic reviews (n=20) to identify articles that the database searches might have missed. We did not impose any limits based on language or date of publication. We will conduct updated searches during peer review of the draft report.

Study Selection

Two investigators screened title and abstracts independently and excluded them if both investigators agreed that the article met one or more of the exclusion criteria. (Table A) We resolved differences between investigators regarding abstract eligibility through consensus.

We independently screened citations promoted on the basis of title and abstract using the full-text article. We resolved differences regarding article inclusion through consensus. Paired investigators conducted an additional independent review of full-text articles to determine inclusion or exclusion from the full-data abstraction.

We included RCTs in which the control group was matched in time and attention to the intervention group for the purpose of matching expectations of benefit. The inclusion of such trials allowed us to evaluate the specific effects of meditation programs separate from the non-specific effects of attention and expectation. Our team thought this was the most rigorous way to determine the efficacy of the interventions. We did not include observational studies because they are likely to have an extremely high risk of bias due to problems such as self-selection of interventions (people who believe in the benefits of meditation or who have prior experience with meditation are more likely to enroll in a meditation program) and use of outcome measures that can be easily biased by participants' beliefs in the benefits of meditation.

For inclusion in this review, we required that studies reported on participants with a clinical condition such as medical or psychiatric populations. Although meditation programs may have an impact on healthy populations, we limited our evaluation of these meditation programs to clinical populations. Since trials study meditation programs in diverse populations, we have defined a clinical condition broadly, to include mental health/psychiatric conditions (e.g., anxiety or stress) and physical conditions (e.g., low back pain, heart disease, or advanced age). Additionally, since stress was of particular interest in meditation studies, we also included trials that studied stressed populations even though they may not have a defined medical or psychiatric diagnosis. We excluded studies among otherwise healthy populations.

Table A. Study inclusion and exclusion criteria

	Inclusion	Exclusion
Population and Condition of Interest	<ul style="list-style-type: none"> • Adult populations (18 years or older) • Clinical (medical or psychiatric) diagnosis, defined as any condition (e.g. high blood pressure, anxiety) including a stressor. 	<ul style="list-style-type: none"> • Studies of children. The type and nature of meditation children receive is significantly different from adults. • Studies of otherwise healthy individuals
Interventions	<p>Structured meditation programs (any systematic or protocolized meditation programs that follow predetermined curricula) consisting of, at a minimum, at least 4 hours of training with instructions to practice outside the training session.</p> <p>These include: Mindfulness-based:</p> <ul style="list-style-type: none"> • MBSR • MBCT • Vipassana • Zen • Other mindfulness meditation <p>Mantra-based:</p> <ul style="list-style-type: none"> • Transcendental Meditation • Other mantra meditation <p>Other meditation</p>	<p>Meditation programs in which the meditation is not the foundation and majority of the intervention. These include:</p> <ul style="list-style-type: none"> • Dialectical Behavioral Therapy (DBT) • Acceptance and Commitment Therapy (ACT). • Any of the movement-based meditations such as Yoga (e.g. Iyengar, Hatha, Shavasana), Tai chi, and Qi gong (Chi kung) • Aromatherapy • Biofeedback • Neurofeedback • Hypnosis • Autogenic training • Psychotherapy • Laughter therapy • Therapeutic touch • Eye movement desensitization reprocessing • Relaxation therapy • Spiritual therapy • Breathing exercise, Pranayama • Exercise • Any intervention that is given remotely, or only by video or audio to an individual without the involvement of a meditation teacher physically present
Comparisons of Interest	<p>Active control, defined as a program that is matched in time and attention to the intervention group for the purpose of matching expectations of benefit. Examples include “attention control,” “educational control,” or another therapy, such as progressive muscle relaxation, that the study compares to the intervention.</p> <ul style="list-style-type: none"> • A non-specific active control only matches time and attention, and is not a known therapy. • A specific active control compares the intervention to another known therapy, such as progressive muscle relaxation. 	<p>Studies that only evaluate a wait-list/usual-care control or do not include a comparison group</p>
Outcomes	See Figure A	
Study Design	Randomized controlled trials with an active control	Non-randomized designs, such as observational studies.
Timing and Setting	Longitudinal studies that occur in general and clinical settings	

MBSR = Mindfulness-based Stress Reduction; MBCT = Mindfulness-based Cognitive Therapy; TM = Transcendental Meditation; KQ = Key Question; DBT = Dialectical Behavioral Therapy; ACT = Acceptance and Commitment Therapy
 We excluded articles with no original data (reviews, editorials, and comments), studies published in abstract form only, and dissertations.

Data Abstraction and Data Management

We used DistillerSR (Evidence Partners, 2010) to manage the screening process. DistillerSR is a Web-based database management program that manages all levels of the review process. We uploaded to the system all citations identified by our search.

We created standardized forms for data extraction, and pilot tested the forms prior to data extraction. Reviewers extracted information on general study characteristics, study participants, eligibility criteria, interventions, and the outcomes. Two investigators reviewed each article for data abstraction. For study characteristics, participant characteristics, and intervention characteristics, the second reviewer confirmed the first reviewer's data abstraction for completeness and accuracy. For outcome data and risk of bias scoring, we used dual and independent review. Reviewer pairs included personnel with both clinical and methodological expertise. We resolved differences between investigators regarding data through consensus.

For each meditation program we extracted information on measures of intervention fidelity including dose, training, and receipt of intervention. We measured duration and maximal hours of structured training in meditation, amount of home practice recommended, description of instructor qualifications, and description of participant compliance, if any.

Data Synthesis

For each key question, we created a detailed set of evidence tables containing all information abstracted from eligible studies.

To display the outcome data, we calculated relative difference in change scores (i.e., the change from baseline in an outcome measure in the treatment group minus the change from baseline in the outcome measure in the control group, divided by the baseline score in the treatment group). However, many studies did not report enough information to calculate confidence intervals for the relative difference in change scores. When we evaluated point estimates and confidence intervals for just the post-intervention or end-of-study differences between groups, and compared these to the point estimates for the relative difference in change scores for those time points, some of the estimates that did not account for baseline differences appeared to favor a different group (i.e., treatment or control) when compared with the estimates that did account for baseline differences. We therefore used the relative difference in change scores to estimate the direction and approximate magnitude of effect for all outcomes. For the purpose of generating an aggregate quantitative estimate of the effect of an intervention and the associated 95 percent confidence interval, we performed meta-analysis using standardized mean differences (effect sizes) calculated by Cohen's method (Cohen's *d*). These were used to also assess precision of individual studies, which was factored into the overall strength of evidence. For each outcome, we displayed the resulting effect size estimate according to the type of control group and duration of followup. Some studies did not report enough information to be included in meta-analysis. For that reason, we decided to display the relative difference in change scores along with the effect size estimates from meta-analysis so that readers can see the full extent of the available data.

We considered a five percent relative difference in change score to be potentially clinically significant. In synthesizing the results of these trials, we considered both statistical and clinical significance. Statistical significance is according to study-specific criteria, for which we reported *p*-values and confidence intervals where present.

Assessment of Methodological Quality of Individual Trials

We assessed the risk of bias in studies independently and in duplicate based on the recommendations in the EPC Methods Guide.³⁰ We supplemented these tools with additional assessment questions based on the Cochrane Collaboration’s Risk of Bias Tool.^{31 32} While many of the tools to evaluate risk of bias are common to behavioral as well as pharmacologic interventions, some items are more specific to behavioral interventions. After discussion with experts in meditation programs and clinical trials, we emphasized four major and four minor criteria. We assigned 2 points each to the major criteria, weighting them more in assessing risk of bias. We assigned 1 point each to the minor criteria. Studies could therefore receive a total of 12 points. If studies met a minimum of three major criteria and three minor criteria (9-12 points), we classified it as having “low risk of bias.” Studies receiving 6-8 points were classified as having “medium risk of bias,” and studies receiving 5 or less points were classified as having “high risk of bias.” (Table B)

Table B. List of major and minor criteria in assessing risk of bias

Major Criteria*	Minor Criteria*
<ul style="list-style-type: none"> • Was the control matched for time and attention by the instructors? • Was there a description of withdrawals and dropouts? • Was attrition < 20% at the end of treatment? As several studies did not calculate attrition starting from the original number randomized, we recalculated the attrition from the original number randomized. • Were those who collected data on the participants blind to the allocation? 	<ul style="list-style-type: none"> • Was the method of randomization described in the paper? To answer “yes” for this question, the trials had to give some description of the randomization procedure. • Was allocation concealed? • Was intent-to-treat analysis used? To answer “yes” for this question, the trial must impute non completer or other missing data, and it must do this from the original number randomized. • Did the trial evaluate the credibility, and if so, was it comparable? If the trial did not evaluate credibility, or if it evaluated credibility but did not find it comparable, then we did not give the trial a point.

*We assigned 2 points each to the major criteria, weighting them more in assessing risk of bias, and 1 point each to the minor criteria.

Assessment of Potential Publication Bias

We planned to use funnel plots to assess potential publication bias if numerous studies reported on an outcome of interest. We also searched for any trials that completed recruitment 3 or more years ago that did not publish results, or that listed outcomes for which they did not report results.

Strength of the Body of Evidence

Two reviewers graded the strength of evidence for each outcome for each of the key questions using the grading scheme recommended by the Methods Guide for Conducting Comparative Effectiveness Reviews. In assigning evidence grades, we considered four domains: risk of bias of included studies; directness, consistency, and precision (Figure B). We classified evidence into four basic categories: 1) “High” grade (indicating high confidence that the

evidence reflects the true effect, and further research is very unlikely to change our confidence in the estimate of the effect); 2) “Moderate” grade (indicating moderate confidence that the evidence reflects the true effect, and further research may change our confidence in the estimate of the effect and may change the estimate); 3) “Low” grade (indicating low confidence that the evidence reflects the true effect, and further research is likely to change our confidence in the estimate of the effect and is likely to change the estimate); and 4) “Insufficient” grade (evidence is unavailable or inadequate to draw a higher grade).

Applicability

We assessed applicability separately for the different outcomes of benefit and harm for the entire body of evidence guided by the PICOTS (Population, Intervention, Comparator, Outcomes, Timing, and Setting) framework as recommended in the EPC Methods Guide.³⁰ We assessed whether findings were applicable to various ethnic groups, or whether race, ethnicity, or education limited the applicability of the evidence.

Results

Results of the Search Results

The literature search identified 14,788 unique citations. During the title and abstract screening, we excluded 13,282 citations. During the article screening, we excluded 1,352 citations. During Key Question applicability screening, we excluded an additional 121 articles that did not meet one or more of the inclusion criteria. We included 34 articles in the review.

Most trials were short-term but ranged from 4 weeks to 3 years in duration. Since the amount of training and practice in any meditation program may affect its results, we collected this information and found a fair range in the quality of information. Not all trials reported on amount of training and home practice recommended. Mindfulness-based stress reduction programs typically provided 20-27.5 hours of training over 8 weeks. The mindfulness meditation trials typically provided about half this amount. Transcendental meditation trials provided 16-39 hours over 3-12 months, while other mantra meditation program provided about half this amount. Only four of the trials reported the trainers' actual meditation experience (ranging between 4 months-25 years) and five reported the trainers' actual teaching experience (ranging between 0-7 years).

Results

The strength of evidence on the outcomes of our review is shown in figures C and D. Since there were numerous scales for the different measures of affect, as well as subgroups within each affect, the scales reported upon were organized to best represent the clinically relevant aspects of each affect. For this review, the comparisons with non-specific active controls allowed a consistent comparison with a similar control group across all outcomes. Comparisons with specific active controls were difficult to draw conclusions from due to the large heterogeneity of type and strength of control groups. Therefore, our results are presented first for all the comparisons with non-specific active controls, and then for the specific active controls.

The figures C1 and C2 show results for all outcomes, separated by type of control (non-specific or specific). The direction and magnitude was determined by the relative difference between groups in the change score. When compared with a non-specific active control, mindfulness meditation programs had low strength of evidence to improve any dimension of negative affect, ranging from a 1% to 21% improvement. A meta-analysis showed an effect size of 0.39 (0.06 to 0.71) favoring mindfulness. A sensitivity analysis corroborated these findings. Mantra meditation programs had low strength of evidence to improve anxiety with a range of -3% to +16% improvement and an effect size of 0.27 (0.02 to 0.52). Mindfulness had moderate strength of evidence to improve pain, ranging from 5% to 31% improvement and an overall effect size of 0.27 (0.02 to 0.51) favoring mindfulness. One trial among women with irritable bowel syndrome had a large statistically significant improvement in visceral pain while three other trials had small nonsignificant improvements for musculoskeletal pain. The strength of evidence was insufficient for most other outcomes. The evidence also was insufficient to support that any meditation program was superior to a specific active control for any outcome.

Harm Outcomes for all Key Questions

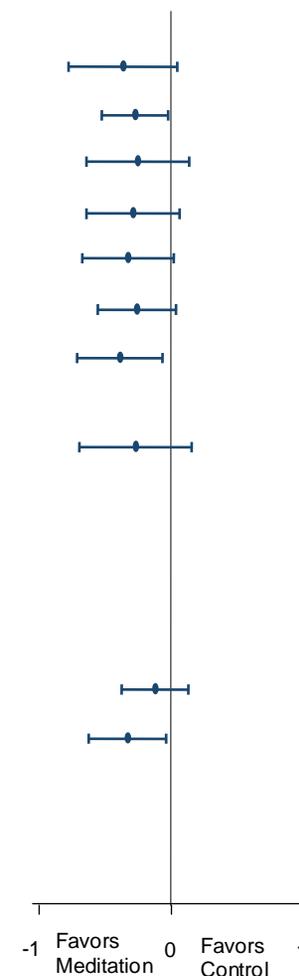
Few trials reported on potential harms of meditation programs. Of the nine trials that reported on harms, none reported any harms of the intervention. One trial specified that they looked for toxicities of meditation to hematologic, renal, and liver markers and found none. The remaining eight trials did not specify the type of adverse event they were looking for. Seven reported that no significant adverse events were found while one did not comment on adverse events. The remaining 25 trials did not report whether they monitored for adverse events.

Assessment of Potential Publication Bias

We could not conduct any reliable quantitative tests for publication bias since few studies were available for most outcomes, and we were unable to include all eligible studies in the meta-analysis due to missing data. Consequently, funnel plots were unlikely to provide much useful information regarding the possibility of publication bias. Our review of clinicaltrials.gov registration database did not provide sufficient information on the scales trials used to measure outcomes, or on the types of controls they used. This did not allow us to verify whether a potentially applicable outcome could have been included in our review. While examining for selective outcome reporting, we found only one trial that selectively reported on positive outcomes.⁴⁵ Among 101 outcomes in 34 trials, trials did not give enough information to calculate a relative difference in the change score (our primary analysis) for seven outcomes due to statistically insignificant findings. These are represented as solid grey boxes in the figures. Trials did not give enough information to conduct a meta-analysis on thirty outcomes. Our findings from the primary analysis are therefore less likely to be affected by publication bias than the meta-analysis.

Figure C1: Summary across measurement domains of comparisons of meditation with non-specific active controls

Outcome	Meditation Program	Population	Direction ¹ (Magnitude ²) of effect	No. of trials Total: PA (MA) ³ , total N	SOE ⁴
Anxiety (KQ1)	Mindfulness	Various	↑ (+4% to +15%)	6: 4 (4), N=494	Low for ↑
	Mantra	Various	↑↓ (-3% to +16%)	5: 4 (4), N=342	Low for ↑
Depression (KQ1)	Mindfulness	Various	↑ (0% to +49%)	7: 6 (5), N=518	Low for ↑
	Mantra	Various	↑↓ (-19% to +46%)	5: 4 (2), N=328	Insufficient
Stress/distress (KQ1)	Mindfulness	Various	↑ (+1% to +21%)	5: 4 (3), N=200	Low for ↑
	Mantra	Select	∅ (-6% to +1%)	3: 3 (2), N=219	Low for ∅
Negative affect (KQ1)	Mindfulness	Various	↑ (+1% to +21%)	9: 7 (6), N=600	Low for ↑
	Mantra	Various	↑↓ (-3% to +46%)	6: 5 (0)*, N=369	Insufficient
Positive affect (KQ1)	Mindfulness	Select	↑↓ (+1% to +7%)	2: 2 (2), N=237	Insufficient
	TM (Mantra)	CHF	∅ (+2%)	1: 1 (0), N=23	Insufficient
Quality of Life (KQ1)	Mindfulness	Select	↑ (+5% to +8%)	2: 2 (0), N=186	Insufficient
Attention (KQ2)	Mindfulness	Caregivers	↑ (+15% to +81%)	1: 1 (0), N=21	Insufficient
	TM (Mantra)	Elderly	↑ (20%)	1: 1 (0), N=62	Insufficient
Sleep (KQ3)	Mindfulness	Various	↑↓ (-3% to +24%)	3: 3 (3), N=265	Insufficient
Pain (KQ4)	Mindfulness	Select	↑ (+5% to +31%)	4: 4 (4), N=341	Moderate for ↑
	TM (Mantra)	CHF	∅ (-2%)	1: 1 (0), N=23	Low for ∅
Weight (KQ4)	Mindfulness	Breast CA	∅ (-2%)	1: 1 (0), N=99	Insufficient
	TM (Mantra)	Select	∅ (-2% to +1%)	2: 2 (0), N=114	Insufficient

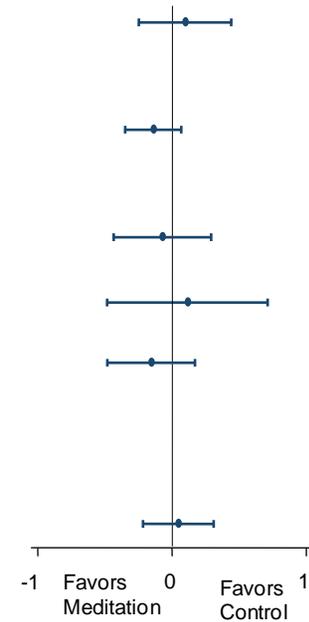


SOE = Strength of Evidence; PA = Primary Analysis; MA = Meta-analysis; CSM = Clinically Standardized Meditation, a mantra meditation program; TM=Transcendental Meditation, a mantra meditation program; CHF = Congestive Heart Failure; CA = Cancer
 Meta-analysis figure shows Cohen's d with the 95% CI

* Meta-analysis on this outcome was not performed since it would duplicate the anxiety meta-analysis for mantra. Only one additional trial could be added (on depression) but did not have usable data that could be added to the anxiety meta-analysis. Anxiety and depression are indirect measures of negative affect, and therefore resulted in a lower strength of evidence than for the outcome of mantra on anxiety.

Figure C2. Summary across measurement domains of comparisons of meditation with specific active controls

Outcome	Meditation Program	Population	Direction ¹ (Magnitude ²) of effect	No. of trials Total: PA (MA) ³ , total N	SOE ⁴
Anxiety (KQ1)	Mindfulness	Various	↑↓ (-39% to +8%)	7: 7 (6), N=372	Insufficient
	CSM (mantra)	Anxiety	↓ (-6%)	1: 1 (0), N=42	Insufficient
Depression (KQ1)	Mindfulness	Various	↑↓ (-32% to +15%)	9: 9 (7), N=579	Insufficient
	CSM (mantra)	Anxiety	↓ (-28%)	1: 1 (0), N=42	Insufficient
Stress/distress (KQ1)	Mindfulness	emotional distress	↓ (-5% to -24%)	3: 3 (3), N=168	Low for ↓
Positive affect (KQ1)	Mindfulness	Select	↑↓ (-45% to 0%)	2: 2 (2), N=142	Insufficient
Quality of Life (KQ1)	Mindfulness	Various	↑↓ (-23% to +9%)	5: 5 (4), N=374	Insufficient
KQ3: all 3 behaviors	Mindfulness	Various	↑↓ (-6% to +21%)	4: 3 (0), N=228	Insufficient
KQ3: alcohol only	Mantra	Alcoholic	↓ (-5% to -36%)	2: 2 (0), N=145	Low for ↓
Pain (KQ4)	Mindfulness	Select	∅ (-1% to -6%)	3: 3 (3), N=234	Low for ∅



SOE = Strength of Evidence; PA = Primary Analysis; MA = Meta-analysis; CSM = Clinically Standardized Meditation, a mantra meditation program; CHF = Congestive Heart Failure; CA = Cancer

Meta-analysis figure shows Cohen's d with the 95% CI

Legend for figure C

The figure on the far-right shows the effect size estimates using Cohen's d (in standard deviation units with the associated 95 percent confidence interval) whenever sufficient data were available to perform a meta-analysis. For comparisons with non-specific active control (NSAC), all eligible studies were included in the analysis for the outcomes of pain, sleep, and positive affect. For comparisons with specific active control (SAC), all eligible studies were included in the analysis for the outcome of stress/distress and pain. For all other meta-analyses, only a subset of eligible studies was included because data was missing in some studies. The meta-analysis results should be interpreted with caution because the inconsistent reporting of data suggests possible reporting bias.

- 1. Direction:** direction of change in the outcome across trials, based on the relative difference between groups in how the outcome measure changed from baseline in each trial. This is calculated as the difference between the change over time in the meditation group and the change over time in the control group, divided by the baseline mean for the meditation group.
 - ↑ indicates that the meditation group improved relative to the control group (with a relative difference generally greater than or equal to 5% across trials).
 - ↓ indicates the meditation group worsened relative to the control group (with a relative difference generally greater than or equal to 5% across trials).
 - ∅ indicates a null effect (with a relative difference generally less than 5% across trials).
 - ↑↓ inconsistent findings (some trials reported improvement with meditation (relative to control) while others showed no improvement or improvement in the control group (relative to meditation)).
- 2. Magnitude:** range of estimates across all trials in a particular domain based on the relative difference between groups in how the outcome measure changed from baseline in each trial. This is a relative percentage difference calculated as: $\frac{(\text{Meditation T2} - \text{Meditation T1}) - (\text{Control T2} - \text{Control T1})}{(\text{Meditation T1})}$ where T1 = baseline mean and T2 = followup mean (after intervention or at the end of the study). This is a simple range of estimates, not a meta-analysis.
- 3. Total number:** the number of trials that measured this outcome; **PA** – the primary analysis (PA) - refers to the number of trials which reported information allowing calculation of the relative difference between groups in the change score; **MA** – refers to the number of trials reporting sufficient information to be included in a meta-analysis. **N** refers to the total sample size.
- 4. Strength of evidence (SOE):** based on aggregate risk of bias, consistency across studies, directness of measures, and precision of estimates. SOE rating is given for the direction of effect in most cases. In some cases, such as mantra meditation programs for anxiety, although the relative differences between groups in the change scores showed inconsistency in findings, the meta-analysis gave a precise estimate favoring one direction.

Discussion

Thirty-four randomized controlled trials (RCTs) assessed the effects of different types of meditation programs. Our review reports one finding with a moderate strength of evidence, a number of findings with low strength of evidence, and the majority of findings with insufficient evidence. Mindfulness meditation programs had low strength of evidence that they improved negative affect, including anxiety, depression, and perceived stress/general distress. The directionality of the findings were fairly consistent across these domains, although the magnitude of the effect tended to be small, on the order of 5% to 10% in the relative difference in change scores. However, two trials showed much larger effects on depressive symptoms, on the order of 25% to 50%, and it is unclear whether these may be representative of a stronger effect in certain populations. One trial was conducted in organ transplant recipients and the other in breast cancer patients. In most trials, the magnitude of effect was much smaller for depression outcomes, but none of those trials were conducted in depressed populations.

While the mindfulness trials that used a specific active control showed significant inconsistency in results, there were two trials of mindfulness-based cognitive therapy conducted among patients in full or partial remission from a major depressive episode that showed improvements in depressive symptoms and relapse rates. These two trials^{46,47} used a clinically important outcome of relapse rate among a depression population, compared mindfulness-based cognitive therapy with tapering of antidepressant medication with maintenance antidepressant medication, and found consistent 8% to 13% absolute reductions in relapse rates. Both trials were rated as having low risk of bias. These findings warrant further investigation, and are generally consistent with prior reviews.

Mantra meditation programs had low strength of evidence that it improved anxiety, insufficient evidence about its effect on depressive symptoms, and low strength of evidence that it did not affect perceived stress. In general, there was inconsistency in the effects of mantra programs on subdomains of negative affect and for negative affect as a whole.

The strength of evidence was insufficient to suggest any effect on positive affect for mindfulness meditation program or mantra meditation program. However, these conclusions were limited by a paucity of studies reporting on this outcome. Some of the differences may also be due to the type of populations studied, whether they had high levels of a particular dimension of negative affect to begin with, length of follow up, and amount of training.

Surprisingly, very few trials reported on perceived stress. We found low strength of evidence that mindfulness meditation program resulted in small improvements in stress and distress when compared with non-specific active controls. Among three mantra trials, two were low risk of bias Transcendental meditation trials among cardiac patients. The effects for all three trials were consistently null. Although it would appear that mantra meditation program do not have an effect on stress, it is unclear if cardiac patients have the level of stress that can be affected by these programs.

Well-being and positive mood are positive dimensions of mental health. Meditation programs seek not only to reduce negative symptomatology, but also to improve the positive dimensions of health. The available evidence did not show any effects on these dimensions, but very few studies reported on positive outcomes. Mindfulness meditation programs similarly did not affect the overall mental component of health-related quality of life. However, very few trials addressed this outcome.

Two randomized controlled trials compared meditation programs with active controls on the outcome of attention. Although there were trends suggesting that meditation programs performed better than non-specific active controls, there were no statistically significant differences between groups on any components of the two measures of attention included in the trials (the Attentional Network Test and the Stroop Color Word Interference Test). These findings indicate the need for more comprehensive trials with a variety of clinical populations (e.g., disorders where attention may be compromised) to provide a clearer understanding of the impact of meditation programs on attention.

Among the nine trials evaluating the effects of meditation programs on health-related behaviors affected by stress, four trials evaluated the effect of meditation on substance use,³³⁻³⁸ one trial evaluated the effect on eating,³⁹ and four trials evaluated the effect on sleep disorders.⁴⁰⁻⁴³ Overall, the evidence was insufficient to draw any conclusion about whether meditation programs alter health-related behaviors affected by stress. The four trials evaluating substance use were all conducted in substance using populations. One trial of mindfulness-based stress reduction among breast cancer patients failed to show an effect on reducing calorie consumption.³⁹ Among the four trials in which sleep was an outcome, one used an insomnia population⁴⁰, and failed to provide evidence of an effect on sleep time or quality. Three other trials, which assessed sleep as a secondary outcome among various clinical populations, had inconsistent results on sleep quality. Our findings are consistent with systematic reviews in this area, in which uncontrolled studies have usually found a benefit while very few controlled studies have not found a benefit for the effects of meditation programs on health-related behaviors affected by stress.¹⁵⁻¹⁷

Among the 11 randomized controlled trials evaluating the effect on pain and weight, we found moderate strength of evidence that mindfulness-based stress reduction reduces pain severity to a small degree when compared with a non-specific active control. This is based on four trials, of which two were conducted in musculoskeletal pain patients, one in patients with irritable bowel syndrome, and one in a non-pain population. Visceral pain had a large and statistically significant relative 30% improvement in pain severity, while musculoskeletal pain showed 5% to 8% improvements that were considered nonsignificant. We also found low strength of evidence that when mindfulness-based stress reduction was compared with various specific active controls including massage, mindfulness-based stress reduction was not superior in reducing pain severity. Very few trials evaluated weight as an outcome, and it was not a primary outcome for any. The evidence was insufficient to determine whether transcendental meditation or mindfulness-based stress reduction have an effect on weight.

The comparative effectiveness of an intervention obviously depends heavily on what is done for the comparison group. A strength of our review is our focus on randomized trials with non-specific active controls, which despite the low strength of evidence should give us greater confidence that the reported benefits are not due to having a flawed comparison group.

Limitations of the Primary Studies

Although we collected information on amount of training, the trials did not provide enough information to make use of that data. We could not draw definitive conclusions about effect modifiers (such as dose and duration) because of the limited amount of data.

It may be that specific outcome measurement scales may be more relevant for a particular form of meditation. In many cases, only certain measures were assessed and the scales may have been limited in their ability to detect an effect.

We intended to evaluate the effects of meditation programs on a broad range of medical and psychiatric conditions since stress outcomes are not limited to any particular medical or psychiatric condition. Despite our focus on active randomized controlled trials, we were unable to detect a specific effect of meditation on most outcomes, with the majority of our evidence grades being insufficient or low. This was mostly driven by two important evaluation criteria: the risk of bias and the inconsistencies in the body of evidence. The reasons for such inconsistencies may have included the differences in the particular clinical conditions, as well as the type of control groups used. When a study compared a meditation program with a specific active control, we could not easily compare these trials with those that used a non-specific active control. We therefore separated these comparisons to be able to evaluate the effects against a relatively homogenous nonspecific active control group. Comparing trials that used one specific active control to another specific active control in general led to large inconsistencies that could be explained by differences in the control groups.

Another possibility is that there was no real effect of the programs on many of the outcomes that had inconsistent findings. While some of the outcomes were primary outcomes, many were secondary outcomes and the studies may not have been appropriately powered to detect changes in these domains.

Limitations of the Review

Our assessment of a five percent relative difference between groups in change scores as being potentially clinically significant needs to be interpreted in the context of heterogeneous scales reporting on various measures. The literature does not clearly define the appropriate threshold for what is clinically significant on these scales. Some may consider a higher or lower threshold as being relevant.

While this review sought to assess the effectiveness of meditation programs above and beyond the nonspecific effects of expectation and attention, it did not assess the preferences of patients. For many patients, even though one therapy may not be better than another, they may still prefer it for personal or philosophical reasons.

We were limited in our ability to determine the overall applicability of the body of evidence to the broad population of patients that could benefit from mindfulness meditation because the studies varied so much in many ways other than just the specific targeted population (i.e., varied in characteristics of the intervention, comparator, outcomes, timing, and setting). Also, the studies generally did not provide enough information to be able to determine whether the effectiveness of mindfulness meditation varied by race, ethnicity, or education.

Future Directions

Further research in meditation would benefit from several considerations. First, since meditation is a skill, more training with an expert and more practice in daily life should lead to greater competency in the skill, which should lead to better outcomes. When compared with other skills that require training, the amount of training afforded in the current paradigm is quite low. Researchers should consider placing greater emphasis on developing the skills of meditation. To facilitate this, better measurement tools are needed. The currently available mindfulness scales have not been well validated and do not appear to distinguish different forms of meditation. Thus, further work on the operationalization and measurement of the particular meditative skill is needed.

Second, trials should document the amount of training instructors provide and patients receive, along with the amount of home practice patients complete. This gives an indication of how effective the program is at delivering training and how adherent participants were.

Third, studies should place emphasis on teacher qualifications. The range of experience in meditation and competence as a teacher of this skill likely plays a role in outcomes.

Fourth, when using a specific active control, if one finds no statistically significant superiority over the control, one is left with the issue of whether the meditation is equivalent to or not inferior to the control, or whether the trial was just underpowered to detect any difference. Conducting comparative effectiveness trials require prior specification of the hypothesis (superiority, equivalence, non-inferiority), and appropriate determination of the margins of clinical significance and minimum importance difference.⁴⁴ In the case of equivalence and non-inferiority trials, trials also need to have appropriate sensitivity. None of the trials showed statistically significant effects against a specific active control, nor did they appear adequately powered to assess non-inferiority or equivalence. This leaves a lot of uncertainty in such trial designs.

Fifth, positive outcomes are a key focus of meditative practices. However, positive outcomes were not included as primary or even secondary outcomes for most trials. Future studies should expand upon these domains.

Future trials should appropriately report key design characteristics to enable the assessment of risk of bias. Future trials should register the trial on a national register, standardize training using trainers who meet specified criteria, specify primary and secondary outcomes *a priori*, power the trial based on the primary outcomes, use CONSORT (CONsolidated Standards of Reporting Trials) recommendations for reporting results, and operationalize and measure the practice of meditation by study participants.

Conclusions

Our review found moderate strength of evidence that mindfulness meditation programs are beneficial for reducing pain severity, and low strength of evidence that meditation programs may lead to improvement in dimensions of negative affect, including anxiety, depression, and perceived stress/general distress. Otherwise, much of the evidence was insufficient to address the comparisons for most of the questions.

Given the large number of outcomes for which the evidence was insufficient, we believe there are a number of reasons for this general lack of evidence. First, while we sought to review the highest standards of behavioral randomized controlled trials, there was wide variation in risk of bias among these trials. Second, we found a limited number of trials for most outcomes, resulting in limited data available for meta-analysis or descriptive synthesis. Third, the reasons for a lack of a significant reduction of stress-related outcomes may be related to the way the research community conceptualizes meditation programs, the difficulties of acquiring such skills, and the limited duration of randomized controlled trials. Historically, the general public did not conceptualize meditation as a quick fix toward anything. It was a skill one learns and practices over time to increase one's awareness, and through this awareness gain insight and understanding into the various subtleties of existence. Trials of short duration and training may be insufficient to develop the skills necessary to affect stress outcomes.

Reference List

1. The National Center for Complementary and Alternative Medicine (NCCAM). Available at: <http://nccam.nih.gov/>
2. Barnes PM, Bloom B, Nahin RL. Complementary and alternative medicine use among adults and children: United States, 2007. *Natl Health Stat Report* 2008; (12):1-23.
3. Goyal M, Haythornthwaite J, Levine D *et al*. Intensive meditation for refractory pain and symptoms. *J Altern Complement Med* 2010; 16(6):627-31.
4. Patient Reported Outcomes Measurement Information System (PROMIS[®]). Available at: <http://www.nihpromis.org/>. Accessed August 10, 2011. [Web Page].
5. Bohlmeijer E, Prenger R, Taal E, Cuijpers P. The effects of mindfulness-based stress reduction therapy on mental health of adults with a chronic medical disease: a meta-analysis. *J Psychosom Res* 2010; 68(6):539-44.
6. Chambers R GEANB. Mindful emotion regulation: An integrative review. *Clin Psychol Rev* 2009; 29(6):560-72.
7. Chiesa A, Serretti A. Mindfulness-based stress reduction for stress management in healthy people: a review and meta-analysis. *J Altern Complement Med* 2009; 15(5):593-600.
8. Chiesa A, Calati R, Serretti A. Does mindfulness training improve cognitive abilities? A systematic review of neuropsychological findings. *Clin Psychol Rev* 2011; 31(3):449-64.
9. Chiesa A, Serretti A. Mindfulness based cognitive therapy for psychiatric disorders: a systematic review and meta-analysis. *Psychiatry Res* 2011; 187(3):441-53.
10. Hofmann SG, Sawyer AT, Witt AA, Oh D.. The effect of mindfulness-based therapy on anxiety and depression: A meta-analytic review. *J Consult Clin Psychol* 2010; 78(2):169-83.
11. Krisanaprakornkit T, Ngamjarus C, Witoonchart C, Piyavhatkul N. Meditation therapies for attention-deficit/hyperactivity disorder (ADHD). *Cochrane Database Syst Rev* 2010; (6):CD006507.
12. Ledesma D, Kumano H. Mindfulness-based stress reduction and cancer: a meta-analysis. *Psychooncology* 2009; 18(6):571-9.
13. Matchim Y, Armer JM, Stewart BR. Mindfulness-based stress reduction among breast cancer survivors: a literature review and discussion. *Oncol Nurs Forum* 2011; 38(2):E61-71.
14. Piet J, Hougaard E. The effect of mindfulness-based cognitive therapy for prevention of relapse in recurrent major depressive disorder: a systematic review and meta-analysis. *Clin Psychol Rev* 2011; 31(6):1032-40.
15. Wanden-Berghe RG, Sanz-Valero J, Wanden-Berghe C. The application of mindfulness to eating disorders treatment: a systematic review. *Eat Disord* 2011; 19(1):34-48.
16. Winbush NY, Gross CR, Kreitzer MJ. The effects of mindfulness-based stress reduction on sleep disturbance: a systematic review. *Explore (NY)* 2007; 3(6):585-91.
17. Zgierska A, Rabago D, Chawla N, Kushner K, Koehler R, Marlatt A. Mindfulness meditation for substance use disorders: a systematic review. *Subst Abus* 2009; 30(4):266-94.
18. Alexander CN, Langer EJ, Newman RI, Chandler HM, Davies JL. Transcendental meditation, mindfulness, and longevity: an experimental study with the elderly. *J Pers Soc Psychol* 1989; 57(6):950-64.
19. Bernardy K, Füber N, Köllner V, Häuser W. Efficacy of cognitive-behavioral therapies in fibromyalgia syndrome - a systematic review and metaanalysis of randomized controlled trials. *J Rheumatol* 2010; 37(10):1991-2005.
20. Rainforth MV, Schneider RH, Nidich SI, Gaylord-King C, Salerno JW, Anderson JW. Stress reduction programs in patients with elevated blood pressure: a systematic review and meta-analysis. *Curr Hypertens Rep* 2007; 9(6):520-8.
21. Anderson JW, Liu C, Kryscio RJ. Blood pressure response to transcendental meditation: a meta-analysis. *Am J Hypertens* 2008; 21(3):310-6.

22. Canter PH, Ernst E. The cumulative effects of Transcendental Meditation on cognitive function-- a systematic review of randomised controlled trials. *Wien Klin Wochenschr* 2003; 115(21-22):758-66.
23. So K.T., Orme-Johnson D. W.. Three randomized experiments on the longitudinal effects of the Transcendental Meditation technique on cognition. *Intelligence* 2001; 419-40.
24. Travis F GS, Stixrud W. ADHD, Brain Functioning, and Transcendental Meditation Practice. *Mind & Brain, The Journal of Psychiatry* 2011; 73-81.
25. Chen KW, Berger CC, Manheimer E et al.. Meditative therapies for reducing anxiety: a systematic review and meta-analysis of randomized controlled trials. *Depress Anxiety* 2012; 29(7):545-62.
26. Chambless DL, Hollon SD. Defining empirically supported therapies. *J Consult Clin Psychol* 1998; 66(1):7-18.
27. Hollon SD, Ponniah K. A review of empirically supported psychological therapies for mood disorders in adults. *Depress Anxiety* 2010; 27(10):891-932.
28. Chiesa A, Malinowski P. Mindfulness-based approaches: are they all the same? *J Clin Psychol* 2011; 67(4):404-24.
29. Rappay L, Bystrisky A. Classical mindfulness: an introduction to its theory and practice for clinical application. *Ann N Y Acad Sci* 2009; 1172:148-62.
30. *Methods Guide for Conducting Comparative Effectiveness Reviews*. Rockville, MD: Agency for Healthcare Research and Quality; August 2007. AHRQ Publication No. 10(11)-EHC063-EF.
31. Higgins JP, Altman DG, Gotzsche PC *et al.* The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011; 343:d5928.
32. Higgins JPT, Green S, eds. *Cochrane handbook for systematic reviews of Interventions* Version 5.1.0. London: The Cochrane Collaboration; Updated March 2011. Available at: <http://www.cochrane.org/training/cochrane-handbook>. Accessed February 17, 2012.
33. Brewer JA, Mallik S, Babuscio TA *et al.* Mindfulness training for smoking cessation: Results from a randomized controlled trial. *Drug Alcohol Depend* 2011.
34. Castillo-Richmond A, Schneider RH, Alexander CN *et al.* Effects of stress reduction on carotid atherosclerosis in hypertensive African Americans. *Stroke* 2000; 31(3):568-73.
35. Garland EL, Gaylord SA, Boettiger CA, Howard MO. Mindfulness training modifies cognitive, affective, and physiological mechanisms implicated in alcohol dependence: results of a randomized controlled pilot trial. *J Psychoactive Drugs* 2010; 42(2):177-92.
36. Brewer JA, Sinha R, Chen JA *et al.* Mindfulness training and stress reactivity in substance abuse: results from a randomized, controlled stage I pilot study. *Subst Abus* 2009; 30(4):306-17.
37. Murphy TJ, Pagano RR, Marlatt GA. Lifestyle modification with heavy alcohol drinkers: effects of aerobic exercise and meditation. *Addict Behav* 1986; 11(2):175-86.
38. Taub E, Steiner SS, Weingarten E, Walton KG. Effectiveness of broad spectrum approaches to relapse prevention in severe alcoholism: A long-term, randomized, controlled trial of Transcendental Meditation, EMG biofeedback and electronic neurotherapy. *Alcoholism Treatment Quarterly* 1994; 11(1-2):187-220.
39. Hebert JR, Ebbeling CB, Olenzki BC *et al.* Change in women's diet and body mass following intensive intervention for early-stage breast cancer. *J Am Diet Assoc* 2001; 101(4):421-31.
40. Gross CR, Kreitzer MJ, Reilly-Spong M *et al.* Mindfulness-based stress reduction versus pharmacotherapy for chronic primary insomnia: a randomized controlled clinical trial. *Explore (NY)* 2011; 7(2):76-87.
41. Schmidt S, Grossman P, Schwarzer B, Jena S, Naumann J, Walach H. Treating fibromyalgia with mindfulness-based stress reduction: results from a 3-armed randomized controlled trial. *Pain* 2011; 152(2):361-9.
42. Oken BS, Fonareva I, Haas M *et al.* Pilot

controlled trial of mindfulness meditation and education for dementia caregivers. *J Altern Complement Med* 2010; 16(10):1031-8.

43. Gross CR, Kreitzer MJ, Thomas W *et al.* Mindfulness-based stress reduction for solid organ transplant recipients: a randomized controlled trial. *Altern Ther Health Med* 2010; 16(5):30-8.
44. Treadwell JR, Singh S, Talati R, et al. A Framework for "Best Evidence" Approaches in Systematic Reviews. Methods Research Report (Prepared by the ECRI Institute Evidence-based Practice Center under Contract No. HHS A 290-2007-10063-I). Rockville, MD: Agency for Healthcare Research and Quality; June 2011. AHRQ Publication No. 11-EHC046-EF.
45. Henderson VP, Clemow L, Massion AO, Hurley TG, Druker S, Hebert JR. The effects of mindfulness-based stress reduction on psychosocial outcomes and quality of life in early-stage breast cancer patients: a randomized trial. *Breast Cancer Res Treat* 2011
46. Segal ZV, Bieling P, Young T *et al.* Antidepressant monotherapy vs sequential pharmacotherapy and mindfulness-based cognitive therapy, or placebo, for relapse prophylaxis in recurrent depression. *Arch Gen Psychiatry* 2010; 67(12):1256-64.
47. Kuyken W, Byford S, Taylor RS *et al.* Mindfulness-based cognitive therapy to prevent relapse in recurrent depression. *J Consult Clin Psychol* 2008; 76(6):966-78.

Introduction

Background

Definition of Meditation

The National Center for Complementary and Alternative Medicine considers meditation to be a mind-body method. This category of complementary and alternative medicine includes interventions that employ a variety of techniques designed to facilitate the mind's capacity to affect bodily function and symptoms. In meditation, a person learns to focus attention. Some forms of meditation instruct the practitioner to become mindful of thoughts, feelings, and sensations and to observe them in a nonjudgmental way. Practitioners generally believe these results in a state of greater calmness, physical relaxation, and psychological balance.¹

Current Practice and Prevalence of Use

Many people use meditation to treat stress and stress-related conditions, as well as to promote health.^{2,3} A national survey in 2008 found that the number of people meditating has been increasing over the years, with approximately 10 percent of the population having some experience with meditation.² A number of hospitals and programs offer courses in meditation to patients seeking alternative or additional methods to relieve ailments or to promote health.

Forms of Meditation

Researchers have categorized meditative techniques as emphasizing “mindfulness” meditation such as mindfulness-based stress reduction (MBSR) or “concentration,” such as transcendental meditation; however this distinction may not differentiate the effects of the techniques or the particular skills they teach.⁴

Mindfulness-based programs include mindfulness-based stress reduction (MBSR) and its adaptation, mindfulness-based cognitive therapy (MBCT). Most consider MBSR and MBCT to be standardized programs. However, instructors vary somewhat in how they teach the programs, partly depending on the clientele. Typically, the programs consist of weekly meetings for 8 weeks, each lasting 2 to 2.5 hours, with an additional 6-8 hour retreat on a weekend day in the middle of the 8-week training. In addition, students receive instructions for daily home practice. MBCT maintains an 8-week course length, similar to MBSR, but instructors modify MBCT for the particular condition of depression. Other adaptations have tried (usually) shorter versions of the program lasting 4 or more weeks targeting different conditions and providing varying amounts of meditation training during that time. Vipassana and Zen are also considered mindfulness-based techniques.

The “concentration”-based techniques consist of transcendental meditation, a program established by Maharishi Mahesh Yogi around 1955, and a few others which used a mantra as part of their meditative technique. Many also consider the transcendental meditation program to be a standardized program that generally consists of daily 1-1.5 hour meetings for 1 week, then periodic meetings, roughly weekly, after the first week for the first month or so, and less frequently after that. Students receive instructions for daily home practice.

Some “mindfulness” approaches such as dialectical behavioral therapy and acceptance and commitment therapy do not use mindfulness as the foundation but rather as an ancillary

component. Others, such as yoga and tai chi, involve a significant amount of movement that produces their own physiological effects apart from the mental exercises. Although these techniques also contain a meditative component, it is often difficult to ascertain the effects of meditation itself on various outcomes, separate from the effects of the exercise component.^{5 6} Many of the yoga interventions, in particular, do not clearly indicate how much meditation is involved in the intervention. Like yoga, qi gong is a broad term encompassing both meditation and movement; it comes with some of the same difficulties as yoga in terms of parsing the effects of movement from the effects of meditation.

Stress Outcomes

Researchers have postulated that meditation programs may affect a range of outcomes related to stress and well-being.⁷ Since practitioners and clinicians from the behavioral sciences or alternative and complementary medical sciences have conducted most of these studies, outcomes largely include self-reported changes in various stress-related symptoms. These symptoms have ranged from the rare examination of positive outcomes, such as increased well-being, to the more common approach, which seeks to examine reductions in negative outcomes, such as anxiety or sleep disturbance. Some studies address symptoms related to the primary condition (e.g., pain in patients with low back pain, or anxiety in patients with social phobia) whereas others address similar emotional symptoms in clinical groups who may or may not present with clinically significant symptoms (e.g., anxiety or depression in individuals with cancer). The effectiveness of these interventions is unclear and may vary among different subgroups such as those with a particular clinical condition (e.g., anxiety or pain).

Evidence to Date

Studies and reviews to date have demonstrated that both “mindfulness” and “concentration” meditation techniques reduce emotional symptoms (e.g., anxiety and depression, stress) and improve physical symptoms (e.g., pain) from a small to moderate degree.⁸⁻²⁷ The populations studied have included healthy adults as well as those with a range of clinical and psychiatric conditions. For the most part these reviews have included uncontrolled studies or studies that used control groups for which they did not provide any additional treatment (i.e., usual care or “waiting list”). In wait-list controlled studies, the control group receives usual care while “waiting” to receive the intervention at some time in the future, providing a usual-care control for the purposes of the study. Thus, it is unclear whether the apparently beneficial effects of meditation training are a result of the expectations for improvement that participants naturally form when obtaining this type of treatment. Additionally, many programs involve lengthy and sustained efforts on the part of both participants and trainers, possibly yielding beneficial effects from the added attention, group participation, and support participants receive as well as the suggestion from trainers that they expect symptoms to improve with these efforts.^{28 29}

The meditation literature has significant limitations related to inadequate control comparisons. An informative analogy is the use of placebos in pharmaceutical or surgical trials. Researchers typically design placebos to match to the “active intervention” in order to elicit the same expectations of benefit on the part of both provider and patient. Additionally, placebo treatment includes all components of care received by the “active” group, including office visits and patient-provider interactions in which the provider engages with the patient in the same way irrespective of which group they are randomized to. These non-specific factors are particularly

important to control when evaluation of outcome relies on patient reporting. In this situation where double blinding is not feasible, the challenge to execute studies that are not biased by these non-specific factors is more pressing.⁵ As inquiry in this field has moved forward over the last few decades, a larger number of trials have moved to a more rigorous design standard of using higher quality controls. Thus, there is a clear need to examine the specific effects of meditation in randomized trials in which expectations for outcome and attentional support from health care professionals are controlled.

Clinical and Policy Relevance

Much uncertainty exists about the differences and similarities between the effects of different forms of meditation.^{4 30} Given the increasing use of meditation across a large number of conditions, it is important for patients, clinicians, and policymakers to understand the effects of meditation, type of meditation, and the conditions for which meditation is efficacious. While some reviews have focused on randomized controlled trials (RCTs), many if not most of the included studies involved wait-list or usual-care controls. Thus, we need to examine the specific effects of meditation interventions relative to control conditions in which expectations for outcome and attentional support from health care professionals are controlled.

Objectives

The objectives of this systematic review are to evaluate the effects of meditation programs on affect, attention, and health-related behaviors affected by stress, pain, and weight, among those with a medical or psychiatric condition in randomized controlled trials with appropriate comparators.

Scope and Key Questions

This report reviews the efficacy of meditation programs on stress-related outcomes among those with a clinical condition. Affect refers to emotion or mood. It can be positive such as the feeling of well-being, or negative such as anxiousness, depression, or stress. Studies usually measure affect through self-reported questionnaires designed to gauge how much someone experiences a particular affect. In some cases, clinicians measure these affects. Attention refers to our ability to maintain focus on particular stimuli; clinicians measure this directly. Studies measure substance use as the amount consumed or smoked over a period of time, and include alcohol consumption, cigarette smoking, or other drugs such as cocaine. Studies measure sleep as the amount of time spent sleeping versus awake or as overall sleep quality. They measure sleep time through either polysomnography or actigraphy, and sleep quality through self-reported questionnaires. Studies measure eating by eating diaries to calculate how much energy or fat a person has consumed over a particular period of time. They measure pain similar to affect, by a self-reported questionnaire to assess how much pain an individual is experiencing. It has two dimensions, pain severity and pain interference. Studies usually measure pain severity on a numerical rating scale from 0-10 or other self-reported questionnaire. Pain interference measures how much the pain is interfering with life and studies measure it on a self-reported scale. Studies measure weight in pounds or kilograms.

The Key Questions (KQs) are as follows.

Key Question 1. What are the efficacy and harms of meditation programs on negative affect (e.g. anxiety, stress) and positive affect (e.g. well-being) among those with a clinical condition (medical or psychiatric)?

Key Question 2. What are the efficacy and harms of meditation programs on attention among those with a clinical condition (medical or psychiatric)?

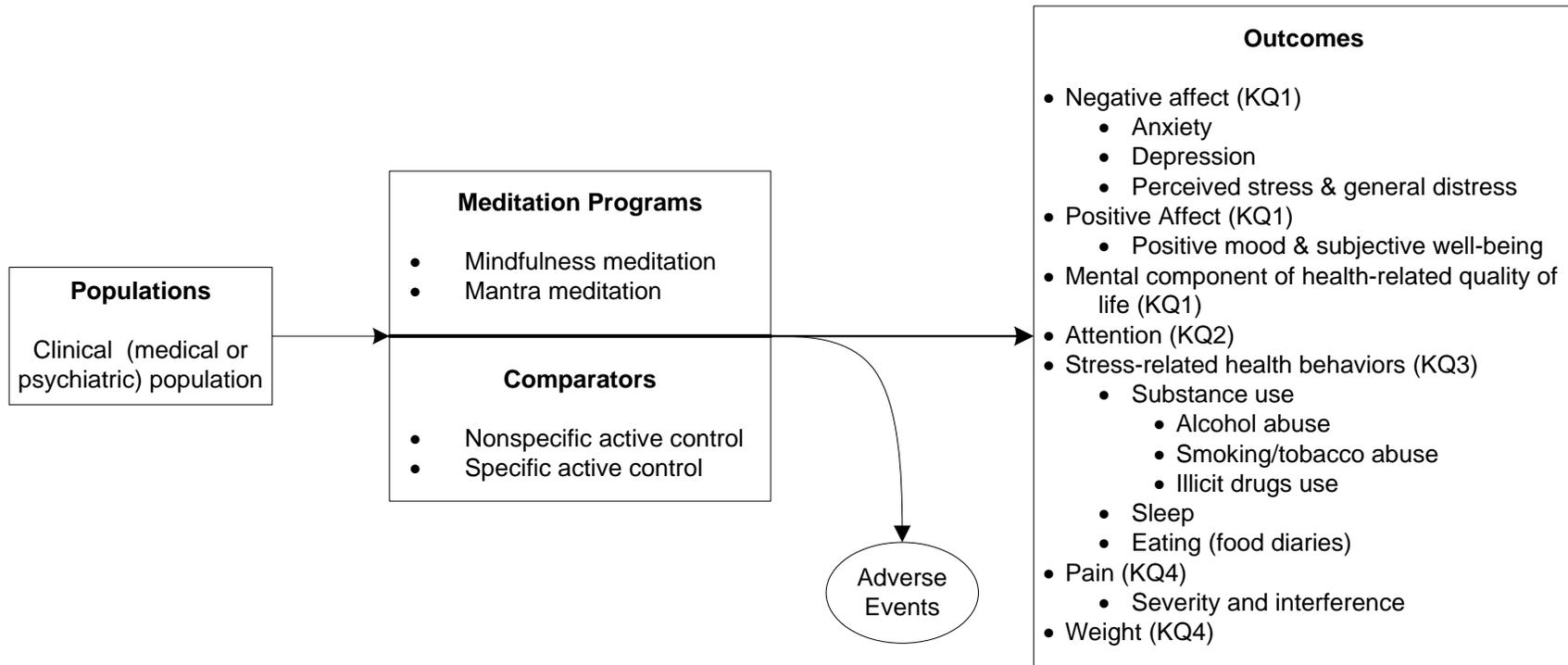
Key Question 3. What are the efficacy and harms of meditation programs on health-related behaviors affected by stress, specifically substance use, sleep, and eating, among those with a clinical condition (medical or psychiatric)?

Key Question 4. What are the efficacy and harms of meditation programs on pain and weight among those with a clinical condition (medical or psychiatric)?

Analytic Framework

We present our analytic framework for the systematic review in Figure 1. The figure illustrates the populations of interest, the meditation programs, and the outcomes that we reviewed. This figure depicts the key questions within the context of the PICOTS framework described in Table 1. Adverse events may occur at any point after the meditation program.

Figure 1. Analytic framework for meditation programs conducted in clinical and psychiatric populations



Methods

The methods for this comparative effectiveness review follow the methods suggested in the Agency for Healthcare Research and Quality (AHRQ) Methods Guide for Effectiveness and Comparative Effectiveness Reviews (<http://www.effectivehealthcare.ahrq.gov/methods-guide.cfm>). The main sections of this chapter reflect the elements of the protocol established for the comparative effectiveness review; certain methods map to the PRISMA checklist.³¹ We carried out this systematic review according to a pre-specified protocol registered at the AHRQ website.³²

Topic Development

The Division of Extramural Research of the National Center for Complementary and Alternative Medicine, National Institutes of Health, nominated the topic for this report in a public process. We recruited six key informants to provide input on the selection and refinement of the questions for the systematic review. To develop the key questions, we reviewed existing systematic reviews, developed an analytic framework, and solicited input from our key informants through e-mail and conference calls. We posted our draft key questions on the Effective Health Care Program website for public comment on October 14, 2011. We revised the key questions, as necessary, based on comments.

We drafted a protocol and recruited a multidisciplinary Technical Expert Panel, including methods experts, Tai Chi and Qigong experts, and meditation experts. With input from the Technical Expert Panel and representatives from AHRQ, we finalized the protocol. We uploaded the protocol to the Effective Health Care Program Web site on February 22, 2012.

Search Strategy

We searched the following databases for primary studies: MEDLINE®, PsycINFO, EMBASE®, PsycArticles, SCOPUS, CINAHL, AMED, and the Cochrane Library through October 11, 2011. We developed a search strategy for MEDLINE, accessed via PubMed®, based on medical subject headings (MeSH®) terms and text words of key articles that we identified a priori (Appendix B). We reviewed the reference lists of included articles, relevant review articles, and 20 related systematic reviews to identify articles that the database searches might have missed. Our search did not have any language restrictions. We will update the search during the peer review process.

We selected databases after internal deliberation and input from the Technical Expert Panel. We did not include meeting proceedings or abstracts of reports of unpublished studies. We searched clinicaltrials.gov. We evaluated the search strategy by examining whether it retrieved a sample of key articles. We did not limit our searches to any geographic regions.

Study Selection

Two investigators independently screened title and abstracts, and excluded them if both investigators agreed that the article met one or more of the exclusion criteria. (Inclusion and exclusion criteria listed in Table 2 and the Abstract Review Form in Appendix C.) We resolved differences between investigators regarding abstract eligibility through consensus.

Citations that we promoted on the basis of title and abstract screen underwent independent screening using the full-text article (Appendix C, Article Review Form). We resolved differences

regarding article inclusion through consensus. Paired investigators conducted another independent review of full-text articles to determine whether they should be included in the full-data abstraction (Appendix C, Key Question Applicability Form). If we deemed articles to have applicable information, we included them in the data abstraction. We resolved disagreements about the eligibility of an article by discussion between the two reviewers or by adjudication of a third reviewer.

For inclusion in this review, we required that studies reported on those with a clinical condition such as medical or psychiatric populations. Although meditation programs may have an impact on healthy populations, we limited our evaluation to clinical populations. Since trials examine meditation programs in diverse populations, we defined a clinical condition broadly to include mental health/psychiatric conditions (e.g., anxiety or stress) and physical conditions (e.g., low back pain, heart disease, or advanced age). Additionally, since stress was of particular interest for meditation studies, we also included trials that studied stressed populations even though they may not have a defined medical or psychiatric diagnosis. We excluded studies among the otherwise healthy. We excluded studies among children or adolescents. Meditation instructors teach children and adults differently, due to differences in maturity, understanding, and discipline. These studies would measure outcomes differently, making a synthesis difficult.

We excluded movement-based techniques that involve meditation due to the confounding effects of the exercise component of those techniques on outcomes (Table 1). To evaluate programs that are more than a brief mental exercise, yet remain broadly inclusive, we defined a meditation program as any systematic or protocolized meditation program that follows a predetermined curriculum. We defined these programs to involve, at a minimum, at least 4 hours of training with instructions to practice outside the training session.

We included both specific and non-specific active controlled trials. We defined any control group which does not match time and attention for the purposes of matching expectation as an inactive control. Examples include wait-list or usual-care controls. We excluded such trials since it would be difficult to assess whether any changes in outcomes were due to the non-specific effects of time and attention. We excluded observational studies susceptible to confounding and selection biases.

We evaluated the effect of these meditation programs on a range of stress-related outcomes and used the Patient Reported Outcomes Measurement Information System (PROMIS) framework to help guide selection and categorization of outcomes.⁷ The PROMIS framework is a National Institutes of Health-sponsored project to optimize and standardize patient reported health status tools. This framework breaks self-reported outcomes into the three broad categories of physical, mental, and social health, and then subdivides these categories further. Our outcomes included negative affect, positive affect, well-being, cognition, and health-related behaviors affected by stress such as substance abuse, sleeping, and eating.⁷ Based on Technical Expert Panel recommendations, we also evaluated the effect of meditation programs on the clinical outcomes of pain and weight, which are not in the PROMIS framework but are stress-related outcomes we deemed important.

We included randomized controlled trials in which the control group was matched in time and attention to the intervention group for the purpose of matching expectations of benefit. The inclusion of such trials allowed us to evaluate the specific effects of meditation programs separate from the non-specific effects of attention and expectation. Our team thought this was the most rigorous way to determine the efficacy of the interventions. We did not include observational studies because they are likely to have an extremely high risk of bias due to

problems such as self-selection of interventions (people who believe in the benefits of meditation or who have prior experience with meditation are more likely to enroll in a meditation program) and use of outcome measures that can be easily biased by participants' beliefs in the benefits of meditation.

We defined an active control as any control in which the control group is matched in time and attention to the intervention group for the purpose of matching expectations of benefit. Examples include “attention control,” “educational control,” or another therapy such as progressive muscle relaxation. A non-specific active control only matches time and attention, and is not a known therapy. A specific active control compares the intervention to another known therapy, such as progressive muscle relaxation.^{28 29 33 34}

Table 1. Study inclusion and exclusion criteria

	Inclusion	Exclusion
Population and Condition of Interest	<ul style="list-style-type: none"> • Adult populations (18 years or older) • Clinical (medical or psychiatric) diagnosis, defined as any condition (e.g. high blood pressure, anxiety) including a stressor. 	<ul style="list-style-type: none"> • Studies of children. The type and nature of meditation children receive is significantly different from adults. • Studies of otherwise healthy individuals
Interventions	<p>Structured meditation programs (any systematic or protocolized meditation programs that follow predetermined curricula) consisting of, at a minimum, at least 4 hours of training with instructions to practice outside the training session.</p> <p>These include:</p> <p>Mindfulness-based:</p> <ul style="list-style-type: none"> • MBSR • MBCT • Vipassana • Zen • Other mindfulness meditation <p>Mantra-based:</p> <ul style="list-style-type: none"> • TM • Other mantra meditation <p>Other meditation</p>	<p>Meditation programs in which the meditation is not the foundation and majority of the intervention. These include:</p> <ul style="list-style-type: none"> • Dialectical Behavioral Therapy (DBT) • Acceptance and Commitment Therapy (ACT). • Any of the movement-based meditations such as Yoga (e.g. Iyenger, Hatha, Shavasana), Tai chi, and Qi gong (Chi kung) • Aromatherapy • Biofeedback • Neurofeedback • Hypnosis • Autogenic training • Psychotherapy • Laughter therapy • Therapeutic touch • Eye movement desensitization reprocessing • Relaxation therapy • Spiritual therapy • Breathing exercise, Pranayama • Exercise • Any intervention that is given remotely, or only by video or audio to an individual without the involvement of a meditation teacher physically present
Comparisons of Interest	<p>Active control, defined as a program that is matched in time and attention to the intervention group for the purpose of matching expectations of benefit. Examples include “attention control,” “educational control,” or another therapy, such as progressive muscle relaxation, that the study compares to the intervention.</p> <ul style="list-style-type: none"> • A nonspecific active control only matches time and attention, and is not a known therapy. • A specific active control compares the intervention to another known therapy, 	<p>Studies that only evaluate a wait-list/usual-care control or do not include a comparison group</p>

	such as progressive muscle relaxation.	
Outcomes	See Figure A	
Study Design	Randomized controlled trials with an active control	Non-randomized designs, such as observational studies.
Timing and Setting	Longitudinal studies that occur in general and clinical settings	

We excluded articles with no original data (reviews, editorials, and comments), studies published in abstract form only, and dissertations.

DBT = Dialectical Behavioral Therapy; ACT = Acceptance and Commitment Therapy; KQ = Key Question; MBCT = Mindfulness-based Cognitive Therapy; MBSR = Mindfulness-based Stress Reduction; TM = Transcendental Meditation

Data Abstraction and Data Management

We used Distiller SR (Evidence Partners, 2010) to manage the screening and review process. We uploaded all citations identified by the search strategies to the system.

We created standardized forms for data extraction (Appendix C). We pilot tested the forms prior to beginning the data extraction. Reviewers extracted information on general study characteristics, study participants, eligibility criteria, interventions, and the outcomes. Two investigators reviewed each article for data abstraction. For study characteristics, participant characteristics, and intervention characteristics, the second reviewer confirmed the first reviewer's data abstraction for completeness and accuracy. For outcome data and risk of bias scoring, we used dual and independent review. Reviewer pairs included personnel with both clinical and methodological expertise. We resolved differences between investigators regarding data through consensus.

For each meditation program we extracted information on measures of intervention fidelity including dose, training, and receipt of intervention. We measured duration and maximal hours of structured training in meditation, amount of home practice recommended, description of instructor qualifications, and description of participant compliance, if any (Tables 5 and 6). Many of the meditation techniques do not have clearly defined training and certification requirements for instructors. However, when available, we extracted data on whether instructors had specialized training or course certification in the particular meditative technique being assessed.

Since studies provided a variety of measures for many of our key questions, we included any randomized controlled trial (RCT) of a meditation program with an active control that potentially applied to any key question. We then went through each of the papers to identify all the scales (instruments or measurement tools) that could potentially apply to a key question. We then revised this list and organized instruments according to relevance for the key questions. We extracted data from instruments that have broad experience and were commonly used to measure relevant outcomes. We prioritized instruments that were used most by other trials in our review, so as to allow more direct comparisons between trials (Table 2).

We entered all information from the article review process into the Distiller SR database. We used the DistillerSR database to maintain the data, which we then exported into Excel for the preparation of evidence tables.

Table 2. Organization of various scales (instruments or measurement tools) for each Key Question

Key Question 1. What are the efficacy and harms of meditation programs on negative affect (e.g. anxiety, stress) and positive affect (e.g. well-being) among those with a clinical condition (medical or psychiatric)?	
Anxiety	
General anxiety	Beck Anxiety Inventory (BAI)
	Profile of Mood States, Tension (POMS)
	Symptom Checklist-90 Anxiety Subscale (SL-90)
	State Trait Anxiety Inventory, State (STAI)
	State Trait Anxiety Inventory, Trait (STAI)
	Brief Symptom Inventory (18), Anxiety Subscale (BSI-18)
	Hamilton Anxiety Rating Scale
	Institute for Personality and Ability Testing (IPAT) Anxiety Inventory
Worry	Penn State Worry Questionnaire
Thought emotion/suppression	Courtauld Emotional Control, Anxiety (CEC)
	White Bear Inventory (thought suppression)
Social anxiety	Liebowitz Social Anxiety, Fear
	Liebowitz Social Anxiety, Avoidance
	Liebowitz Social Anxiety, Fear and Avoidance Combined
	Social Interactions, Fear
	Social Phobia
	Fear of Negative Evaluation (brief version)
Depression	
Self-reported depression	Beck Depression Inventory (BDI)
	Symptom Checklist-90 Depression Subscale (SCL-90)
	Center for Epidemiologic Studies Depression Scale (CES-D)
	Profile of Mood States, Depression (POMS)
	Brief Symptom Inventory (18), Depression (BSI-18)
	Beck Depression Inventory (BDI)
	Beck Depression Inventory II (BDI-II)
	Interpersonal Sensitivity
	Self Rating Depression Scale (SDS)
	Institute for Personality and Ability Testing (IPAT) Depression Scale
Clinician-rated depression	Structured Clinical Interview, Relapse (Y/N) (SCID)
	Hamilton Psychiatric Rating Scale for Depression (HAM-D)
Stress	
	Perceived Stress Scale (10 and 14 item) (PSS)
	Life Stress Instrument (LSI)
General Distress	
	Brief Symptom Inventory (18), General Symptom Severity Index (BSI-18)
	Brief Symptom Inventory (53) Global Psychiatric Symptoms (BSI-53)
	Positive and Negative Affect Scale (PANAS) - Negative mood
	Symptom Checklist-90-R Global Severity Index (SL-90)
	Short Form-36 Mental Health Subscale (SF-36)
	Profile of Mood States, Total Mood Disturbance (POMS)
Negative Affect	
	Positive and Negative Affect Scale (PANAS) - Negative Mood
Well-being	
	Sense of Coherence Scale (meaningfulness subscale)
	Quality of Well-Being Scale
Positive Mood	
	Short Form (SF) 36 Vitality Subscale
	Positive and Negative Affect Scale (PANAS) - Positive Mood
Positive Affect	

	Positive and Negative Affect Scale (PANAS) - Positive Mood
Mental component of health-related quality of life	
	Short Form (SF) 12, SF 36, Veterans Rand 36 (VR 36): mental component score for all
	World Health Organization Quality of Life (WHOQL)-Psychological
Key Question 2. What are the efficacy and harms of meditation programs on attention among those with a clinical condition (medical or psychiatric)?	
Attention	
	Attentional Network
	Stroop Color-Word Test (sustained attention)
Key Question 3. What are the efficacy and harms of meditation programs on health-related behaviors affected by stress, specifically substance use, sleep, and eating, among those with a clinical condition (medical or psychiatric)?	
Substance Use	
ETOH	Penn Alcohol Craving Scale
	Attention (dot probe)
	Impaired Response Inhibition Scale for Alcohol (IRISA)
	Weekly Diary
	Daily Diary
Cocaine	Weekly Diary
Smoking	Cigarette Use
Sleep	
Summary measures	Pittsburgh Sleep Quality Index (PSQI)
	Insomnia Severity Index (ISI)
	Epworth Sleepiness Scale (ESS)
Diary	Diary (total sleep time, wake after sleep onset)
Actigraphy	Actigraphy (total sleep time, wake after sleep onset)
Eating	
Diary	7-Day Food Recall (fat/fiber/carbs)
Key Question 4. What are the efficacy and harms of meditation programs on pain and weight among those with a clinical condition (medical or psychiatric)?	
Pain	
Severity	Numeric Rating Scale 0-10 (sensation and/or unpleasantness)
	Irritable Bowel Syndrome (IBS) Abdomen Pain Severity
	Pain Perception (sensory and affective)
	Short Form-36 Bodily Pain Subscale
	McGill Pain Questionnaire (current pain score)
Interference	Fibromyalgia Impact Questionnaire
	Roland Morris Disability Questionnaire
Weight (pounds or kilograms)	

All measures are direct except:

Penn Alcohol Craving Scale which is an indirect measure of alcohol consumption

Anxiety, Depression and Stress/Distress measures which are indirect measures of Negative Affect

Positive Mood and Subjective Well Being measures which are indirect measures of Positive Affect

Data Synthesis

For each key question, we created a detailed set of evidence tables containing all information abstracted from eligible studies.

To display the outcome data, we calculated relative difference-in-change scores (i.e., the change from baseline in an outcome measure in the treatment group minus the change from baseline in the outcome measure in the control group, divided by the baseline score in the treatment group). However, many studies did not report enough information to calculate confidence intervals for the relative difference in change scores. When we evaluated point estimates and confidence intervals for just the post-intervention or end-of-study differences between groups, and compared these to the point estimates for the relative difference-in-change scores for those time points, some of the estimates that did not account for baseline differences appeared to favor a different group (i.e. treatment or control), when compared with the estimates that did account for baseline differences. We therefore used the relative difference-in-change scores to estimate the direction and approximate magnitude of effect for all outcomes. The relative difference in change graphs were used to determine consistency. They are not a statistical analysis, but a visual way to display the data. This was done by the following formula: $\frac{(\text{meditation } T2-T1) - (\text{control } T2-T1)}{(\text{meditation } T1)}$ where T1 is the baseline means score and T2 is the followup mean score.

For the purpose of generating an aggregate quantitative estimate of the effect of an intervention and the associated 95 percent confidence interval, we performed meta-analysis using standardized mean differences (effect sizes) calculated by Cohen's method (Cohen's d).³⁵ For each outcome, we displayed the resulting effect size estimate according to the type of control group and duration of followup. Some studies did not report enough information to be included in meta-analysis. For that reason, we decided to display the relative difference in change scores along with the effect size estimates from meta-analysis so that readers can see the full extent of the available data. We used statistical significance of the metaanalytic result to guide our reporting of precision.

We calculated point estimates for the difference-in-change scores for all outcomes. Since these studies were looking at short interventions and relatively low doses of meditation, we considered a five percent relative difference in change score to be potentially clinically significant. In synthesizing the results of these trials, we considered both statistical and clinical significance. Statistical significance is according to study-specific criteria, and we reported p-values and confidence intervals where present. We defined clinical significance as a 5 percent relative difference-in-change.

Some scales show improvement with more positive numbers, and others show more improvement with less positive numbers. After calculating the relative difference in change scores, we reversed the sign on the scales which showed improvement with more negative numbers so that all scales showed an improvement in the positive direction. We oriented the meta-analysis graphs similarly, so that effect sizes are shown in the direction of which treatment arm they favored rather than increases and decreases in each scale.

During data synthesis, if trials reported on more than one scale for a particular outcome, we prioritized the scale that was most common to all the trials to improve comparability between trials. To arrive at an overall strength of evidence, we used only one scale per outcome per trial in order to avoid giving extra weight to trials that reported on the same outcome with multiple scales. For this reason, although we describe the various scales reported on by the trials in the

text, the graphical displays show only the scale that was compared with other studies to arrive at the strength of evidence. Since many trials reported on the same scale at multiple time points, we provided graphs showing the effects at the end of intervention and at the end of study. Wherever meta-analysis was possible, we separated outcomes by time point. For most, these were at 2-3 months (post intervention) and beyond 3 months (end of study). We describe relevant changes in outcomes over time in the results, but for purposes of consistency we used the first time point only for describing the magnitude of change in the strength of evidence tables.

We combined stress and distress into a single outcome due to the paucity of studies and similarities between these outcomes. For studies that reported on both a stress and a distress scale, we prioritized using the scale that was most common in the group of studies. For the same reasons, we also combined well-being and positive mood into the single outcome of positive affect.³⁶

To analyze the effects of meditation programs on negative affect, we combined one negative affect scale per trial with the others. Since some trials reported on more than one negative affect scale, we prioritized anxiety, then depression, then stress/distress. Anxiety is a primary dimension of negative affect and a common symptom of stress. Anxiety is highly correlated with depressive symptoms, and thus, is expected to be a good primary marker of negative affect in the samples included in these analyses when more than one measure of negative affect was available.³⁷ We also conducted a sensitivity analysis of this analysis by reversing the prioritization order such that stress/distress was prioritized over depression which was prioritized over anxiety. For the large bulk of outcomes, measures were rated as direct measures of that outcome. However, since anxiety, depression, stress and distress are components of negative affect, we rated them as indirect measures of negative affect. If a direct measure of negative affect was available (e.g. PANAS), we used that measure instead of any indirect measures.

Assessment of Methodological Quality of Individual Studies

We assessed the risk of bias in studies independently and in duplicate based on the recommendations in the Guide for Conducting Comparative Effectiveness Reviews.³⁸ We supplemented these tools with additional assessment questions based on the Cochrane Collaboration's Risk of Bias Tool.^{39 40} While many of the tools to evaluate risk of bias are common to behavioral as well as pharmacologic interventions, some items are more specific to behavioral interventions. After discussion with experts in meditation programs and clinical trials, we emphasized four major and four minor criteria. The four major criteria in assessing bias of meditation programs were: matching control for time and attention; description of withdrawals and dropouts; attrition; and blinding of outcome assessors. We considered as minor criteria the description of randomization, allocation concealment, intention to treat analysis, and credibility evaluation (Table 3).

Matching controls for time and attention is prerequisite to matching expectations of benefit. We extracted data on time and attention for both groups and if the control gave at least 75 percent of the time and attention as the intervention arm, we gave it credit for matching. Evaluating credibility is also an important, albeit followup step. Clearly identifying the number of withdrawals and dropouts is necessary for estimating the role that it may play in biasing the results. If attrition was very large, greater than 20 percent, we felt it reflected a potentially large

bias and lower quality of trial. Finally, although double blinding is not possible, single blinding of the data collectors is possible and important in reducing risk of bias. While all studies should clearly describe the randomization procedure rather than just stating that “participants were randomized,” we felt that some studies, especially older ones, may have conducted appropriate randomization but just not reported the procedures in detail. We therefore listed this as a minor criterion. The same applied for intent-to-treat (ITT) analysis. However, if a study stated they conducted an ITT analysis but did not impute missing data, we did not give those studies points for an ITT analysis.

We assigned two points each to the major criteria, weighting them more in assessing risk of bias (Table 3). We assigned one point each to the minor criteria. Studies could therefore receive a total of 12 points. If studies met a minimum of three major criteria and three minor criteria (9-12 points), we classified it as having “low risk of bias.” Studies receiving 6-8 points were classified as having “medium risk of bias,” and studies receiving 5 or less points were classified as having “high risk of bias.” Using this scoring system, we would still consider a study that did not meet one major criterion low risk of bias if it met other minor criteria. We could only grade a study that did not meet two major criteria as medium risk of bias or high risk of bias.

Low risk-of-bias studies had the least bias and we considered the results valid. Medium risk-of-bias studies were susceptible to some bias, but not enough to invalidate the results. High risk-of-bias studies had significant flaws that might have invalidated the results. In addition, if there were other issues with the studies that were not captured by the above criteria, such as greater than 20 percent attrition or significant errors in reporting, we categorized such studies as high risk of bias on a study-by-study basis.

Table 3. List of major and minor criteria in assessing risk of bias

Major Criteria*	Minor Criteria*
<ul style="list-style-type: none"> • Was the control matched for time and attention by the instructors? • Was there a description of withdrawals and dropouts? • Was attrition < 20% at the end of treatment? As several studies did not calculate attrition starting from the original number randomized, we recalculated the attrition from the original number randomized. • Were those who collected data on the participants blind to the allocation? 	<ul style="list-style-type: none"> • Was the method of randomization described in the paper? To answer “yes” for this question, the papers had to give some description of the randomization procedure. • Was allocation concealed? • Was intent-to-treat analysis used? To answer “yes” for this question, the paper must impute noncompleter or other missing data, and do this from the original number randomized. • Was the credibility evaluated, and if so, was it comparable? If credibility was not evaluated, or if it was evaluated but not comparable, then it did not receive a point.

*We assigned 2 points each to the major criteria, weighting them more in assessing risk of bias. We assigned 1 point each to the minor criteria. Studies could therefore receive a total of 12 points. If studies met a minimum of three questions from major and three from minor (9-12 points), we assigned it a grade of “low risk of bias.” For studies ranging 6-8 points, we assigned a “medium risk of bias,” and for studies scoring 5 or less points, we assigned a “high risk of bias.”

Assessment of Potential Publication Bias

Sometimes studies with positive results for a particular outcome get published while studies with negative results do not, erroneously leading the readers to conclude that an intervention has positive effects on a given outcome when it may not. Even when an intervention does have an effect on an outcome, we expect to see a distribution of results by chance, that can include null results. When conducting a meta-analysis, a funnel plot allows us to see if the results of the studies were spread in a distribution reflecting what we might expect by chance. It assumes that

the largest studies will be near the average, and small studies will be spread on both sides of the average. However, this requires that we have the data to represent the results of each study in a meta-analysis. Anticipating that we might not find enough studies to support a quantitative assessment of publication bias, we conducted a qualitative assessment of publication bias by reviewing all the randomized trials of meditation listed in the clinicaltrials.gov registry. We searched for any trials that completed recruitment three or more years ago that did not publish results, or that listed outcomes for which they did not report results.⁴¹ To assess for selective outcomes reporting, we examined the methods section for all the scales used to measure outcomes and assessed whether the studies had reported results for all of them.

Strength of the Body of Evidence

After synthesizing the evidence, two reviewers graded the quantity and quality of the best available evidence addressing key questions one to four by adapting an evidence grading scheme recommended in the *Methods Guide for Conducting Comparative Effectiveness Reviews*.³⁸ In assigning evidence grades, we considered the four recommended domains, including risk of bias in the included studies, consistency across studies, directness of the evidence, and precision of the pooled estimate or the individual study estimates.

We derived the risk of bias for an individual study from the algorithm described above. We assessed the aggregate risk of bias of studies and integrated these assessments into a qualitative assessment of the summary risk-of-bias score. Since the studies in our evidence base were at varying risk of bias, most aggregate scores were based on a combination of high, moderate, or low risk-of-bias ratings. Where there was heterogeneity, we prioritized the lowest risk-of-bias studies.

We used the direction of effect of outcomes falling in the same category, irrespective of statistical significance, to evaluate consistency. In evaluating consistency, due to the heterogeneity of studies, we qualitatively considered giving greater weight to low risk-of-bias studies and/or those with large sample sizes if they were accompanied by one to two other conflicting studies that were of high risk of bias. If all the studies in an evidence base showed a similar direction of effect, we rated the evidence base as consistent. We rated single studies as consistency unknown.

We assessed the precision of individual studies by evaluating the statistical significance of a comparison through meta-analysis. To evaluate precision, we used confidence intervals or p-values. When we did not have a meta-analysis, we prioritized difference-in-change or “group-by-time interaction” confidence intervals or p-values where available. We found that few of the studies reported effect sizes and 95 percent confidence intervals. We estimated the confidence intervals for some of the outcomes. If all studies in an evidence base were precise, we rated the evidence base to be precise. We designated as imprecise studies whose effect size overlapped with the line of no difference. When studies did not report measures of dispersion or variability, we rated the precision as unknown.

We rated the evidence as being direct if the intervention was directly linked to the patient oriented outcomes of interest. We rated the evidence as indirect when the outcome was measured by scales such as Penn alcohol craving scale, impaired response inhibition scale for alcohol use, and attention dot scales, as these were indirect measures of substance use behavior. We conducted internal deliberations to arrive at a consensus of what was direct or indirect. For the large bulk of outcomes, measures were rated as direct measures of that outcome. However, since anxiety, depression, and stress/distress are components of negative affect, we rated them as

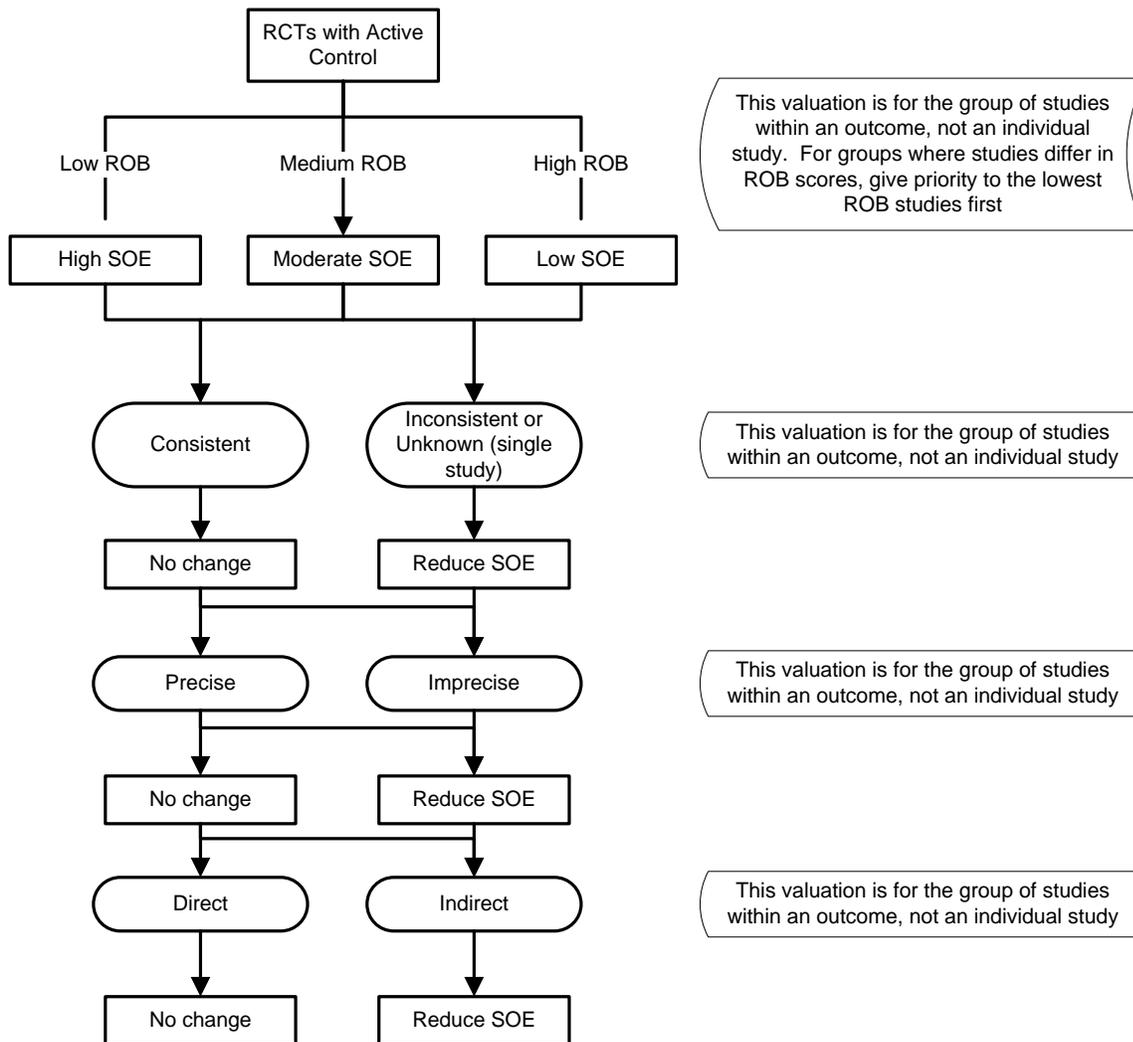
indirect measures of negative affect. If direct measures of negative affect such as the Positive and Negative Affect Scale (PANAS) was available, we used that measure instead of any indirect measures. Similarly, we rated well-being and positive mood as indirect measures of positive affect.

To incorporate multiple domains into an overall grade of the strength of evidence, we used the estimate of the summary risk of bias score, directness, and consistency, along with precision to evaluate an intervention. We used a qualitative approach to incorporating these multiple domains into an overall grade. We initially assigned strength of evidence for all outcomes based on their risk of bias ratings. Low risk of bias studies were assigned a high strength of evidence and vice versa. We rated consistent, precise, and direct evidence from such low risk-of-bias studies as high-grade strength of evidence. We downgraded the strength of evidence when consistency was unknown (i.e., single study) or inconsistent. We downgraded the strength of evidence when evidence was indirect. Imprecision or unknown precision also led to a downgrade in the strength of evidence (Figure 2).

We classified evidence pertaining to Key Questions 1 to 4 into four categories: 1) “High” grade, indicating high confidence that the evidence reflects the true effect, and further research is very unlikely to change our confidence in the estimate of the effect; 2) “Moderate” grade, indicating moderate confidence that the evidence reflects the true effect, and further research may change our confidence in the estimate of the effect and may change the estimate; 3) “Low” grade, indicating low confidence that the evidence reflects the true effect, and further research is likely to change our confidence in the estimate of the effect and is likely to change the estimate; and 4) “Insufficient” grade, indicating evidence is either unavailable or inadequate to draw a higher grade .

We did not incorporate the optional domain of publication bias in the evidence grade. However, if we found qualitative evidence of publication bias, the ultimate conclusions took that into consideration. Thus, low strength of evidence with probable publication bias translated into a very weak conclusion.

Figure 2. Algorithm for rating the strength of evidence



Definitions

Risk of Bias (ROB): Low, Medium, or High based on 4 major and 4 minor criteria
 Consistency: The direction of effect, irrespective of statistical significance
 Precision: Confidence interval or p-values, prioritizing difference-in-change values or “group x time interaction” values
 Directness: If not a direct measure of an outcome, categorized as indirect

Assumptions

- All outcomes have at least 1 study
- Studies start out with a SOE grading based on ROB
- Then based on other criteria, they either maintain that SOE grade or are downgraded one notch. They do not upgrade.

Abbreviations: RCTs = Randomized controlled trials; ROB = Risk of bias; SOE= Strength of evidence

Applicability

We assessed applicability separately for the different outcomes for the entire body of evidence guided by the PICOTS framework as recommended in the Methods Guide for Comparative Effectiveness Reviews of Interventions.³⁸ One of the potential factors we assessed was intervention fidelity (e.g., duration of structured meditation training, total amount of meditation practice (dose of meditation), subject compliance with meditation, subject proficiency with meditation, instructor qualifications, and study selection criteria for participants). We also assessed the selection process of these studies to evaluate the concern that participants in meditation studies are highly selected, such as trained meditators. In addition, we assessed whether findings were applicable to various ethnic groups or whether the applicability of evidence was limited by race, ethnicity, or education.

Peer Review and Public Commentary

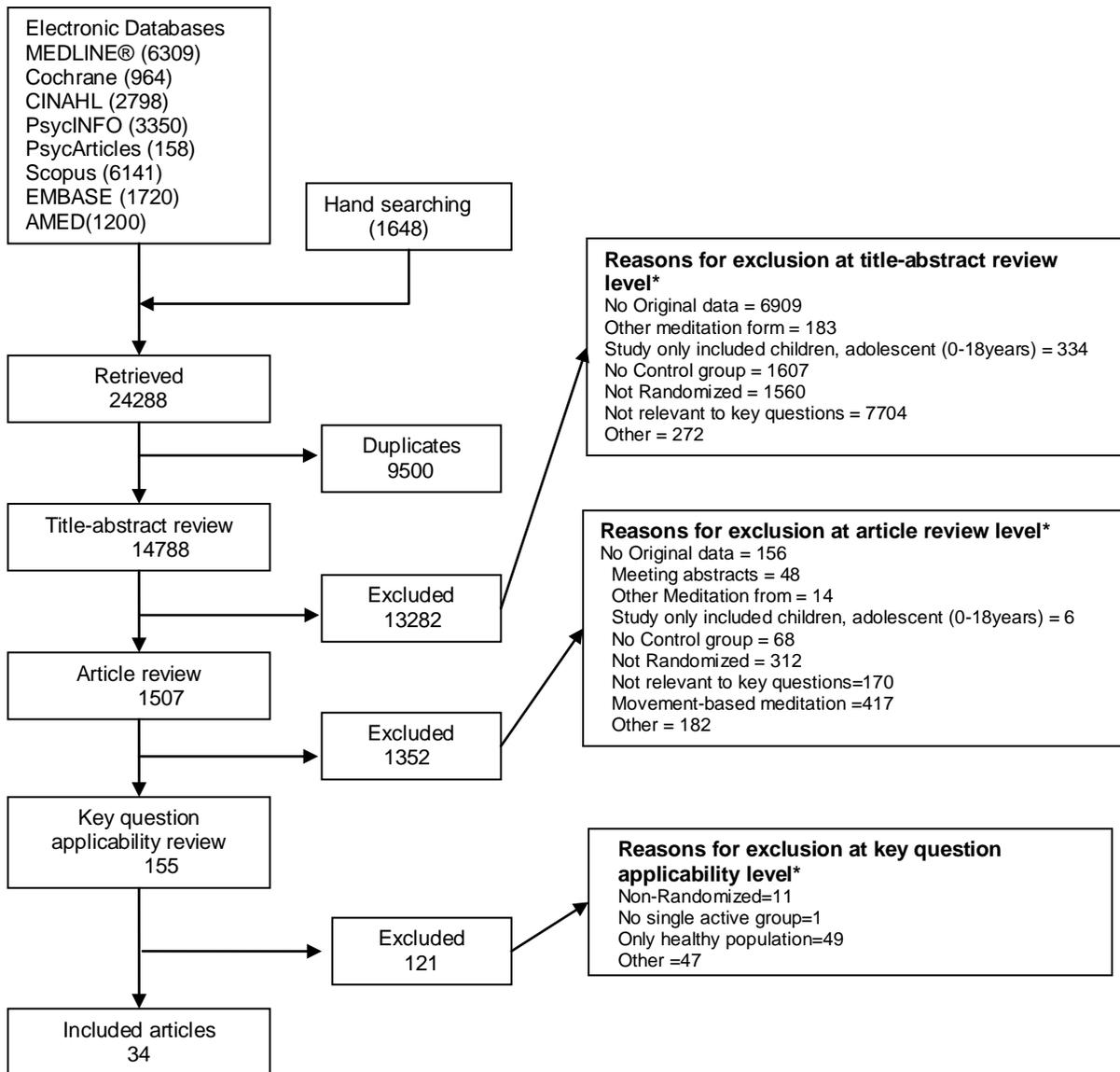
We have invited experts in mind/body medicine, transcendental meditation, and individuals representing stakeholder and user communities to provide external peer review of this comparative effectiveness review; AHRQ and an associate editor will also provide comments. The draft report will be posted on the AHRQ website for 4 weeks to elicit public comment. We will address all reviewer comments, revising the text as appropriate, and document everything in a —disposition of comments report that will be made available 3 months after the Agency posts the final CER on the AHRQ website.

Results

Results of the Search

Figure 3 summarizes the search results. The literature search identified 14,788 unique citations. During the title and abstract screening, we excluded 13,282 citations. During the article screening, we excluded 1,352 citations that met at least one of the exclusion criteria. During Key Question (KQ) applicability screening, we excluded an additional 121 articles that did not meet one or more of the inclusion criteria (Appendix D). We included 34 articles in the review.

Figure 3. Summary of the literature search



* Total exceeds the number in the exclusion box because reviewers were allowed to mark more than 1 reason for exclusion

Description of Types of Trials Retrieved

Of the included trials, 26 addressed KQ1 (negative and positive affect), two trials addressed KQ 2 (attention), 11 trials addressed KQ 3 (health related behaviors affected by stress), and 11 addressed KQ 4 (pain and weight). The majority of trials targeted patient populations with mental health or substance abuse problems (n=15). Other population groups under investigation included individuals with breast cancer (n=2), cardiovascular disease (hypertension and congestive heart failure (CHF); (n=2), chronic pain (n=4), human immunodeficiency virus (HIV) (n=1), irritable bowel syndrome (IBS) (n=1), metabolic disorders (n=2), chronic obstructive pulmonary disorder (COPD) (n=1), tinnitus (n=1), as well as healthy adults (n=1), older persons (n=1), transplant recipients (n=1), nicotine-addicted adults (n=1), and insomniacs (n=1) (Table 4).

The interventions included mindfulness-based stress reduction (MBSR) (n=11), stress/pain management (n=1), and mindfulness-based cognitive therapy (MBCT) (n=4), as well as transcendental meditation (n=8), mantra meditation (n=3), mindfulness training (n=2), mindfulness as treatment (n=1), mindfulness meditation (n=2), mindfulness-based relapse prevention (n=1), and Metta meditation (n=1) (Table 4).

Trials took place in various countries (United States (U.S.) trials (n=23) ; Non-U.S. trials (n=11)) (Table 4).

Since the amount of training and practice in any meditation program may affect its results, we collected this information and found a fair range in the quality of information reported. Not all trials reported on amount of training and home practice recommended. In general, MBSR programs provided 20-27.5 hours of training over 8 weeks. The modified mindfulness trials generally provided about half this level of training (between 8 to 13.5 hours of training over 4 to 8 weeks) as did other mantra programs (7.5-8 hours of training over 5-8 weeks). Transcendental meditation trials generally provided more training (16-39 hours) over longer periods of time (3-12 months) (Tables 5 -6).

Most trials did not describe the specific expertise of the trainers. Only four of the trials reported the trainers' actual meditation experience (ranging between 4 months-25 years) and five reported the trainers' actual teaching experience (ranging between 0-7 years).

Seven trials were rated as low risk of bias, 19 as medium risk of bias, and 8 as high risk of bias (Table 7).

Table 4. Characteristics of included trials

Author, Year	Study Objective	Sample Size (N)	Study Location	Medical or Psychiatric Condition of the Study Population	Intervention and Comparator	Outcome(s) (KQs)
Mindfulness Meditation						
Brewer, 2009 ⁴²	The goals of the study were to assess group MT compared with CBT in substance use and treatment acceptability, and specificity of MT compared with CBT in targeting stress reactivity.	36	U.S.	Patients with alcohol and/or cocaine use disorders	Group MT vs. specific active control (CBT)	Substance use - alcohol and/or cocaine (KQ 3) Adverse Events
Brewer, 2011 ⁴³	The aim of this study was to evaluate the effect of mindfulness training on smoking cessation through randomized clinical trials.	88	U.S.	Nicotine-dependent adults with interest in smoking cessation	MT vs. specific active control (American Lung Association's (FFS) treatment)	Substance use (KQ 3) Adverse Events
Delgado L.C., 2010 ⁴⁴	The objective was to examine psychological and physiological indices of emotional regulation in non-clinical high worriers after a mindfulness-based training program aimed at reducing worry.	36	Spain	Patients with chronic worry	MBCT/modified MBCT vs. specific active control (progressive muscle relaxation)	Worry (KQ 1) General distress (KQ1) Positive mood (KQ 1)
Garland E. L., 2010 ⁴⁵	The objective was to assess the effect of MT to disrupt the risk chain of stress-precipitated alcohol relapses.	53	U.S.	Alcohol-dependent adults	Mindfulness-based interventions vs. NSAC (alcohol abstinence support group)	Stress (KQ 1) General Distress (KQ 1) Substance use (KQ 3)
Gaylord S.A., 2011 ⁴⁶	The aim of this study was to assess the feasibility and efficacy of a group program of mindfulness training, a	97- 22 dropped before intervention started. (75)	U.S.	Women with Irritable Bowel Syndrome	MBSR vs. specific active control (IBS support group)	Depression (KQ 1) General distress (KQ 1) Pain severity (KQ 4)

Author, Year	Study Objective	Sample Size (N)	Study Location	Medical or Psychiatric Condition of the Study Population	Intervention and Comparator	Outcome(s) (KQs)
	cognitive behavioral technique, for women with IBS.					Adverse Events
Gross C.R., 2010 ⁴⁷	The aim of this study was to assess the efficacy of MBSR in reducing symptoms of anxiety, depression, and poor sleep in transplant patients.	150	U.S.	Solid organ transplant recipients	MBSR vs. NSAC (peer-led health education)	Anxiety (KQ 1) Depression (KQ 1) Positive mood (KQ 1) QOL (KQ 1) Sleep (KQ 3) Pain severity (KQ 4) Adverse Events
Gross C.R., 2011 ⁴⁸	The aim of this study was to investigate the potential of MBSR as a treatment for chronic primary insomnia.	30	U.S.	Adults with primary chronic insomnia	MBSR vs. specific active control (PCT with eszopiclone)	Anxiety (KQ 1) Depression (KQ 1) QOL (KQ 1) Sleep (KQ 3) Adverse Events
Hebert J.R., 2001 ⁴⁹	The aim of this study was to determine the effectiveness of an intensive dietary intervention on diet and body mass in women with breast cancer.	172	U.S.	Patients with breast cancer	MBSR-based clinic program vs. NSAC (NEP)	Eating (KQ 3) Weight (KQ 4)
Henderson V.P., 2011 ⁵⁰	The objective of this study was to determine the effectiveness of a MBSR program on QOL and psychosocial outcomes in women with early-stage breast cancer, using a three-	172	U.S.	Women with early stage breast cancer	MBSR vs. NSAC (NEP)	Anxiety (KQ 1) Thoughts/emotion suppression (KQ 1) Depression (KQ 1) Subjective well-being (KQ

Author, Year	Study Objective	Sample Size (N)	Study Location	Medical or Psychiatric Condition of the Study Population	Intervention and Comparator	Outcome(s) (KQs)
	armed randomized controlled clinical trial.					1)
Koszycki D., 2007 ⁵¹	The objective was to evaluate how well MBSR compared with a first-line psychological intervention works for the treatment of SAD	53	Canada	Patients with generalized social anxiety disorder	MBSR vs. specific active control (CBT)	Social anxiety (KQ 1) Depression (KQ 1)
Kuyken W., 2008 ⁵²	The objective was to determine if, among patients with recurrent depression who are treated with antidepressant medication, MBCT is comparable to treatment with m-ADM in (a) depressive relapse prevention, (b) key secondary outcomes, and (c) cost effectiveness.	123	U.K.	Patients with depression	MBCT vs. specific active controls (antidepressant tapering or M-ADM)	Depression (KQ 1) QOL (KQ 1) Adverse Events
Lee S.H., 2006 ⁵³	The objective was to examine the effectiveness of a MBSR program in patients with anxiety disorder.	46	South Korea	Patients with generalized anxiety disorder or panic disorder	MBSR vs. NSAC (anxiety disorder education program)	Anxiety (KQ 1)
Moritz S., 2006 ⁵⁴	The objective was to evaluate the efficacy of a home study-based spirituality program on mood disturbance in emotionally distressed patients.	165	Canada	Patients with psychological distress	MBSR vs. specific active controls (spirituality)	Anxiety (KQ 1) Depression (KQ1) General distress (KQ 1) Positive mood (KQ 1) QOL (KQ 1) Pain severity (KQ 4)
Morone N. E.,	The aim of this study	40	U.S.	Community	MBSR	Pain severity (KQ 4)

Author, Year	Study Objective	Sample Size (N)	Study Location	Medical or Psychiatric Condition of the Study Population	Intervention and Comparator	Outcome(s) (KQs)
2009 ⁵⁵	was to assess 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 to test the education control program for feasibility.			dwelling older adults with chronic low back pain	vs. NSAC (health education program)	Pain interference (KQ 4) Adverse Events
Mularski R. A., 2009 ⁵⁶	The objective was to test the efficacy of MBBT (a hybrid of the Relaxation Response training and MBSR training) on improving Symptoms and health-related QOL in those with COPD.	86	U.S.	Patients with COPD	MBBT vs. NSAC (support group)	Stress (KQ 1) QOL (KQ 1)
Oken B.S., 2010 ⁵⁷	The objective was to evaluate whether a mindfulness meditation intervention may be effective in caregivers of close relatives with dementia and to help refine the protocol for future larger trials.	31	U.S.	Caregivers of close relatives with dementia	MBCT vs. NSAC (education or respite care)	Depression (KQ 1) Stress (KQ 1) Attention (KQ 2)
Philippot P., 2011 ⁵⁸	The objective of this randomized clinical trial was to examine the relative effectiveness of two psychological interventions for treating tinnitus.	30	Belgium	Patients with tinnitus	MBCT/ modified MBCT vs. specific active controls (relaxation training or CBT)	Anxiety (KQ 1) Depression (KQ1) Attention (KQ 2)
Piet J., 2010 ⁵⁹	The aim of the study was to pilot test MBCT alone and in	26	Denmark	Adults with social phobia	MBCT/modified MBCT vs.	Social anxiety (KQ 1) Depression (KQ 1)

Author, Year	Study Objective	Sample Size (N)	Study Location	Medical or Psychiatric Condition of the Study Population	Intervention and Comparator	Outcome(s) (KQs)
	combination with CBGT for young adults with social phobia.				relaxation training specific active control (CBT)	General distress (KQ 1)
Pipe T. B., 2009 ⁶⁰	The aim of this study was to rigorously evaluate a brief stress management intervention for nurse leaders.	33	U.S.	Stressed Nurse Leaders	MBSR vs. Leadership Control Group	Anxiety (KQ 1) Depression (KQ 1) Gen Distress (KQ 1)
Plews-Ogan M., 2005 ⁶¹	The aim of this study was to assess the feasibility of studying MBSR and massage for the management of chronic pain and to estimate their effects on pain and mood.	30	U.S.	Patients with chronic musculoskeletal pain	MBSR vs. specific active control (weekly massage)	Subjective well-being (KQ 1) Pain severity (KQ 4)
Schmidt S., 2010 ⁶²	The aim of this study was to study the efficacy of MBSR for enhanced well-being of fibromyalgia patients investigated in a three-armed trial.	177	Germany	Women with fibromyalgia	MBSR vs. specific active controls (progressive muscle relaxation and stretching)	Anxiety (KQ 1) Depression (KQ 1) Sleep (KQ 3) Pain severity (KQ 4)
Segal Z.V., 2010 ⁶³	The objective was to compare rates of relapse in depressed patients in remission receiving MBCT against maintenance antidepressant pharmacotherapy, the current standard of care.	84	Canada	Patients with recurrent depression	MBCT vs. specific active control (maintenance antidepressant therapy)	Depression (KQ 1)
Wong S.Y-S., 2011 ⁶⁴	The objective of this study was to compare the clinical effectiveness of the MBSR program with an MPI program in	99	Hong Kong	Patients with chronic pain	MBSR vs. specific active control (MPI)	Anxiety (KQ 1) Depression (KQ 1) QOL (KQ 1)

Author, Year	Study Objective	Sample Size (N)	Study Location	Medical or Psychiatric Condition of the Study Population	Intervention and Comparator	Outcome(s) (KQs)
	terms of pain intensity, pain-related distress, QOL, and mood in patients with chronic pain.					Pain severity (KQ 4)
Mantra Meditation						
Alexander, 1989 ⁶⁵	The aim of this study was to determine whether direct change in state of consciousness through specific mental techniques can extend human life and reverse age-related declines.	73	U.S.	Elderly	Mantra meditation vs. (relaxation program and TM)	Attention (KQ 2)
Bormann J.E., 2006 ⁶⁶	The objective was to examine the efficacy of a psycho-spiritual intervention of mantra repetition - a word or phrase with spiritual associations repeated silently throughout the day – on psychological distress (intrusive thoughts, stress, anxiety, anger, and depression), QOL enjoyment, satisfaction, and existential spiritual well-being in HIV-infected adults.	93	U.S.	Adults with HIV infection	Mantra Meditation vs. NSAC (education)	Anxiety (KQ 1) Stress (KQ 1) Depression (KQ 1)
Castillo-Richmond, 2000 ⁶⁷	To determine if stress reduction with the TM program can decrease CHD risk factors and cardiovascular mortality in African Americans.	138	U.S.	Hypertension (high normal blood pressure, stage I, or stage II hypertension)	TM vs. NSAC (health education)	Substance use - smoking (KQ 3) Weight (KQ 4)
Elder, 2006 ⁶⁸	The aim of this study was to assess the	60	U.S.	Diabetic patients in primary care setting	TM vs.	Weight (KQ 4)

Author, Year	Study Objective	Sample Size (N)	Study Location	Medical or Psychiatric Condition of the Study Population	Intervention and Comparator	Outcome(s) (KQs)
	feasibility and clinical impact of a whole-system, Ayurvedic intervention for newly diagnosed people with type 2 diabetes.				NSAC (diabetes education classes)	Adverse Events
Jayadevappa R., 2007 ⁶⁹	The objective was to evaluate the effectiveness of a TM stress reduction program for African Americans with CHF.	23	U.S.	African American patients with CHF	TM vs. NSAC (health education)	Stress (KQ 1) Depression (KQ 1) Subjective well-being (KQ 1) Positive mood (KQ 1) Pain severity (KQ 4)
Lehrer P.M., 1983 ⁷⁰	The objective was to compare mantra meditation and progressive relaxation treatments and their effect on anxiety among anxious participants.	61	U.S.	Adults with anxiety	Mantra meditation vs. specific active control (relaxation program)	Anxiety (KQ 1) Depression (KQ 1)
Murphy TJ, 1986 ⁷¹	The aim of this study was to assess the effects of exercise and meditation on alcohol consumption in social drinkers.	60	U.S.	High-volume drinkers	Mantra meditation vs. specific active control (running (exercise))	Substance use - alcohol (KQ 3)
Paul-Labrador M., 2006 ⁷²	The objective was to evaluate the efficacy of TM on components of the metabolic syndrome and CHD.	103	U.S.	Patients with stable CHD	Mantra Meditation vs. NSAC (health education)	Anxiety (KQ 1) Depression (KQ 1) Stress (KQ 1) Adverse Events
Sheppard W.D., 1997 ⁷³	The objective was to compare the effect of TM and a CSM program on the reduction of	44	U.S.	Employees working in a high stress environment inside a high security	Mantra meditation vs. NSAC (CSM)	Anxiety (KQ 1) Depression (KQ 1)

Author, Year	Study Objective	Sample Size (N)	Study Location	Medical or Psychiatric Condition of the Study Population	Intervention and Comparator	Outcome(s) (KQs)
	stress among high-security government agency workers.			government agency		
Smith J.C., 1976 ⁷⁴	The objective was to assess whether the crucial therapeutic component of TM is or is not the TM exercise	139	U.S.	Anxious college students	Mantra meditation vs. NSAC (relaxation program)	Anxiety (KQ 1)
Taub E., 1994 ⁷⁵	The objective was to assess whether TM has an effect on relapse prevention in alcoholics.	125	U.S.	Alcoholics in recovery program	TM vs. SAC Biofeedback	Substance Use (KQ3)

CBT = Cognitive Behavioral Therapy; CBGT = Cognitive Behavioral Group Therapy; FFS = Freedom from Smoking; M-ADM = Maintenance Antidepressant Mono-Therapy; MBBT = Mindfulness-based Breathing Therapy; MBCT = Mindfulness-based Cognitive Therapy; MBSR = Mindfulness-based Stress Reduction; MPI = Multidisciplinary Pain Intervention; MT = Mindfulness Training; NEP = Nutrition Education Program; PCT = Pharmacotherapy; TM = Transcendental Meditation; CHF = Congestive Heart Failure; IBS = Irritable Bowel Syndrome; MPI = Meditation Practice Institute; SAD = Social Anxiety Disorder, QOL = Quality of Life; COPD = Chronic Obstructive Pulmonary Disorder; CHD = Chronic Heart Disease; HIV = Human Immunodeficiency Virus; KQ = Key Question; NSAC = Non-specific Active Control; SAC = Specific Active Control; CSM = Clinically Standardized Meditation

Table 5. Training dose for included trials over duration of training period (numbers are calculated from information provided in trials)

Author, Year	Intervention	Training Duration (weeks)	Total Training Dose (hours)	Recommended Home Practice over Training Period (hours)
Mindfulness Meditation				
Brewer, 2009 ⁴²	MB Relapse Prevention	9	9	NP
Brewer, 2011 ⁴³	MM	4	12	NP
Delgado L.C., 2010 ⁴⁴	MM	5	10	NP
Garland E. L., 2010 ^{45**}	MBCT	10	NP	NP
Gaylord S.A., 2011 ^{46*}	MM	8	23	NP
Gross C.R., 2010 ^{47*}	MBSR	8	27	NP
Gross C.R., 2011 ⁴⁸	MBSR	8	26	36
Hebert J.R., 2001 ^{49*}	MM	15	45	NP
Henderson V.P., 2011 ⁵⁰	MBSR	8	25	NP
Koszycki D., 2007 ⁵¹	MBSR	8	27.5	28
Kuyken W., 2008 ^{52*}	MBCT	8	24	37.5
Lee S.H., 2006 ⁵³	MM	8	8	NP
Moritz S., 2006 ^{54*}	MBSR	8	12	NP
Morone N. E., 2009 ⁵⁵	MM	8	12	42
Mularski R. A., 2009 ⁵⁶	MBBT	8	8	NP
Oken B.S., 2010 ⁵⁷	MBSR/MBCT	7	9	NP
Philippot P., 2011 ⁵⁸	MM	6	13.5	NP
Piet J., 2010 ⁵⁹	MBCT	8	16	28
Pipe T. B., 2009 ⁶⁰	MBSR	5	10	17.5
Plews-Ogan M., 2005 ⁶¹	MBSR	8	20	NP
Schmidt S., 2010 ⁶²	MBSR	8	27	42
Segal Z.V., 2010 ^{63*}	MBCT	8	23	NP
Wong S.Y-S, 2011 ⁶⁴	MBSR	8	27	NP
Mantra Meditation				
Alexander, 1989 ^{65**}	TM	12	NP	56.3
Bormann J.E., 2006 ⁶⁶	Mantra	5	7.5	NP
Castillo-Riachmond, 2000 ^{67**}	TM	1	NP	120.6
Elder, 2006 ^{68**}	TM	NP	NP	90
Jayadevappa R., 2007 ^{69*}	TM	24	22.5	90
Lehrer P.M., 1983 ⁷⁰	Mantra	5	7.5	NP
Murphy, 1986 ⁷¹	Mantra	8	8	37.52
Paul-Labrador M., 2006 ⁷²	TM	16	39	NP
Sheppard W.D., 1997 ⁷³	TM	12	16	56.3
Smith J.C., 1976 ^{74**}	TM	25	NP	87.5
Taub E., 1994 ⁷⁵	TM	4	19	NP

* These studies did not explicitly describe training amounts. Numbers were estimated from available information.

** These studies did not give enough information to estimate or calculate training dose.

NP=Not Provided; MBSR = Mindfulness-based Stress Reduction; MBCT = Mindfulness-based Cognitive Therapy; MBRP = Mindfulness-based Relapse Prevention; MBBT = Mindfulness-based Breathing Therapy; MM = Mindfulness Meditation, typically a variant of MBSR; TM = Transcendental Meditation

Table 6. Teacher qualifications for included trials

Author, Year	Intervention	Teacher Trained in Meditation Technique?	Certified?	Years of Meditation Experience?	Years of Teaching Experience in Meditation?
Mindfulness Meditation					
Brewer, 2009 ⁴²	MBRP	Y	NP	12	Several
Brewer, 2011 ⁴³	MM	Y	NP	>13	NP
Delgado, 2010 ⁴⁴	MM	NP	NP	NP	NP
Garland, 2010 ⁴⁵	MBCT	NP	NP	NP	NP
Gaylord, 2011 ⁴⁶	MM	Y	NP	NP	NP
Gross, 2010 ⁴⁷	MBSR	Y	NP	NP	NP
Gross, 2011 ⁴⁸	MBSR	Y	Y	NP	NP
Herbert, 2001 ⁴⁹	MM	NP	NP	NP	NP
Henderson V.P., 2011 ⁵⁰	MBSR	Y	NP	NP	NP
Koszycski D., 2007 ⁵¹	MBSR	Y	NP	NP	NP
Kuyken, 2008 ⁵²	MBCT	Y	Y	NP	NP
Lee, 2006 ⁵³	MM	Y	NP	NP	5
Moritz, 2006 ⁵⁴	MBSR	NP	NP	NP	NP
Morone, 2009 ⁵⁵	MM	Y	Y	25	Y
Mularski, 2009 ⁵⁶	MBBT	Y	Y	Several	Several
Oken, 2010 ⁵⁷	MBSR/MBCT	Y	NP	NP	NP
Philippot, 2011 ⁵⁸	MM	Y	NP	3	NP
Piet, 2010 ⁵⁹	MBCT	Y	NP	NP	NP
Pipe, 2009 ⁶⁰	MBSR	Y	NP	NP	NP
Plews-Ogan, 2005 ⁶¹	MBSR	NP	NP	NP	NP
Schmidt S., 2010 ⁶²	MBSR	Y	Y	NP	7
Segal, 2010 ⁶³	MBCT	Y	Y	NP	NP
Wong, 2011 ⁶⁴	MBSR	Y	NP	NP	NP
Mantra Meditation					
Alexander, 1989 ⁶⁵	TM	Y	Y	NP	NP
Borman, 2006 ⁶⁶	Mantra	Y	NP	NP	NP
Castillo-Richmond, 2000 ⁶⁷	TM	NP	Y	NP	NP
Elder, 2006 ⁶⁸	TM	Y	NP	NP	NP
Jayadevappa, 2007 ⁶⁹	TM	Y	Y	NP	NP
Lehrer, 1983 ⁷⁰	Mantra	Y	NP	0.33	0
Murphy, 1986 ⁷¹	Mantra	NP	NP	Y	NP
Paul-Labrador, 2006 ⁷²	TM	Y	NP	NP	NP
Sheppard, 1997 ⁷³	TM	Y	Y	NP	NP
Smith, 1976 ⁷⁴	TM	Y	Y	NP	NP
Taub, 1994 ⁷⁵	TM	Y	Y	NP	NP

NP=Not Provided; MBSR = Mindfulness-based Stress Reduction; MBCT = Mindfulness-based Cognitive Therapy; MBRP = Mindfulness-based Relapse Prevention; MBBT = Mindfulness-based Breathing Therapy; MM = Mindfulness Meditation, typically a variant of MBSR; TM = Transcendental Meditation

Table 7. Risk of bias for included trials

Author, Year	Major Criteria				Minor Criteria				Score	ROB
	Q1: Matched for time / attention	Q2: Withdrawals & Dropouts described	Q3 Attrition less than 20%	Q4: Single Blinding	Q5: random- ization method	Q6: AC	Q7: ITT	Q8: credibility comparable		
Mindfulness										
Brewer,2009 ⁴²	1	1	0	0	1	0	0	1	6**	High
Brewer, 2011 ⁴³	1	1	0	0	1	0	0	0	5	High
Delgado L.C., 2010 ⁴⁴	1	1	1	0	0	0	0	0	6	Medium
Garland E. L., 2010 ⁴⁵	1	1	0	1	0	0	0	1	7	Medium
Gaylord S.A., 2011 ⁴⁶	1	1	0	1	1	0	0	1	8	Medium
Gross C.R., 2010 ⁴⁷	1	1	1	0	1	0	0	0	7	Medium
Gross C.R., 2011 ⁴⁸	1	1	1	0	1	1	0	0	8	Medium
Hebert J.R., 2001 ⁴⁹	1	1	1	0	0	0	0	0	6	Medium
Henderson V.P., 2011 ⁵⁰	1	1	1	0	1	0	0	0	7	Medium
Koszycki D., 2007 ⁵¹	1	1	0	0	0	0	1	0	5	High
Kuyken W., 2008 ⁵²	1	1	1	1	1	0	1	0	10	Low
Lee S.H., 2006 ⁵³	1	1	1	0	0	0	1	0	7	Medium
Moritz S., 2006 ⁵⁴	1	1	1	0	1	1	1	0	9	Low
Morone N. E., 2009 ⁵⁵	1	1	1	1	1	1	0	1	11	Low
Mularski R. A., 2009 ⁵⁶	1	1	0	0	1	1	0	1	7**	High
Oken B.S., 2010 ⁵⁷	1	1	0	1	1	0	0	1	8	Medium
Philippot P., 2011 ⁵⁸	1	1	1	0	1	0	0	0	7	Medium
Piet J., 2010 ⁵⁹	1	1	1	0	1	0	1	0	8	Medium
Pipe T. B., 2009 ⁶⁰	1	1	1	0	1	0	0	0	7	Medium
Plews-Ogan M., 2005 ⁶¹	1	1	0	0	1	0	0	0	5	High
Schmidt S., 2010 ⁶²	1	1	1	0	1	1	0	0	8	Medium
Segal Z.V., 2010 ⁶³	1	1	0	1	1	1	1	0	9	Low
Wong S.Y-S, 2011 ⁶⁴	1	1	1	1	1	1	1	0	11	Low

Author, Year	Major Criteria				Minor Criteria				Score	ROB
	Q1: Matched for time / attention	Q2: Withdrawals & Dropouts described	Q3 Attrition less than 20%	Q4: Single Blinding	Q5: random- ization method	Q6: AC	Q7: ITT	Q8: credibility comparable		
Mantra										
Alexander, 1989 ⁶⁵	1	0	0	1	1	1	0	1	7	Medium
Bormann J.E., 2006 ⁶⁶	1	1	0	0	1	0	1	0	6	Medium
Castillo-Richmond, 2000 ⁶⁷	1	1	0	1	1	0	0	0	7*	High
Elder, 2006 ⁶⁸	0	1	1	0	1	1	0	0	6	Medium
Jayadevappa R., 2007 ⁶⁹	1	1	1	1	1	0	1	0	10	Low
Lehrer P.M., 1983 ⁷⁰	1	1	1	0	0	0	0	1	7	Medium
Murphy TJ, 1986 ⁷¹	1	1	0	0	1	0	0	0	5	High
Paul-Labrador M., 2006 ⁷²	1	1	1	1	1	0	0	0	9	Low
Sheppard W.D., 1997 ⁷³	1	1	0	1	0	0	0	0	6	Medium
Smith J.C., 1976 ⁷⁴	1	1	0	0	1	0	0	0	5	High
Taub E., 1994 ⁷⁵	1	1	1	0	1	0	0	0	7	Medium

Major Criteria: Q 1: Was the Control Matched for Time and Attention by the Instructors? Q2: Was There a Description of Withdrawals and Dropouts? Q3: Was Attrition <20% at the End of Treatment? Q4: Single blinding employed?

Minor Criteria: Q5: Was the Method of Randomization Described in the Paper? Q6: Was Allocation Concealed? Q7: Was ITT Used? Q8: Was the Credibility Comparable? ROB = Risk of Bias.

Score calculated by multiplying each major criteria by two and then adding across all eight questions. < 6= high ROB, 6-8 = medium ROB, 9-12 = low ROB.

* Scored as high due to uncertain sampling method

** Scored as high due to very high attrition, 42% for Mularski and 61% for Brewer

Key Question Results

Since there were numerous scales for the different measures of affect, as well as subgroups within each affect, the scales reported upon were organized to best represent the clinically relevant aspects of each affect. For this review, the comparisons with non-specific active controls were the most meaningful as they allowed a consistent comparison with a similar control group across all outcomes. Comparisons with specific active controls were much more difficult to draw conclusions from due to the large heterogeneity of type and strength of control groups. Therefore, our results are presented first for all the comparisons with non-specific active controls, and then for the specific active controls.

Key Question 1. What are the efficacy and harms of meditation programs on negative affect (e.g. anxiety, stress) and positive affect (e.g. well being) among those with a clinical condition (medical or psychiatric)?

Key Points and Evidence Grades

Comparisons with Non-specific Active Controls

Anxiety

- The strength of evidence is low that mindfulness meditation programs result in a small improvement in anxiety among various clinical populations when compared with a non-specific active control. We based this rating on overall medium risk of bias, consistent findings for a small positive effect, directness of measures, and imprecise estimates.
- The strength of evidence is low that mantra meditation programs result in a small improvement in anxiety among various clinical populations when compared with a non-specific active control. We based this rating on overall medium risk of bias, inconsistent findings, directness of measures, and precise estimates.

Depression

- The strength of evidence is low that mindfulness meditation programs improve symptoms of depression among various clinical populations when compared with a non-specific active control. We based this rating on overall medium risk of bias, consistent findings for a positive effect, directness of measures, and imprecise estimates.
- The strength of evidence is insufficient that mantra meditations have an effect on symptoms of depression among various clinical populations when compared with a non-specific active control. We based this rating on overall medium risk of bias, inconsistent findings, directness of measures, and imprecise estimates.

Stress/Distress

- The strength of evidence is low that mindfulness meditation programs result in a small improvement in stress and distress among various clinical populations when compared with a non-specific active control. We based this rating on overall medium risk of bias, consistent findings, directness of measures, and imprecise estimates.
- The strength of evidence is low that mantra meditation programs have no effect on stress when compared with a non-specific active control. We based this rating on overall medium risk of bias, consistent findings of a null effect, directness of measures, and imprecise estimates.

Negative Affect

- The strength of evidence is low that mindfulness meditation programs improve negative affect among various clinical populations when compared with a non-specific active control. We based this rating on overall medium risk of bias, consistent results, indirect measures of negative affect, and precise estimates.
- The strength of evidence is insufficient that mantra programs have an effect on negative affect among various clinical populations when compared with a non-specific active control. We based this rating on overall medium risk of bias, inconsistent results, indirect measures of negative affect, and imprecise estimates.

Positive Affect

- The strength of evidence is insufficient that mindfulness meditation programs have an effect on positive affect when compared with a non-specific active control. We based this rating on medium risk of bias, inconsistent findings, indirect measures, and imprecise estimates.
- The strength of evidence is insufficient about the effects of transcendental meditation on positive affect when compared with a non-specific active control. We based this rating on a single low risk of bias study, unknown consistency, indirect measures, and imprecise estimates.

Mental Component of Health-related Quality of Life

- The strength of evidence is insufficient that mindfulness meditation programs have an effect on the mental component of health-related quality of life when compared with a non-specific active control. We based this rating on overall high risk of bias, consistent findings, direct measures, and imprecise estimates.

Comparisons with Specific Active Controls

Anxiety

- The strength of evidence is insufficient that mindfulness meditation programs have an effect on anxiety among various clinical populations when compared with a variety of specific active controls. We based this rating on overall medium risk of bias, inconsistent findings, directness of measures, and imprecise estimates.
- The strength of evidence is insufficient about the effects of clinically standardized meditation on anxiety in an anxious population when compared with progressive muscle relaxation. We

based this rating on a single study with medium risk of bias, unknown consistency, directness of measures, and imprecise estimates.

Depression

- The strength of evidence is insufficient that mindfulness meditation programs have an effect on depressive symptoms among various clinical populations compared with a variety of specific active controls. We based this rating on overall medium risk of bias, inconsistent results, direct measures, and imprecise estimates.
- The strength of evidence is insufficient that clinically standardized meditation has an effect on depressive symptoms in an anxious population compared with progressive muscle relaxation. We based this rating on a single study with medium risk of bias, unknown consistency, direct measures, and imprecise estimates.

Stress/Distress

- The strength of evidence is low that mindfulness meditation programs do not improve distress among those with mood disturbance or symptoms of anxiety compared with a variety of specific active controls. We based this rating on overall medium risk of bias, consistent results, direct measures, and imprecise estimates.

Positive Affect

- The strength of evidence is insufficient that mindfulness meditation programs have an effect on positive affect among those with a mood disturbance or symptoms of anxiety when compared with a variety of specific active controls. We based this rating on overall medium risk of bias, inconsistent findings, indirect measures, and imprecise estimates.

Mental Component of Health-related Quality of Life

- The strength of evidence is insufficient that mindfulness meditation programs have an effect on the mental component of health related quality of life among various clinical populations when compared with a variety of specific active controls. We based this rating on overall medium risk of bias, inconsistent findings, direct measures, and imprecise estimates.

Harms (All trials in key question1)

- Four studies reported on adverse events, but participants experienced no adverse events and 22 studies did not report on adverse events.

Trial Characteristics

We included 26 trials for this key question, of which 15 took place in the U.S. Three trials took place in Canada. Six trials took place in Europe, including Belgium, the United Kingdom (two trials), Spain, Denmark, and Germany. The remaining two trials were done in Hong Kong and South Korea. Sixteen of the trials took place in an outpatient setting, two in an inpatient or hospital setting, two in a university setting, and one in multiple settings; five trials did not report the setting or it was unclear.

Six trials explicitly reported the time period of recruitment. The year when recruitment started ranged from 2000 to 2008 in these trials. Twenty-three of 26 trials reported the trial

duration; it ranged from four weeks to three years. Twenty-one trials reported the length of treatment as well as followup information, with length of treatment ranging from 1 week to 4 months. Length of additional followup after treatment ranged from none (i.e. treatment assessed at its end) to three years.

Three trials excluded patients with past or present substance abuse, eight trials excluded patients with psychiatric conditions, and 10 trials excluded patients according to some medical diagnostic criteria (Appendix E, Evidence Table 2). Most trials (N=16) were of medium risk of bias, four were of high risk of bias, and only six were of low risk of bias.

Population Characteristics

The majority of trials recruited populations with chronic medical conditions, anxiety, or depression. Information was not available for the majority of trials on racial, ethnic, education, or gender composition.

The sample size of the trials ranged from 23 to 180, with a median sample size of 60. In nine trials the participants were from populations with psychiatric disorders, and in 16 trials the participants were from medical populations, including substance abuse, chronic pain, and fibromyalgia. Of the trials in medical populations, three trials were of subjects with acute or chronic pain or fibromyalgia;^{55 61 62 64} six trials were of subjects with anxiety disorders, anxiety trait, or worry;^{44 51 53 59 70 74} two trials were of subjects with depression;^{52 63} and 10 trials were of subjects with chronic medical conditions, including metabolic syndrome, COPD, HIV, and congestive heart failure.^{46-48 50 56-58 66 69 72} Nineteen trials provided information on the gender characteristics of the participants. In four trials, the population was 100 percent female.^{44 46 50 62} The median percentage of female participants in the remaining trials was 33 percent.

Twenty-two trials provided information on the age distribution of the trial population. The mean age in these trials ranged from 18.7 to 67.7 years (median=48). Only 12 trials provided information on racial or ethnic characteristics of their trial population. The proportion of white subjects among these populations ranged from 0 percent (in a trial of African Americans with congestive heart failure) to 95 percent.⁶⁹ Fifteen trials provided information on the level of completed education among trial participants (Appendix E, Evidence Table 3).

Intervention Characteristics

In the intervention arms, nine trials administered mindfulness-based stress reduction (MBSR), three administered mindfulness-based cognitive therapy (MBCT), seven administered a mindfulness variant, five administered transcendental meditation, and two administered other mantra meditations.

Mindfulness Trials

All the mindfulness trials conducted a weekly training session that ran for 6 to 8 weeks. Exceptions include one mindfulness meditation trial that ran for four weeks on stressed employees,⁶⁰ another that ran for 5 weeks on high worriers,⁴⁴ and one that ran for 10 weeks on alcohol-dependent people.⁴⁵ The ten mindfulness-based stress reduction (MBSR) trials provided training that generally ranged from 20 to 27.5 hours except for two trials. One used MBSR as a control group for a spirituality intervention; we estimated the maximal training time for that trial at 12 hours.⁵⁴ Another trial ran it for 15 weeks and we estimate the maximal training at 45 hours.⁴⁹ All MBSR trials, except two,^{50 49} noted that they provided homework. Three MBSR

trials specified the amount of homework, which ranged from 28-42 hours over an 8-week period. Seven of ten trials noted that the teachers were trained; two noted they were certified, and two trials noted that their teachers had between 5 and 7 years of teaching experience. Two trials did not report on teacher qualifications. Four of the trials used a non-specific active control and four used a specific active control.

For the three mindfulness-based cognitive therapy (MBCT) trials, the amount of meditation training ranged from 16 to 24 hours over an 8-week period. All three recommended home practice, and two specified the amount, which ranged from 28-37.5 hours over the 8-week period. One reported the teacher was trained, and two reported the teachers were trained and certified. None gave details on amount of meditation or teaching experience. All three used a specific active control (Table 5).

Among the remaining nine mindfulness-variant trials, the amount of training ranged from 8 to 13.5 hours over 4 to 9 weeks. All except one recommended home practice and two trials specified the amount of home practice, which ranged from 14-17.5 hours over the training period. Six of seven trials reported that their teachers were trained; one reported that the teacher was also certified, and two noted that the amount of teaching experience ranged from 3 to 5 years. One trial did not report anything regarding teacher qualifications. Five used a non-specific active control and two used a specific active control (Table 6).

Mantra Trials

The five transcendental meditation trials generally had a different format for training.^{65 69 72-74} There was an initial period of daily training for 1 to 1.5 hours for about 1 week, followed by periodic checks lasting 30-60 minutes over the followup period. Two transcendental meditation trials did not give enough information to calculate a training amount. All trials recommended daily homework, ranging from 56.3 hours for the two 3-month trials to 90 hours for the two 6-month trials. The transcendental meditation trials all use trained and certified teachers, although none specified the amount of meditation or teaching experience these teachers had. All five trials used a non-specific active control.

Two trials used a mantra and were not of the transcendental meditation tradition. Bormann et al. used mantras representing various spiritual traditions, based on the Easwaran approach.^{66 76} Lehrer et al. used a clinically standardized meditation program.⁷⁰ Both trials consisted of no more than 7.5 hours of training over a 5-week period, with instructions to practice at home. Both studies reported that teachers were trained. The teachers for clinically standardized meditation were undergraduate and graduate students who had four months of training and had no prior meditation teaching experience.

Outcomes

Comparisons with Non-specific Active Controls

Anxiety

Six mindfulness meditation programs and five mantra meditation programs trials examined the effect of the meditation program on anxiety as compared with a non-specific active control.^{46 47 50 53 60 62 46-48 51 54 60 62 64} The trials included in this analysis used four measures of anxiety. We selected measures that are widely used in trials of anxiety, giving preference to those that most of

the other trials in their comparison group used. This was to maintain as much homogeneity in the outcome scale as possible (Appendix E).

One mindfulness meditation program trial found nonsignificant results for its anxiety measure and did not report the data.⁵⁰ Another mindfulness meditation program trial did not report enough information to make quantitative comparisons.⁶⁰

Mindfulness Meditation Programs versus Non-specific Active Controls

Six trials compared mindfulness meditation programs to non-specific active controls for this outcome, and tended to show a small effect (Figure 4). Four were mindfulness-based stress reduction (MBSR) trials and two were modified versions of MBSR. Three trials used State Trait Anxiety Inventory, while others used the Brief Symptom Inventory Anxiety Subscale (BSI-18), Symptom Checklist-90 Anxiety Subscale (SL-90), and Beck Anxiety Inventory (BAI) scale. The four MBSR trials gave an equivalent amount of training, ranging from 23-27 hours, while the modified mindfulness trials gave 8 hours of training. The trials did not give enough information on the amount of home practice recommended or completed.

Among the trials that reported scores, a difference-in-change calculation shows that all had a 4 to 15.5 percent improvement post intervention (eight weeks), and a 4.6 to 6.8 percent improvement at the end of the trial (3-6 months). The trial conducted in Korea showed statistically significant results by the end of treatment, and the results reached statistical significance at the end of the study period for two other trials.

Gross et al. randomized patients with an organ transplant (n=138) to 8 weeks of MBSR or health education arms.⁴⁷ Anxiety was a primary outcome measure and it saw non-significant changes at 8 weeks and 6 months. Schmidt et al. randomized women with fibromyalgia (n=177) to one of three arms: (1) MBSR, (2) a non-specific active control, or (3) a wait list.⁶² The anxiety scale was a secondary outcome. The MBSR group showed a statistically significant 4.6 percent decrease in State Trait Anxiety Inventory (STAI) Trait score at 4 months (p=0.02) compared with the non-specific active control. Gaylord et al. randomized women to an MBSR program adapted for individuals with irritable bowel syndrome or a non-specific active control (n=97).⁴⁶ The MBSR group showed a 6.8 percent change over baseline at 3 months (p=0.02). In a three-arm randomized clinical trial of women with early stage breast cancer, Henderson et al.⁵⁰ examined the effect of MBSR (n=100). They found no differences in scores of the Beck Anxiety Inventory or the SCL-90 Phobic Anxiety scores, and did not report either set of scores.

Pipe et al. evaluated a 4-week abbreviated mindfulness-based stress reduction (MBSR) course for 33 nurse leaders who were believed to be experiencing work-related stress.⁶⁰ It provided 8 hours of training with a maximum of 14 hours of home practice over four weeks. At 4 weeks, the trial showed a small non-significant improvement favoring the mindfulness meditation group, but did not provide baseline scores for comparison. This trial had a medium risk of bias.

Lee et al. randomized patients with anxiety disorders (n=46) recruited from a psychiatric hospital or its clinics in South Korea, to either an 8-week mindfulness-based stress management program or non-specific active control (anxiety disorder-based education).⁵³ The Korean meditation program did not appear to be a direct derivative of mindfulness-based stress reduction (MBSR) as most other trials in this review are, but shared overlapping features of mindfulness meditation. Outcome measures included both self-report measures (State-Trait Anxiety Inventory, State and Trait subscales; SCL-90 Anxiety subscale; and a clinician-rated measure

(HAM-A). The trial standardized all of the self-report measures in Korean. The program provided 8 hours of training targeted towards anxiety reduction, with unspecified amount of home practice. At the end of 8 weeks of treatment, the meditation group showed a significantly greater improvement ($p < .05$) in all outcome measures compared with the education group, with relatively large effects (15 to 43 percent overall reduction on the measures compared with the education group). Of note, the trial saw the largest reduction (43%) on the clinician-rated Hamilton Anxiety Rating Scale. This trial had a medium risk of bias.

We conducted two meta-analyses, one of post-intervention outcomes at eight weeks and one of end of study outcomes at three to six months (Figures 5- 6). Both showed small nonsignificant effect sizes favoring meditation, generally consistent with the difference in change analysis (Figure 4). Of note, these effect sizes do not account for the baseline differences and therefore may not be entirely consistent with the difference in change graphs.

In summary, the Korean meditation trial used an anxious population and showed large effect sizes on all measures of anxiety. The remaining trials used diverse clinical populations, and among these two trials showed small significant effects at three to four months. There was general consistency among all four measures of anxiety. All six trials had a medium risk of bias.

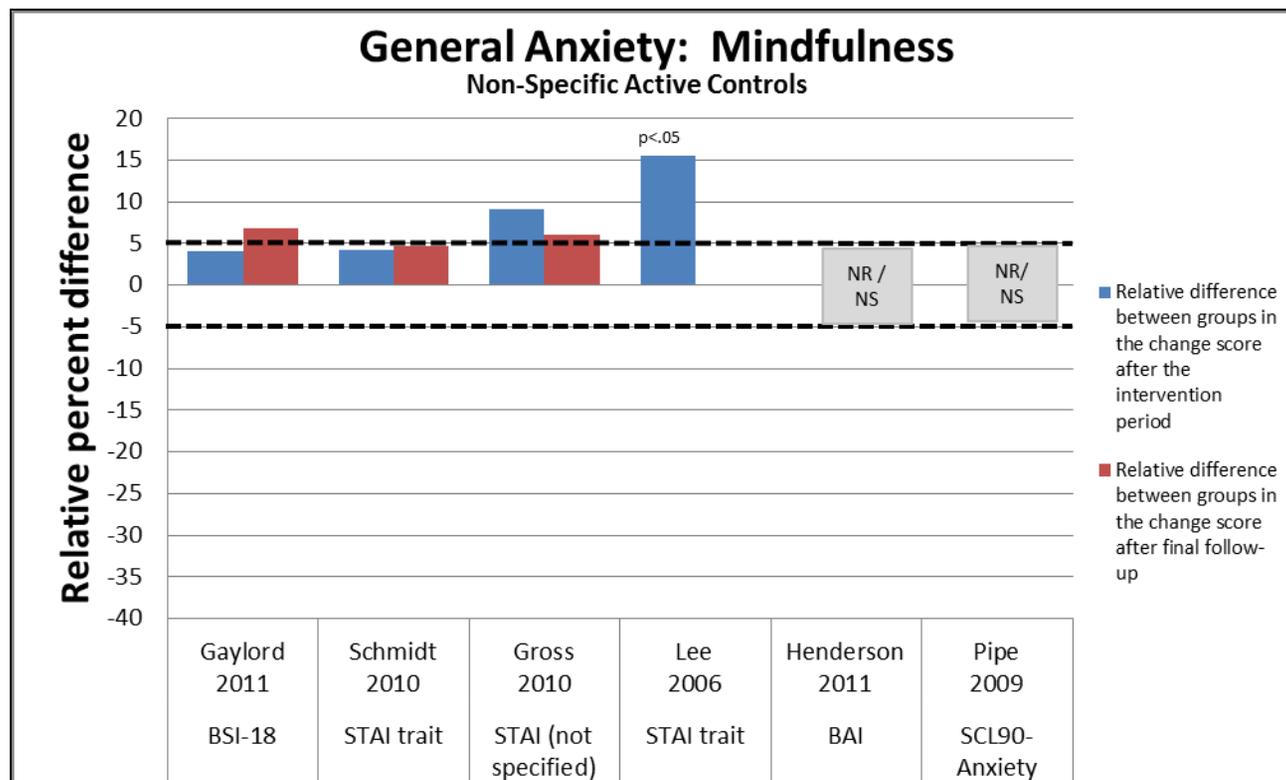
The strength of evidence is low that mindfulness meditation programs result in a small improvement in anxiety among various clinical populations when compared with a non-specific active control. We based this rating on overall medium risk of bias, consistent findings for a small positive effect, directness of measures, and imprecise estimates (Table 8).

Table 8. Grade of trials addressing the efficacy of mindfulness meditation program on anxiety compared with non-specific active controls among various populations

Number of Trials; Subjects	Domains Pertaining to Strength of Evidence				Magnitude of Effect and Strength of Evidence
	Risk of Bias	Consistency	Directness	Precision	
Anxiety					Low SOE of an improvement
6; 494	Medium	Consistent	Direct	Imprecise	4% to 15.5% improvement favoring meditation

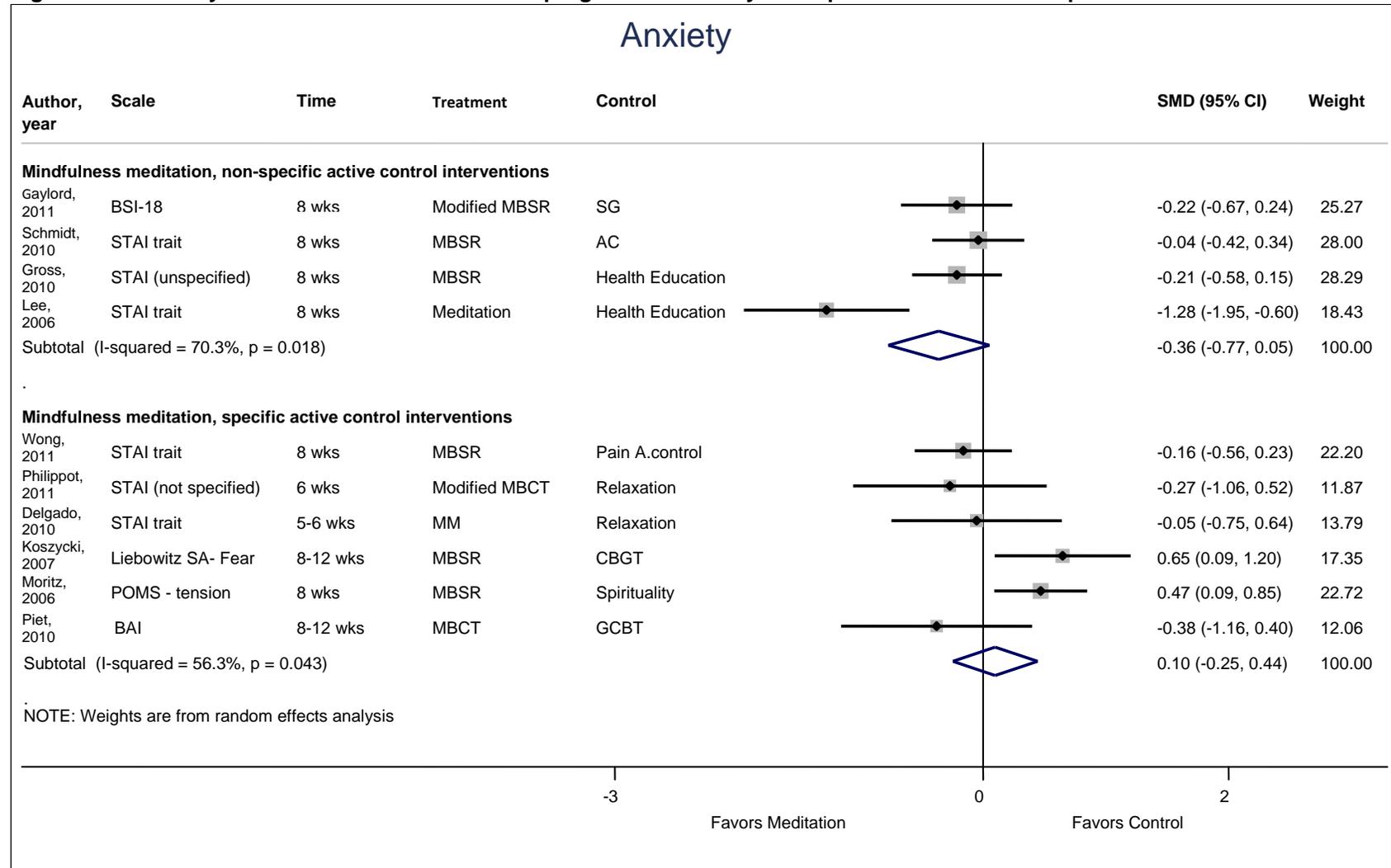
SOE = Strength of Evidence

Figure 4. Relative difference between groups in the changes in measures of general anxiety, in the mindfulness versus non-specific active control studies



- Relative difference between groups in the change score.** This is a relative percent difference, using the baseline mean in the meditation group as the denominator. For example, if the meditation group improves from a 10 to 19 on a mental health scale and the control group improves from 11 to 16 on the same scale, the relative difference between groups in the change score is: $((19-10)-(16-11))/10 \times 100 = 40\%$. The interpretation is that there is a 40% relative improvement on the mental health scale in the meditation group compared with the control group. See appendix E for absolute difference in change score values. Improvement in all scales is indicated in the positive direction. A positive relative percent difference means that the score improved more in the intervention group than in the control group
- NR / NS = Not Reported/Not significant. The trial measured this outcome and stated they were non-significant, and did not report actual results.
- Black dotted lines from -5% to +5% indicate our criteria for no effect. It does not indicate statistical significance.
- A p value above or below a bar indicates statistical significance reported in the original study publication. If there is no p value with a bar, the outcome was not significant in the original study publication.
- BSI-18= Brief Symptom Inventory 18, Anxiety subscale; STAI = State Trait Anxiety Inventory; BAI = Beck Anxiety Inventory; SCL90 = Symptom Checklist 90, anxiety subscale

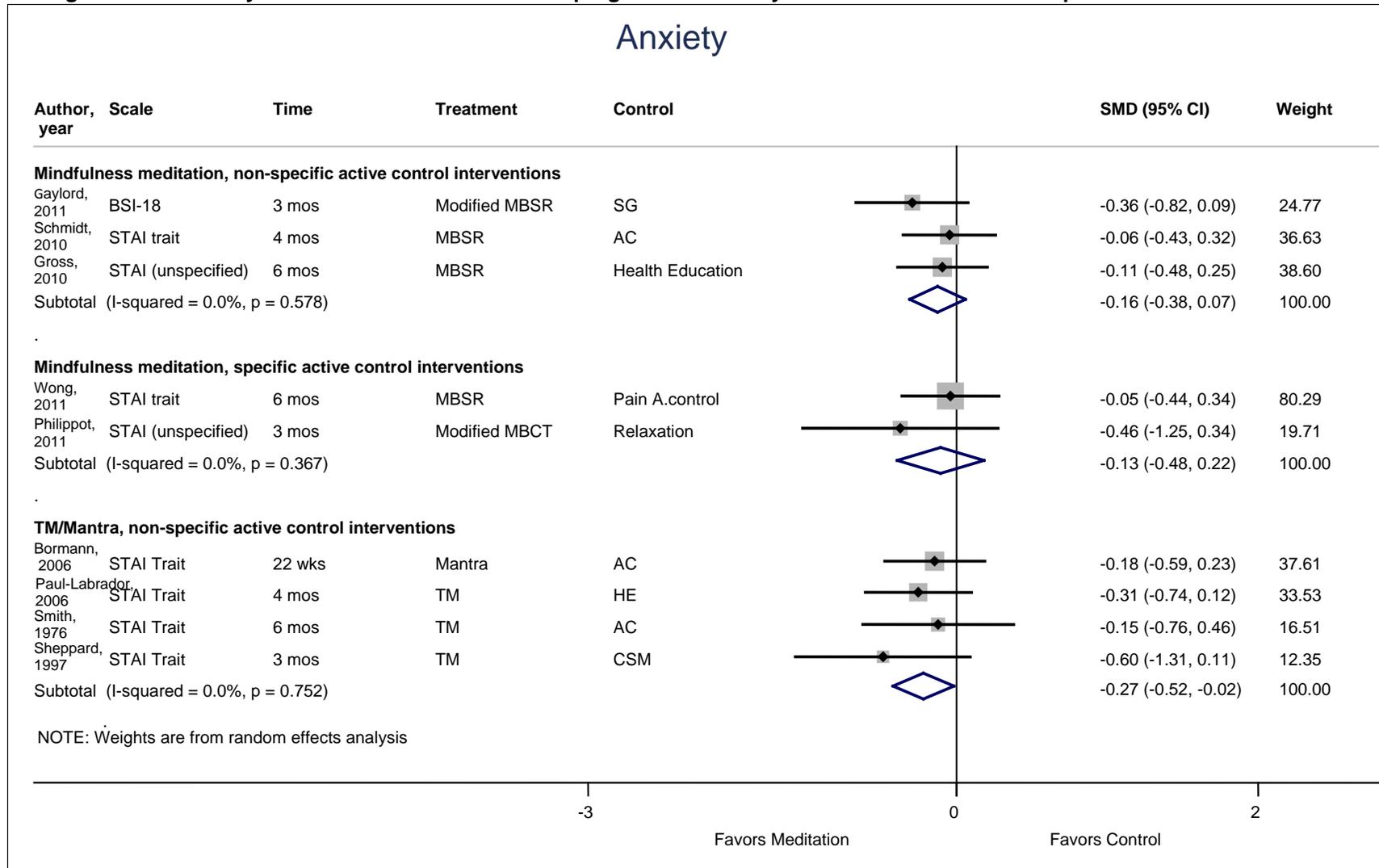
Figure 5. Meta-analysis of the effects of meditation programs on anxiety with up to 8 weeks of followup



STAI = State Trait Anxiety Inventory; BSI = Brief Symptom Inventory; BAI = Beck Anxiety Inventory; SCL = Symptom Checklist; POMS = Profile of Mood States; wks = weeks; MM = Mindfulness Meditation; CBGT = Cognitive Behavioral Group Therapy; MBSR = Mindfulness Based Stress Reduction; AC = Active Control; SG = Support Group

Text describing results for comparisons with specific active controls for anxiety starts on page 77

Figure 6. Meta-analysis of the effects of meditation programs on anxiety after 3-6 months of followup



STAI = State Trait Anxiety Inventory; BSI = Brief Symptom Inventory; wks = weeks; TM = Transcendental Meditation; MBSR = Mindfulness Based Stress Reduction; AC = Active Control; SG = Support Group; HE = Health Education; mos = Months; CSM = Clinically Standardized Meditation

Text describing results for comparisons with specific active controls for anxiety starts on page 77

Mantra Mindfulness Programs versus Non-specific Active Controls

Four trials of transcendental meditation and one trial of another mantra meditation programs evaluated an anxiety outcome. Paul-Labrador et al. randomized participants with stable coronary heart disease (n=103) to 16 weeks of either transcendental meditation or health education.⁷² The state trait anxiety inventory (STAI) measured anxiety as a secondary outcome. The program provided up to 39 hours of training over 16 weeks with an unspecified amount of home practice. At 16 weeks of followup, the difference-in-change between the two groups was only 2.8 percent favoring the control, and was non-significant. This was a well-designed trial with a low risk of bias and relatively large sample size.

Alexander et al. randomized residents (n=73) of eight homes for the elderly to transcendental meditation and two different non-specific active controls: a guided attention technique and a mental relaxation technique in which the patient chose a familiar verse or phrase to silently repeat instead of a specific assigned mantra.⁶⁵ This program did not report on the amount of training provided, but asked participants to do home practice up to a maximum of 56.3 hours over 12 weeks. After 3 months of practice, STAI scores were no different between the groups. This trial had a medium risk of bias.

Sheppard et al. randomized employees of the federal government (n=44) to participate in a 3-month stress management program, either transcendental meditation or an educational control.⁷³ Both STAI Trait and State scores were measured at 3 months and 3 years. This trial provided up to 16 hours of training and up to 56.3 hours of home practice over 12 weeks. In a difference-in-change analysis, at 3 months both STAI state and trait scores had improved by 12-16 percent ($p < .05$ for Trait), and by 3 years both STAI state and trait had improved by 19-26 percent ($p < .05$ for both). This trial had a medium risk of bias.

Smith et al. randomized university students (n=100) interested in an anxiety reducing technique to either transcendental meditation or a sham meditation program to match expectations, time, and attention.⁷⁴ This trial had 59 percent attrition and was also categorized as high risk of bias. The trial did not report on amount of meditation training given but it estimated a maximum home practice of 87.5 hours over 6 months. At 6 months, the difference-in-change scores were not different between the two groups.

Bormann et al. randomized HIV-infected adults (n=93) to mantra meditation or an education group. The intervention was 10 weeks with a 22-week followup, and provided 7.5 hours of training and unspecified amount of home practice over 10 weeks.⁶⁶ At 10 weeks, the difference-in-change score on the STAI Trait scale was 6.1 percent favoring the mantra group; however, this was not statistically significant. This difference reduced to 2.1 percent at 22 weeks. This trial had a medium risk of bias. It listed anxiety as one of seven primary outcomes.

Overall, three transcendental meditation trials had point estimates favoring the null, and the smallest trial that was conducted among stressed employees had large statistically significant results favoring transcendental meditation that persisted for three years. The largest and highest quality trial using cardiac patients showed no effect of transcendental meditation compared with a non-specific control trial.⁷² The other mantra trial among HIV patients had similarly null effects on anxiety. The difference in change graphs showed inconsistent results (Figure 7). However, the meta-analysis suggested a small statistically significant effect of mantra meditation programs on anxiety (Figure 6).

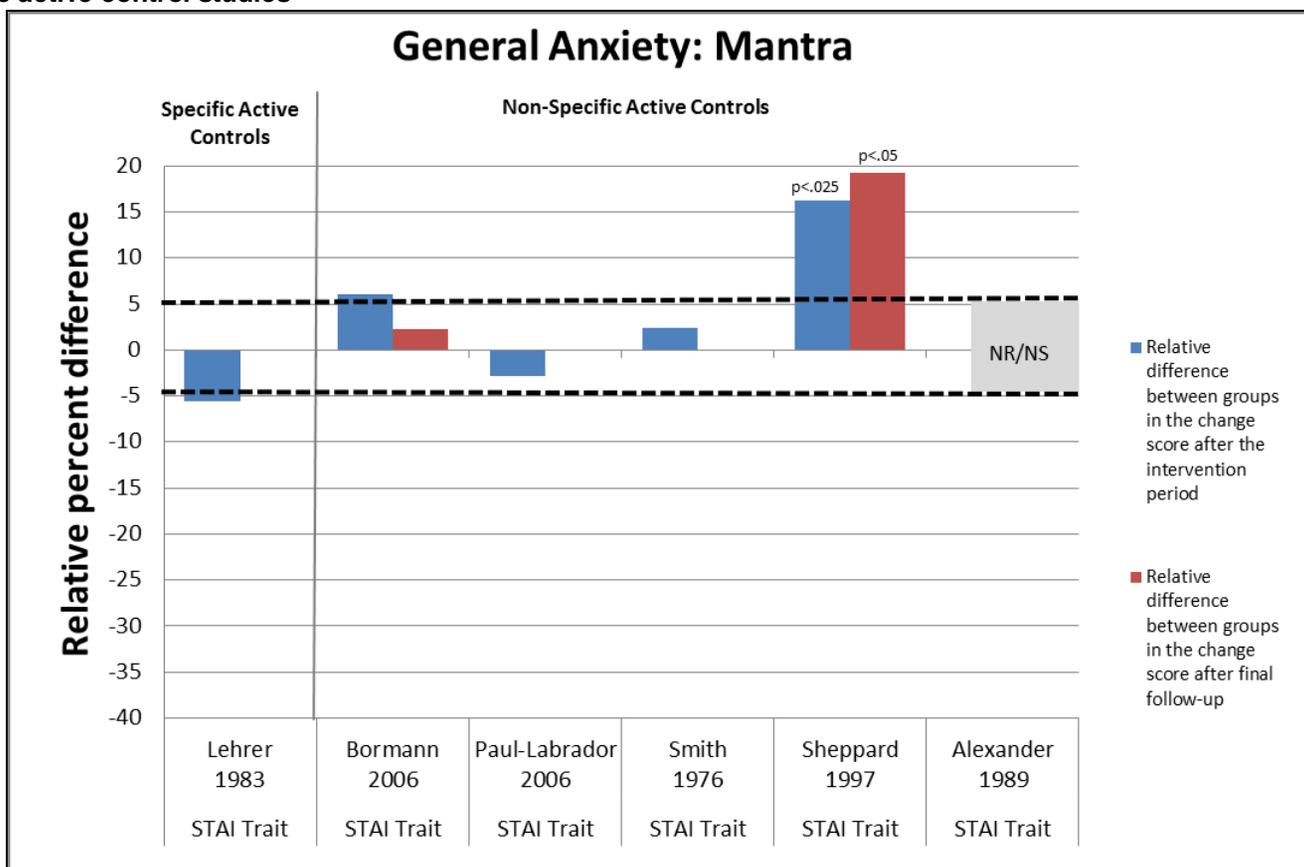
The strength of evidence is low that mantra meditation programs result in a small improvement in anxiety among various clinical populations when compared with a non-specific active control. We based this rating on overall medium risk of bias, inconsistent findings, directness of measures, and precise estimates (Table 9).

Table 9. Grade of trials addressing the efficacy of mantra meditation programs on anxiety compared with non-specific active controls among various populations.

Number of Trials; Subjects	Domains Pertaining to Strength of Evidence				Magnitude of Effect and Strength of Evidence
	Risk of Bias	Consistency	Directness	Precision	
Anxiety					Low SOE of an improvement
5; 342	Medium	Inconsistent	Direct	Precise	-2.8% to +16.3%

SOE = Strength of Evidence; TM = Transcendental Meditation

Figure 7. Relative difference between groups in the changes in measures of general anxiety, in the mantra versus non-specific active control/ specific active control studies



1. Relative difference between groups in the change score. This is a relative percent difference, using the baseline mean in the meditation group as the denominator. For example, if the meditation group improves from a 10 to 19 on a mental health scale and the control group improves from 11 to 16 on the same scale, the relative difference between groups in the change score is: $((19-10)-(16-11))/10 \times 100 = 40\%$. The interpretation is that there is a 40% relative improvement on the mental health scale in the meditation group compared with the control group. See appendix E for absolute difference in change score values. Improvement in all scales is indicated in the positive direction. A positive relative percent difference means that the score improved more in the intervention group than in the control group

2. NR / NS = Not Reported/Not significant. The trial measured this outcome and stated they were non-significant, and did not report actual results.

3. Black dotted lines from -5% to +5% indicate our criteria for no effect. It does not indicate statistical significance.

4. A p value above or below a bar indicates statistical significance reported in the original study publication. If there is no p value with a bar, the outcome was not significant in the original study publication.

5. STAI = State Trait Anxiety Inventory

6. Text describing results for comparisons with specific active controls for anxiety starts on page 80

Depression

Mindfulness Meditation Programs versus Non-specific Active Control

Four trials compared mindfulness-based stress reduction (MBSR) with a non-specific active control.^{46 47 50 62} All were at medium risk of bias and had sample sizes ranging from 75 to 137. These four trials provided between 23 to 27 hours of training with unclear amounts of home practice. In addition, three trials compared a modified mindfulness-based stress reduction (MBSR) program with a non-specific active control. These three were at a medium risk of bias, provided eight-nine hours of training with unclear amounts of home practice, and had sample sizes ranging from 19 to 41. These seven trials included diverse populations. Three trials used the Center for Epidemiologic Studies Depression Scale (CES-D), three used the Symptom Checklist 90 (SCL90) Depression subscale, and one used the Brief Symptom Inventory (BSI-18) depression subscale.

Henderson et al. randomized patients with early-stage breast cancer (n=100) to MBSR or a nutrition education program. They used two scales to measure depression. They found non-significant results on their main measure of depression, the Beck Depression Inventory (BDI), and did not report values. However, this trial measured numerous outcomes and did not correct for multiple comparisons. A difference-in-change estimate revealed a 49 percent improvement on the SCL-90 depression subscale ($p < .05$). Gaylord et al. randomized women with irritable bowel syndrome (IBS) (n=75) to MBSR versus support program for women with IBS and showed no significant difference between trial arms at 2 or 3 months.⁴⁶ Schmidt et al. randomized women with fibromyalgia (n=109) to MBSR or non-specific active control. The MBSR arm showed no changes at 8 weeks but showed a 12.4 percent non-significant improvement in the center for epidemiologic studies depression scale (CES-D) at 4 months compared with the control arm.⁶² Gross et al. randomized solid organ transplant patients, post-surgery, (n=137) to MBSR versus health education. A difference-in-change calculation showed that MBSR participants had 25.8 to 31.8 percent reductions in the CES-D that were consistently maintained between 2 and 12 months. However, these changes did not reach significance ($p = 0.10$).⁴⁷

Three trials evaluated other mindfulness programs against a non-specific active control. Oken et al. randomized people who take care of elderly relatives with dementia (n=19) to mindfulness meditation program or a non-specific active control.⁵⁷ This trial found a non-significant 10.1 percent improvement on CES-D favoring the mindfulness group. This trial had a medium risk of bias, provided 9 hours of training over 7 weeks by a trained teacher and an unspecified amount of home practice.

Pipe et al. compared a 4-week abbreviated MBSR course for 32 nurse leaders, who were believed to be under work-related stress, to a non-specific active control.⁶⁰ It provided 8 hours of training with a maximum of 14 hours of home practice over 4 weeks. At 4 weeks, the trial showed a small non-significant improvement favoring the mindfulness meditation group on the SCL-90 Depression (absolute difference of .44 (95% CI: -.88 to +.01)), but did not provide baseline scores for comparison of the size of effect. This trial had a medium risk of bias.

Lee et al. randomized 46 patients with anxiety disorders recruited from a psychiatric hospital or its clinics in South Korea, to either an 8-week mindfulness-based stress management program or non-specific active control group (anxiety disorder-based education).⁵³ The Korean meditation

program did not appear to be a derivative of MBSR or MBCT as most other trials in this review are, but shared some overlapping features of mindfulness meditation. It found non-significant 30.3 percent reduction in the BDI and 17.4 percent reduction in SCL-90 depression scores. The trial standardized all of the self-report measures in Korean. The program provided 8 hours of training targeted towards anxiety reduction, with unspecified amount of home practice. This trial had a medium risk of bias.

In summary, these seven trials used diverse populations of patients although none of them were overtly depressed. The difference in change graphs showed generally consistent findings favoring an improvement in depressive symptoms across studies, although only one had a statistically significant result (Figure 8). Two meta-analyses were performed, one of two month outcomes and the other of four to six month outcomes. Both meta-analyses found small nonsignificant effects of mindfulness meditation programs on depressive symptoms (Figures 9 and 10).

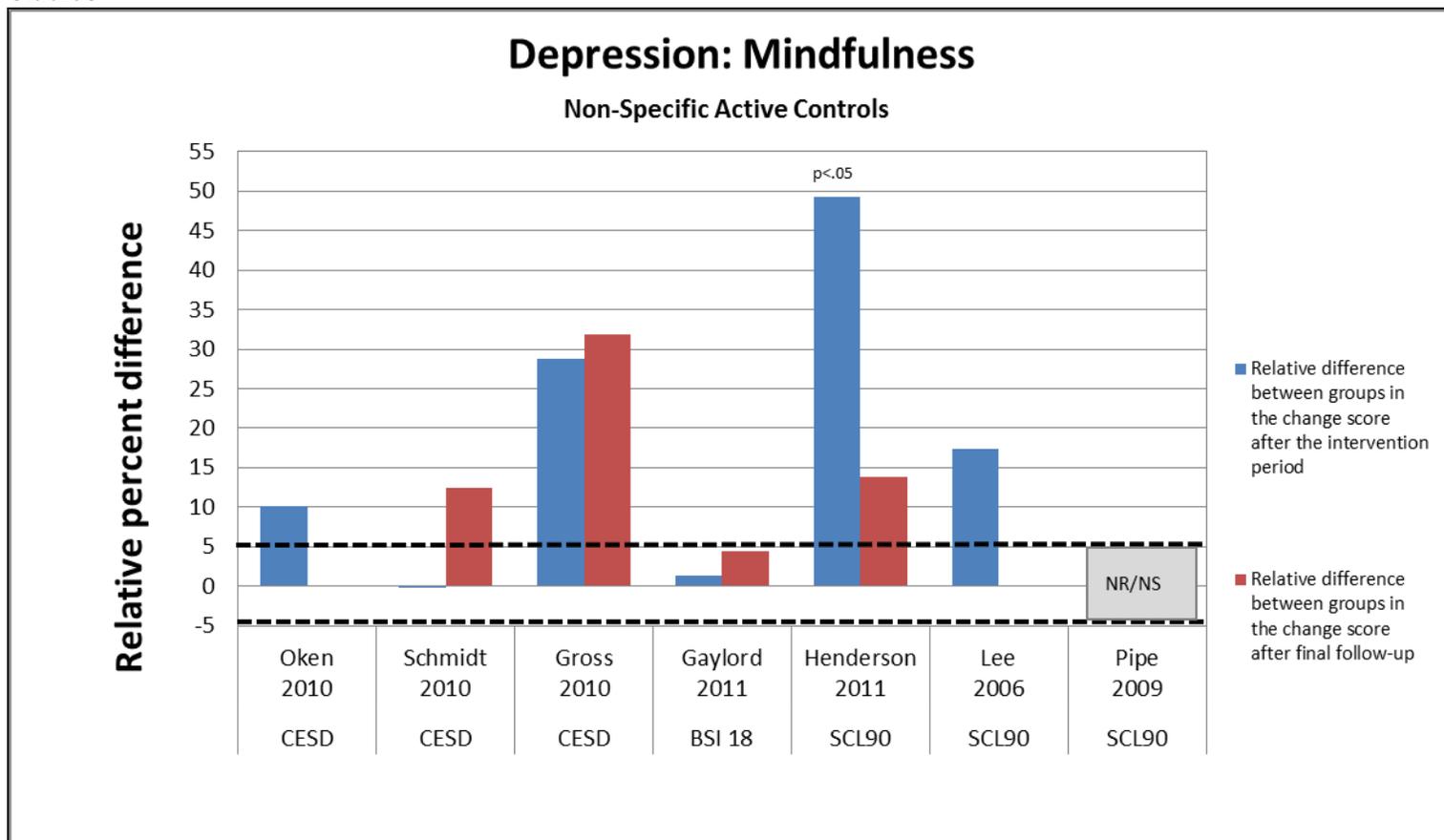
The strength of evidence is low that a mindfulness meditation program improves symptoms of depression among various clinical populations when compared with a non-specific active control. We based this rating on overall medium risk of bias, consistent findings for a positive effect, directness of measures, and imprecise estimates (Table 10).

Table 10. Grade of trials addressing the efficacy of mindfulness meditation programs on symptoms of depression compared with non-specific active controls among clinical populations

Number of Trials; Subjects	Domains Pertaining to Strength of Evidence				Magnitude of Effect and Strength of Evidence
	Risk of Bias	Consistency	Directness	Precision	
Depressive symptoms					Low SOE of an improvement in depressive symptoms
7; 518	Medium	Consistent	Direct	Imprecise	-0.1% (favoring null) to +49.2% (favoring mindfulness meditation program)

SOE = Strength of Evidence

Figure 8. Relative difference between groups in the changes in measures of depression, in the mindfulness versus non-specific active control studies



- Relative difference between groups in the change score.** This is a relative percent difference, using the baseline mean in the meditation group as the denominator. For example, if the meditation group improves from a 10 to 19 on a mental health scale and the control group improves from 11 to 16 on the same scale, the relative difference between groups in the change score is: $((19-10)-(16-11))/10 \times 100 = 40\%$. The interpretation is that there is a 40% relative improvement on the mental health scale in the meditation group compared with the control group. See appendix E for absolute difference in change score values. Improvement in all scales is indicated in the positive direction. A positive relative percent difference means that the score improved more in the intervention group than in the control group
- NR / NS = Not Reported/Not significant. The trial measured this outcome and stated they were non-significant, and did not report actual results.
- Black dotted lines from -5% to +5% indicate our criteria for no effect. It does not indicate statistical significance.
- A p value above or below a bar indicates statistical significance reported in the original study publication. If there is no p value with a bar, the outcome was not significant in the original study publication.
- CESD = Center for Epidemiological Studies Depression Scale; BSI = Beck Stress Inventory; SCL= Symptom Checklist(depression subscale)

Mantra Meditation Programs versus Non-specific Active Control

Transcendental Meditation versus Non-specific Active Control

Four trials of transcendental meditation assessed a depression outcome among cardiac, elderly, and stressed employees. One trial of other mantra assessed depression as an outcome among HIV positive patients. Two of the transcendental meditation studies were of low risk of bias and the remaining studies were rated as medium risk of bias. The transcendental meditation studies ranged from 16 to 39 hours of training over 12 to 25 weeks while the other mantra in HIV patients provided 7.5 hours of training over 5 weeks.

Paul-Labrador et al. randomized 103 participants with stable coronary heart disease to 16 weeks of either transcendental meditation or health education.⁷² Depression was a secondary outcome measured by the center for epidemiologic studies depression scale (CES-D). The program provided up to 39 hours of training over 16 weeks with an unspecified amount of home practice. At 16 weeks of followup, the difference-in-change between the two groups was 19.1 percent favoring the control, and was non-significant. This trial had a low risk of bias

Alexander et al. randomized 73 residents of eight homes for the elderly to transcendental meditation and two different non-specific active controls: a guided attention technique and a mental relaxation technique in which the patient chose a familiar verse or phrase to silently repeat instead of a specific assigned mantra.⁶⁵ This program did not report on the amount of training provided, but it recommended home practice up to a maximum of 56.3 hours over 12 weeks. After 3 months of practice, the Self Rating Depression Scale scores were no different between the groups, and the difference-in-change estimates favored the null. This trial had a medium risk of bias.

Sheppard et al. randomized 44 employees of the federal government to participate in a 3-month stress management program, either transcendental meditation or an educational control.⁷³ It measured institute for personality and ability testing (IPAT) depression scores at 3 months and 3 years. This trial provided up to 16 hours of training and up to 56.3 hours of home practice over 12 weeks. In a difference-in-change analysis, at 3 months IPAT depression scores had improved by 30.3 percent ($p < .05$), and by 3 years the scores had improved by 84.5 percent ($p < .01$). This trial had a medium risk of bias.

Jayadevappa et al. randomized congestive heart failure patients ($n=23$) to either 3 months of transcendental meditation or health education, assessing depression as a secondary outcome using the CES -D scale.⁶⁹ Post-intervention, difference-in-change point estimates were 46.1 and 49 percent at 3 and 6 months respectively. The trial reported these results as non-significant. This trial had a low risk of bias, and provided 22.5 hours of training over 6 months by trained and certified teachers. It recommended up to 90 hours of home practice during this time.

Bormann et al. randomized HIV-infected adults ($n=93$) to mantra meditation or an education group with primary outcomes related to the reduction of intrusive thoughts and improvement in quality of life (QOL) and well-being.⁶⁶ The intervention was 10 weeks with a 22-week followup, and provided 7.5 hours of training and unspecified amount of home practice over 10 weeks.⁶⁶ At 10 weeks, the difference-in-change score on the center for epidemiologic studies depression scale was 1.6 percent and was not statistically significant. This difference increased to 20.1

percent at 22 weeks favoring the control (p=.07). This trial had a medium risk of bias. Depression was listed as one of seven primary outcomes.

In summary, the difference in change graphs showed inconsistent results (Figure 11). We conducted two meta-analyses of trials with available data, one at 2 to 3 months of followup and the other at 4 to 6 months of followup (Figures 9 -10). Both meta-analyses included only two of the studies, and showed small nonsignificant effect sizes. Of note, two of the lowest risk of bias trials which both used cardiac patients and the same scale (center for epidemiologic studies depression scale) found conflicting results.^{69 72} Two other trials of medium risk of bias each used a different scale and also found conflicting results.

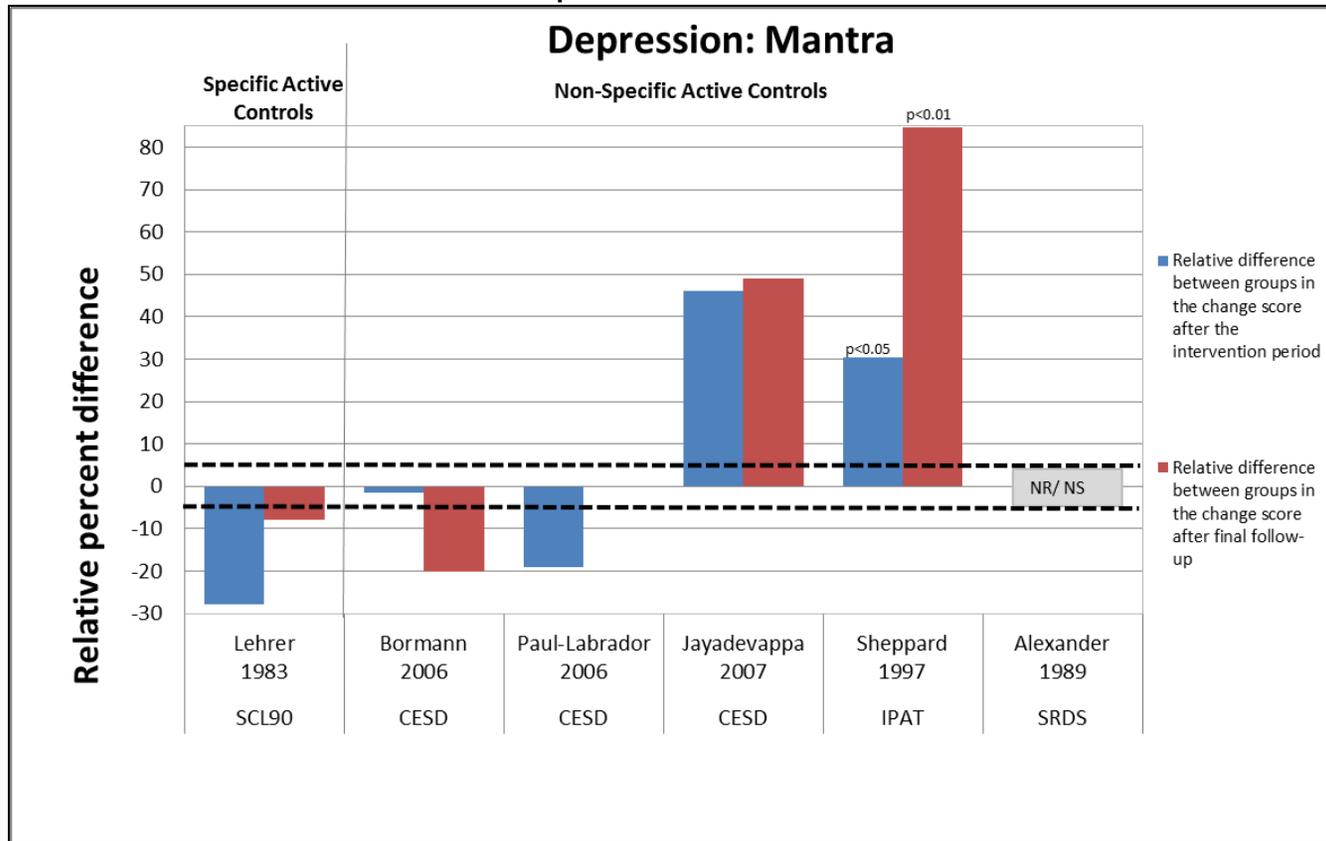
The strength of evidence is insufficient that mantra meditation programs have an effect on symptoms of depression among various clinical populations when compared with a non-specific active control. We based this rating on overall medium risk of bias, inconsistent findings, directness of measures, and imprecise estimates (Table 11).

Table 11. Grade of trials addressing the efficacy of mantra meditation program on symptoms of depression compared with non-specific active controls among clinical populations

Number of Trials; Subjects	Domains Pertaining to Strength of Evidence				Magnitude of Effect and Strength of Evidence
	Risk of Bias	Consistency	Directness	Precision	
Depressive symptoms					Insufficient SOE of an effect
5;328	Medium	Inconsistent	Direct	Imprecise	-19.1% to +46.1%

SOE = Strength of Evidence

Figure 11. Relative difference between groups in the changes in measures of depression, in the mantra versus non-specific active control / specific active control studies



1. **Relative difference between groups in the change score.** This is a relative percent difference, using the baseline mean in the meditation group as the denominator. For example, if the meditation group improves from a 10 to 19 on a mental health scale and the control group improves from 11 to 16 on the same scale, the relative difference between groups in the change score is: $\frac{((19-10)-(16-11))}{10} \times 100 = 40\%$. The interpretation is that there is a 40% relative improvement on the mental health scale in the meditation group compared with the control group. Improvement in all scales is indicated in the positive direction. A positive relative percent difference means that the score improved more in the intervention group than in the control group.
2. NR / NS = Not Reported/Not significant. The trial measured this outcome and stated they were non-significant, and did not report actual results.
3. Black dotted lines from -5% to +5% indicate our criteria for no effect. It does not indicate statistical significance.
4. A p value above or below a bar indicates statistical significance reported in the original study publication. If there is no p value with a bar, the outcome was not significant in the original study publication.
5. SCL = Symptom Checklist; CES-D = Center for Epidemiological Studies Depression Scale; IPAT = Institute for Personality and Ability Testing; SRDS = Self-rating Depression Scale
6. Text describing results for comparisons with **specific** active controls for depression starts on page 84

Stress and Distress

Mindfulness Meditation Programs versus Non-specific Active Control

Five trials compared mindfulness meditation programs with non-specific active controls, and evaluated stress or distress as an outcome.^{45 46 56 57 60} One used mindfulness-based stress reduction (MBSR) and four used mindfulness meditation. Four were of medium risk of bias and one was rated as high risk of bias. These trials involved diverse patient groups including irritable bowel syndrome, caregivers of family members with dementia, alcoholics, chronic obstructive pulmonary disease, and nursing leaders believed to be under job stress. The trial sizes ranged from 19 to 75. Three trials used a measure of stress and two used a measure of distress.

Oken et al. randomized people who take care of elderly relatives with dementia (n=19) to mindfulness meditation or a non-specific active control.⁵⁷ The purpose of this trial was to see if mindfulness meditation would decrease stress in caregivers of relatives with dementia. For inclusion, participants had to endorse greater than 9 points on the perceived stress scale (PSS). Although stress was a primary outcome, the PSS was a secondary measure for this trial. This trial found a non-significant 14.1 percent improvement on the PSS favoring the mindfulness meditation group. This trial had a medium risk of bias, provided 9 hours of training over 7 weeks by a trained teacher, and an unspecified amount of home practice.

Garland et al.⁴⁵ assessed the effects of a modified mindfulness-based cognitive therapy (MBCT) for alcoholics versus a non-specific active control on alcohol dependent adults (n=37) to assess whether mindfulness meditation could disrupt the risk chain of stress-precipitated alcohol relapse. The intervention lasted 10 weeks and did not specify information on the amount of training provided, although participants could have done a maximum of 17.5 hours of home practice over the 10 weeks. This trial had a medium risk of bias and found a statistically significant 21.2 percent reduction in the PSS favoring the mindfulness meditation group (p=.03). This trial studied mostly African American males and had medium risk of bias.

Mularski et al. randomized elderly patients, predominantly men, with moderate to severe COPD (n=49) to mindfulness-based behavioral therapy (MBBT) or an active support group.⁵⁶ It found no difference in perceived stress scores between the two arms of the trial after 2 months. This trial suffered from a 42 percent attrition rate and had a high risk of bias.

Gaylord et al. randomized women with irritable bowel syndrome (IBS) (n=75) to MBSR versus support program for women with IBS and showed no significant difference (3.6 percent favoring MBSR) between trial arms at 2 months on the BSI 18.⁴⁶ At 6 months this had increased slightly to 5.2 percent (p=.049). This was a medium risk-of-bias trial that provided 23 hours of training and unspecified amount of home practice over 8 weeks.

Pipe et al. evaluated a 4-week abbreviated MBSR course for 32 nurse leaders who felt they suffered from work-related stress, compared with a non-specific active control.⁶⁰ At 4 weeks, the trial showed no difference between the mindfulness meditation group on the symptom checklist 90 global severity index (SCL-90 GSI) (absolute difference of .26 favoring mindfulness meditation), but did not provide baseline scores for comparison of the size of effect. It provided 8 hours of training with a maximum of 14 hours of home practice over 4 weeks. This was a small trial with a medium risk of bias.

The difference in change graphs generally showed consistent effects on measures of stress and distress favoring a reduction in the mindfulness groups (Figure 12). A meta-analysis suggested a small nonsignificant effect of these programs on stress and distress. (Figure 13)

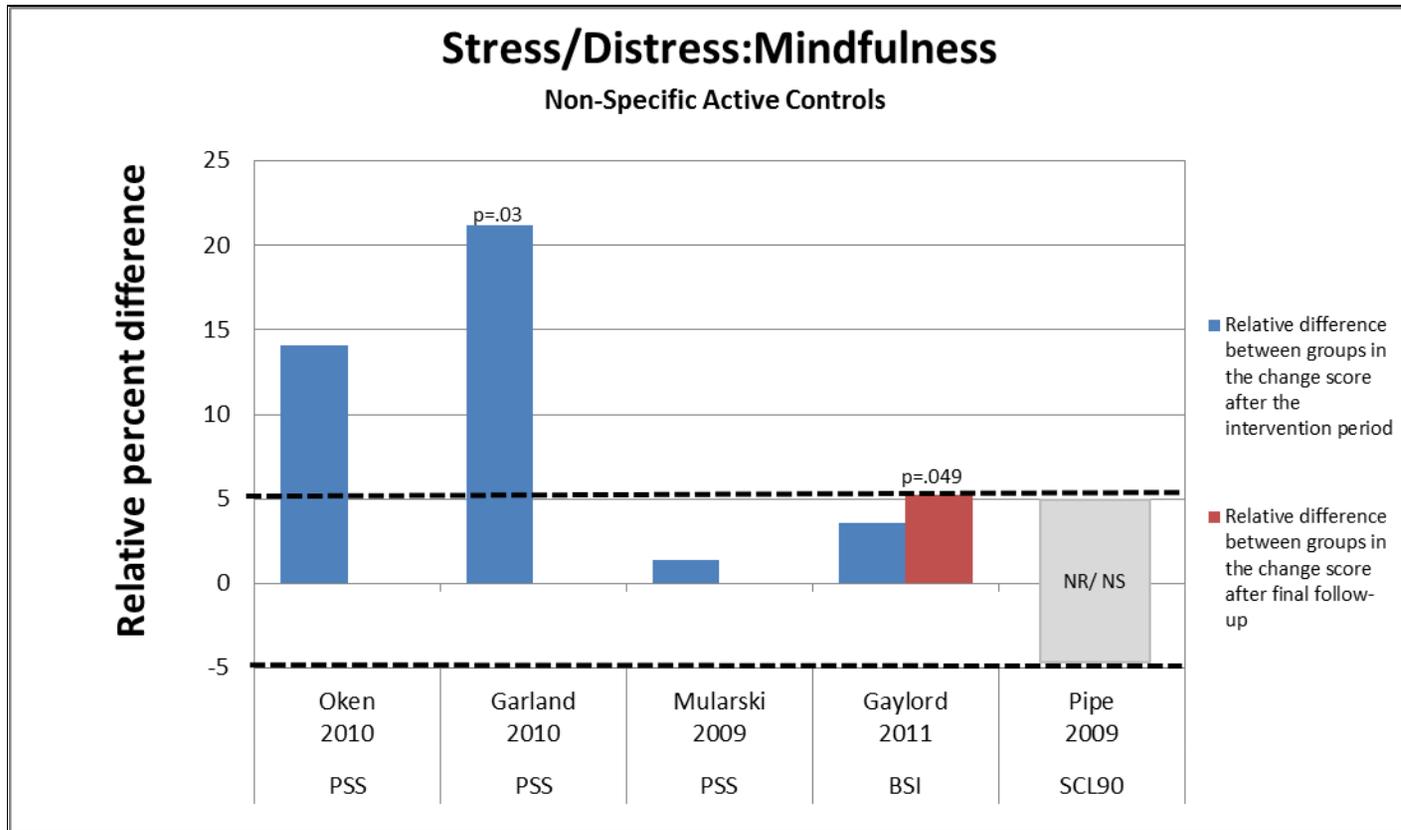
The strength of evidence is low that mindfulness meditation programs result in a small improvement in stress and distress among various clinical populations when compared with a non-specific active control. We based this rating on overall medium risk of bias, consistent findings, directness of measures, and imprecise estimates (Table 12).

Table 12. Grade of trials assessing the efficacy of mindfulness programs on stress and distress compared with non-specific active controls among various populations

Number of Trials; Subjects	Domains Pertaining to Strength of Evidence				Magnitude of Effect and Strength of Evidence
	Risk of Bias	Consistency	Directness	Precision	
Stress & Distress					Low SOE of an effect
5; 200	Medium	Consistent	Direct	Imprecise	1.4% to 21.2% improvement in stress & distress

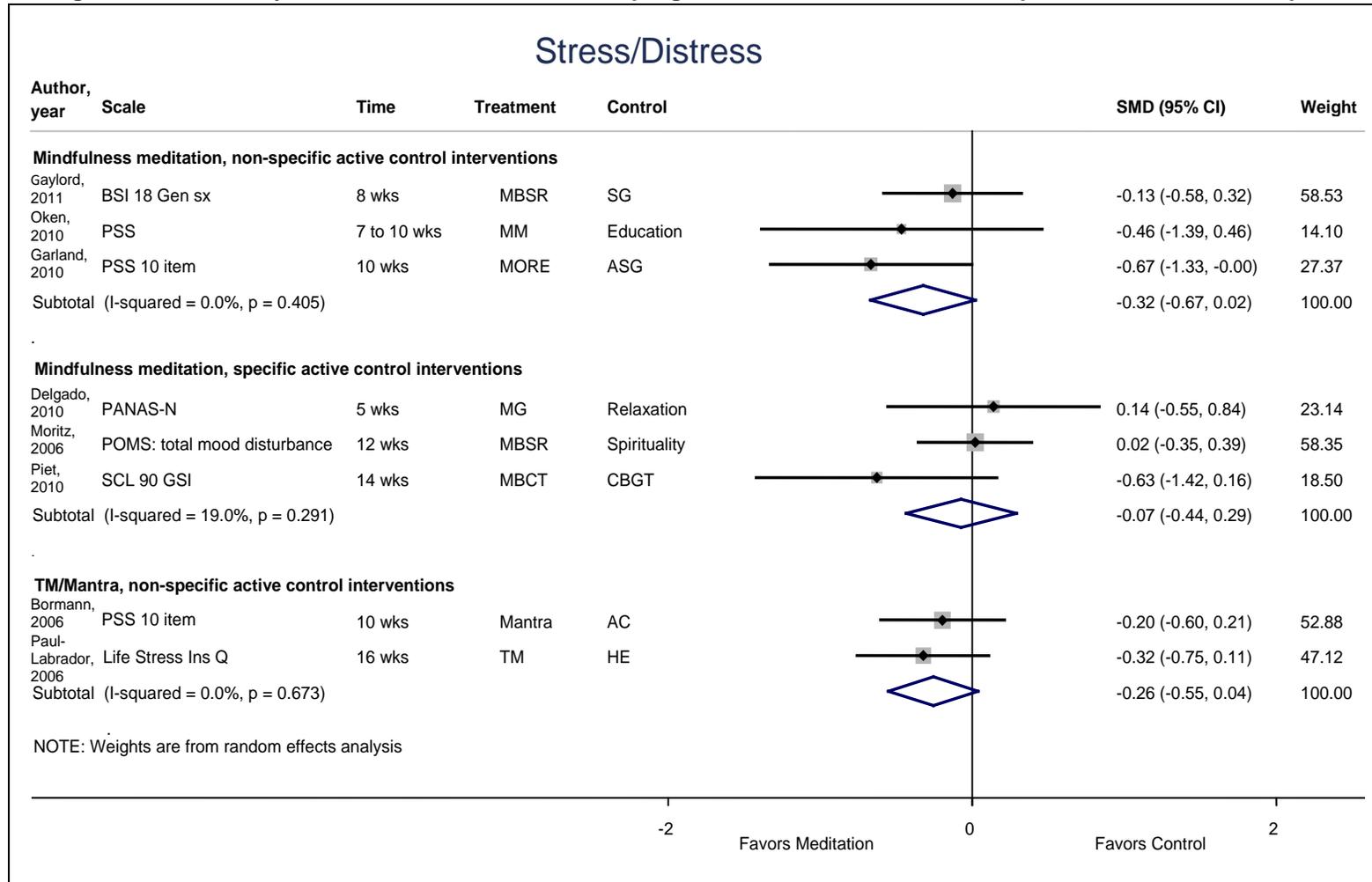
SOE = Strength of Evidence

Figure 12. Relative difference between groups in the changes in measures of stress/distress, in the mindfulness versus non-specific active control studies



- Relative difference between groups in the change score.** This is a relative percent difference, using the baseline mean in the meditation group as the denominator. For example, if the meditation group improves from a 10 to 19 on a mental health scale and the control group improves from 11 to 16 on the same scale, the relative difference between groups in the change score is: $((19-10)-(16-11))/10 \times 100 = 40\%$. The interpretation is that there is a 40% relative improvement on the mental health scale in the meditation group compared with the control group. See appendix E for absolute difference in change score values. Improvement in all scales is indicated in the positive direction. A positive relative percent difference means that the score improved more in the intervention group than in the control group
- NR / NS = Not Reported/Not significant. The trial measured this outcome and stated they were non-significant, and did not report actual results.
- Black dotted lines from -5% to +5% indicate our criteria for no effect. It does not indicate statistical significance.
- A p value above or below a bar indicates statistical significance reported in the original study publication. If there is no p value with a bar, the outcome was not significant in the original study publication.
- PSS = Perceived Stress Scale ; BSI = Beck Stress Inventory; SCL = Symptom Checklist

Figure 13. Meta-analysis of the effects of meditation programs on stress/distress with up to 14 weeks of followup



PSS = Perceived Stress Scale ; BSI = Beck Stress Inventory; SCL = Symptom Checklist; POMS = Profile of Mood States; PANAS-N = Positive and Negative Affect Scale - Negative mood; MM = Mindfulness Meditation; MORE = Mindfulness-oriented Recovery Enhancement; SG = Support Group; ASG = Alcohol Dependence Support Group; TM = Transcendental Meditation; MBSR = Mindfulness-based Stress Reduction; MBCT = Mindfulness-based Cognitive Therapy; AC = Active Control; CBGT = Cognitive Behavioral Group Therapy; HE = Health Education

Text describing results for comparisons with **specific** active controls for stress/distress starts on page 84

Mantra Meditation Programs versus Non-specific Active Control

Three trials of mantra meditation programs evaluated stress as an outcome for cardiac patients. Two were transcendental meditation and one used another mantra meditation program. The transcendental meditation trials were both conducted in cardiac patients and both had a low risk of bias. One used the life stress instrument questionnaire and the other used the perceived stress scale (PSS). The other mantra meditation trial utilized HIV positive patients and used the PSS.

Paul-Labrador et al. randomized patients with stable coronary heart disease (n=103) to 16 weeks of either transcendental meditation or health education.⁷² Stress was a secondary outcome measured by the Life Stress Instrument Questionnaire. The program provided up to 39 hours of training over 16 weeks with an unspecified amount of home practice. At 16 weeks of followup, the difference-in-change between the two groups was 5.9 percent favoring the control, and was non-significant. This trial had a low risk of bias.

Jayadevappa et al. randomized congestive heart failure patients (n=23) to either 3 months of transcendental meditation or health education, assessing stress as a secondary outcome using the PSS scale.⁶⁹ With 100 percent trial completion and a 95 percent compliance rate among the originally randomized subjects, there was no difference in perceived stress scores between the two groups at 3 or 6 months. Difference-in-change point estimates were 0.9 and 1.3 percent at 3 and 6 months respectively. These were reported as non-significant. This trial had a low risk of bias, and provided 22.5 hours of training over six months by trained and certified teachers. It recommended up to 90 hours of home practice during this time.

Bormann et al. randomized HIV-infected adults (n=93) to mantra meditation or an education group with primary outcomes related to the reduction of intrusive thoughts and improvement in quality of life and well-being.⁶⁶ The intervention was 10 weeks with a 22-week followup, and provided 7.5 hours of training and unspecified amount of home practice over 10 weeks.⁶⁶ The difference-in-change score on the PSS was 1.2 and 3 percent at 10 and 22 weeks, favoring the null and was not statistically significant. This trial had a medium risk of bias. Stress was one of seven primary outcomes.

The difference in change graphs showed consistent findings of a null effect of mantra meditation programs on stress (Figure 14). A meta-analysis of two of the trials suggested a small non-significant effect (Figure 13).

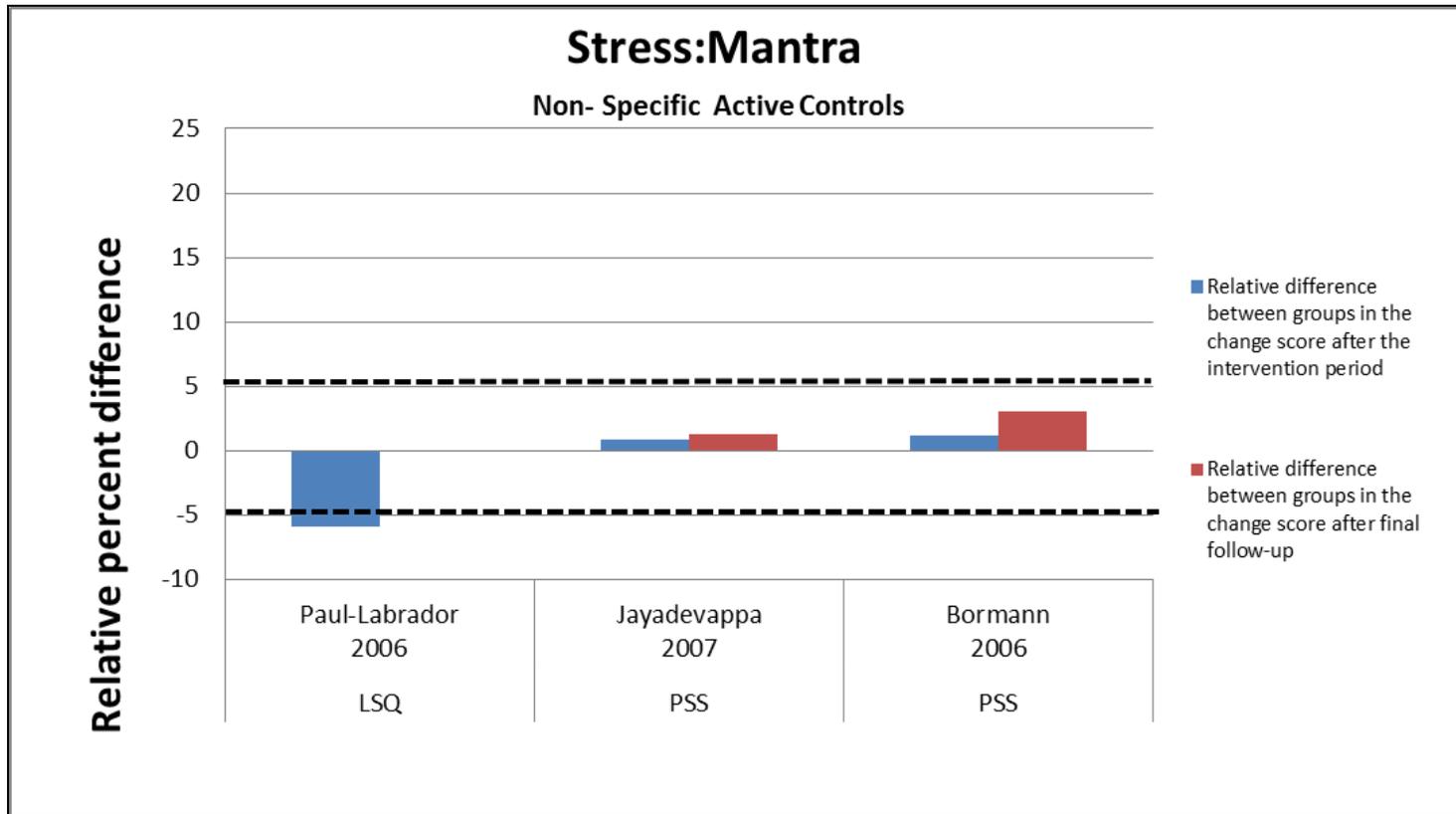
The strength of evidence is low that mantra meditation programs have no effect on stress when compared with a non-specific active control. We based this rating on overall medium risk of bias, consistent findings of a null effect, directness of measures, and imprecise estimates (Table 13).

Table 13. Grade of trials addressing the efficacy of mantra meditation programs on stress compared with non-specific active controls among cardiac and HIV patients

Number of Trials; Subjects	Domains Pertaining to Strength of Evidence				Magnitude of Effect and Strength of Evidence
	Risk of Bias	Consistency	Directness	Precision	
Stress					Low SOE of no effect on measures of stress
3; 219	Medium	Consistent	Direct	Imprecise	-5.9% to +1.2%

SOE = Strength of Evidence

Figure 14. Relative difference between groups in the changes in measures of stress, in the mantra versus non-specific active control studies



- Relative difference between groups in the change score.** This is a relative percent difference, using the baseline mean in the meditation group as the denominator. For example, if the meditation group improves from a 10 to 19 on a mental health scale and the control group improves from 11 to 16 on the same scale, the relative difference between groups in the change score is: $\frac{((19-10)-(16-11))}{10} \times 100 = 40\%$. The interpretation is that there is a 40% relative improvement on the mental health scale in the meditation group compared with the control group. See appendix E for absolute difference in change score values. Improvement in all scales is indicated in the positive direction. A positive relative percent difference means that the score improved more in the intervention group than in the control group.
- NR / NS = Not Reported/Not significant. The trial measured this outcome and stated they were non-significant, and did not report actual results.
- Black dotted lines from -5% to +5% indicate our criteria for no effect. It does not indicate statistical significance.
- A p value above or below a bar indicates statistical significance reported in the original study publication. If there is no p value with a bar, the outcome was not significant in the original study publication.
- PSS = Perceived Stress Scale (PSS); LSQ = Life Stress Ins Q

Negative Affect

Mindfulness Meditation Programs versus Non-specific Active Control

Nine trials compared mindfulness meditation programs with non-specific active controls, and evaluated a negative affect outcome. Since some trials reported on more than one outcome, for these trials we prioritized anxiety over depression and depression over stress/distress as indirect measures of negative affect. None of the trials used a direct measure of negative affect. Six trials reported on anxiety, one on depression, and two on perceived stress. The trials were performed on diverse populations, ranging in sample size from 19 to 137. All trials had a medium risk of bias except one which had a high risk of bias. These trials have been previously described, and are shown in graphical form in Figure 15. The difference in change graphs showed a consistent improvement in negative affect when we compared mindfulness meditation programs to a non-specific active control. Two trials showed small nonsignificant effects which became significant at the end of study, and two trials showed significant effects post-intervention. A meta-analysis of these trials showed a small statistically significant effect size of 0.39 favoring meditation (Figure 16). We conducted a sensitivity analysis prioritizing stress/distress over anxiety to see if this would change our conclusions (Figures 17-18). Both analyses gave similar results.

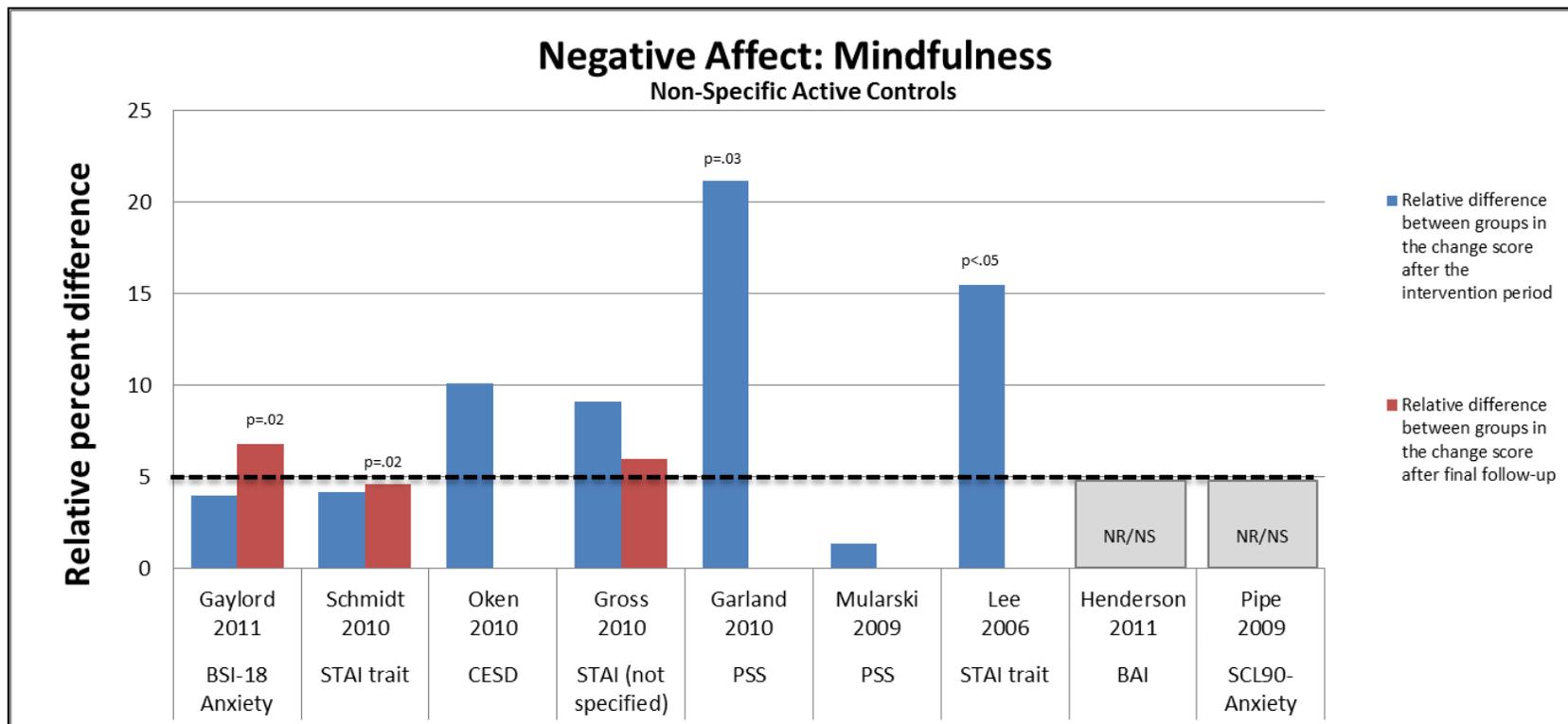
The strength of evidence is low that mindfulness meditation program improve negative affect among various clinical populations when compared with a non-specific active control. We based this rating on overall medium risk of bias, consistent results, indirect measures of negative affect, and precise estimates (Table 14).

Table 14. Grade of trials addressing the efficacy of mindfulness meditation programs on negative affect compared with non-specific active controls among diverse populations

Number of Trials; Subjects	Domains Pertaining to Strength of Evidence				Magnitude of Effect and Strength of Evidence
	Risk of Bias	Consistency	Directness	Precision	
Negative Affect					Low SOE of an improvement in negative affect
9; 600	Medium	Consistent	Indirect	Precise	1.4% to 21.2% improvement

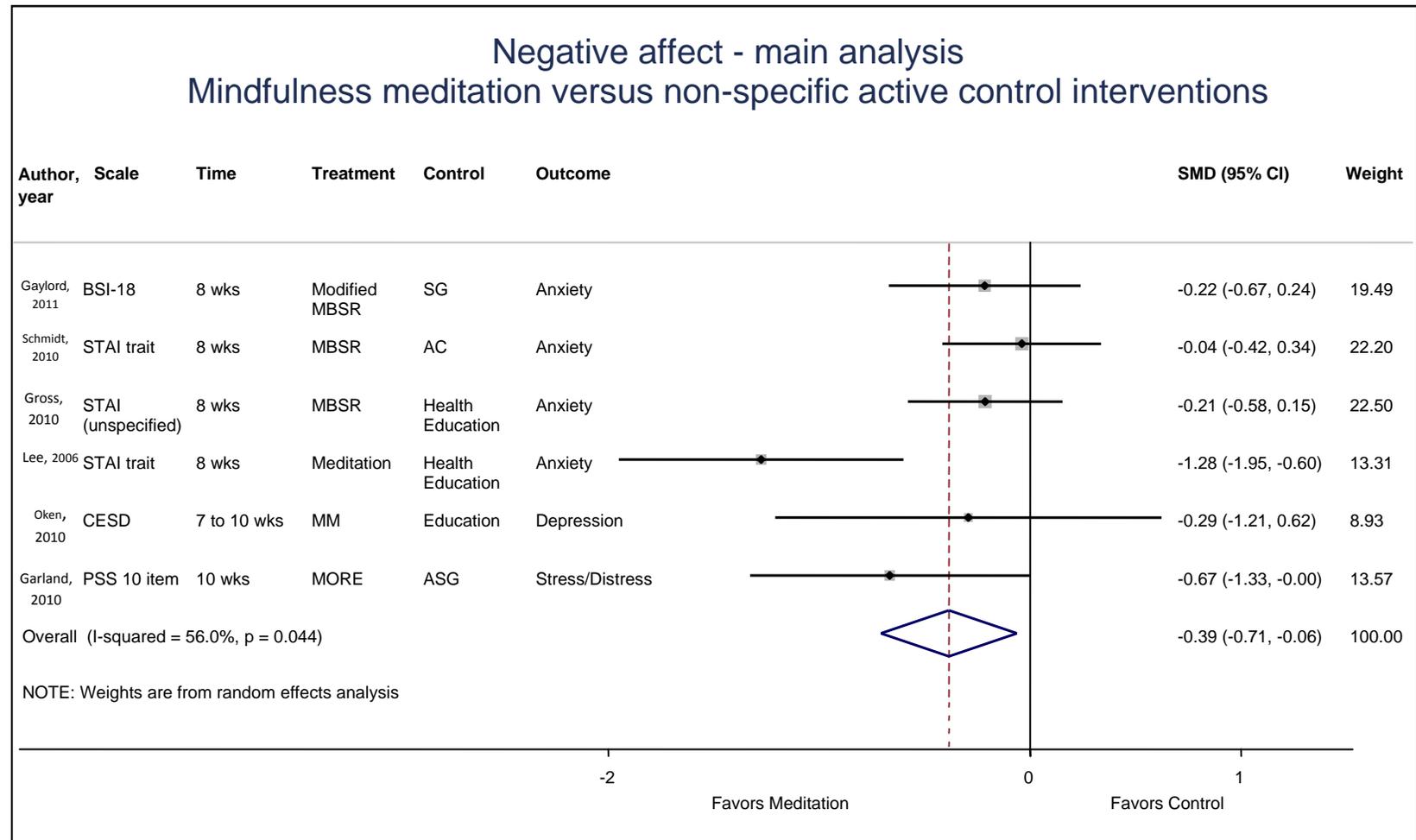
SOE = Strength of Evidence

Figure 15. Relative difference between groups in the changes in measures of negative affect, in the mindfulness versus non-specific active control studies



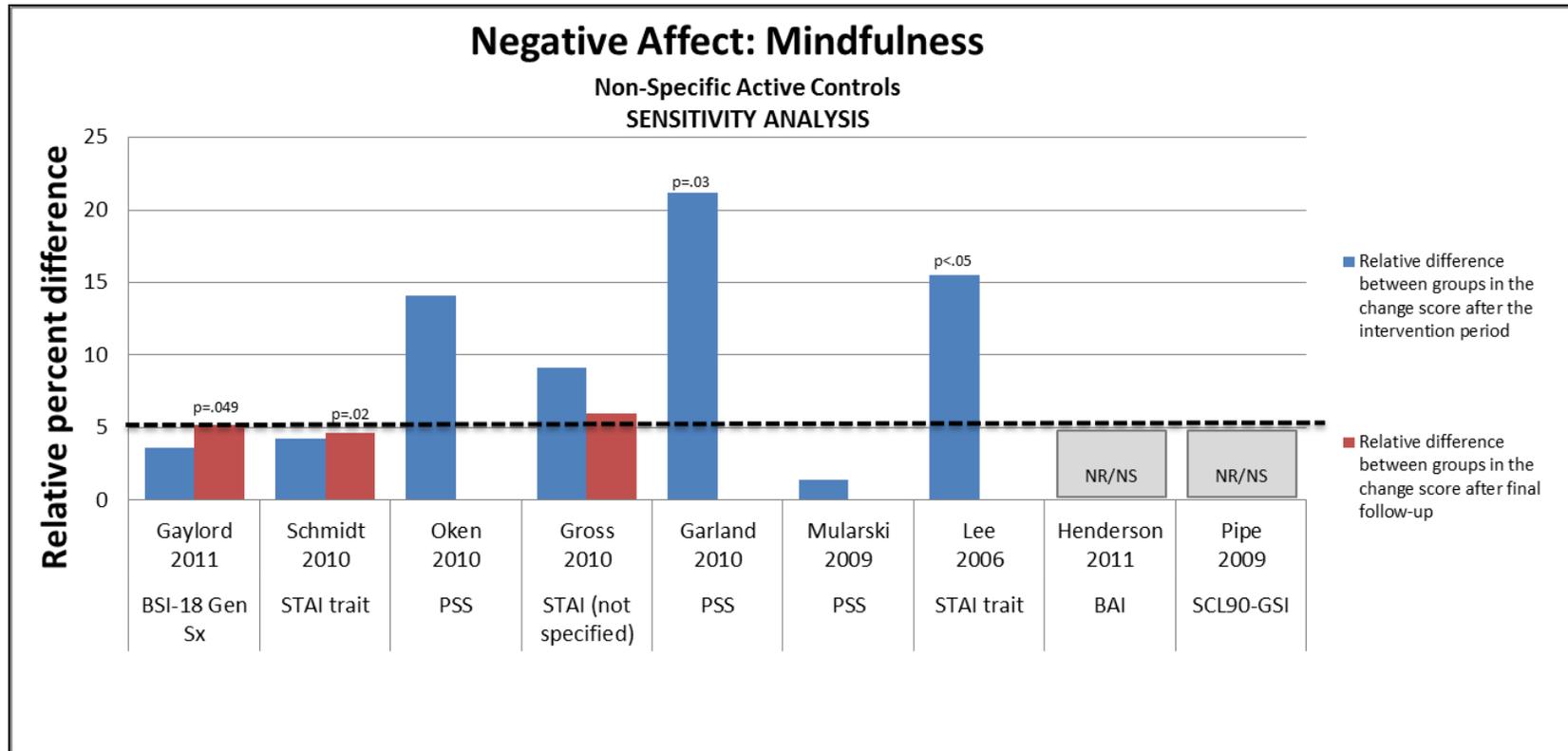
- Relative difference between groups in the change score.** This is a relative percent difference, using the baseline mean in the meditation group as the denominator. For example, if the meditation group improves from a 10 to 19 on a mental health scale and the control group improves from 11 to 16 on the same scale, the relative difference between groups in the change score is: $\frac{((19-10)-(16-11))}{10} \times 100 = 40\%$. The interpretation is that there is a 40% relative improvement on the mental health scale in the meditation group compared with the control group. See Appendix E for absolute difference in change score values. Improvement in all scales is indicated in the positive direction. A positive relative percent difference means that the score improved more in the intervention group than in the control group.
- NR / NS = Not Reported/Not significant. The trial measured this outcome and stated they were non-significant, and did not report actual results.
- Black dotted lines from -5% to +5% indicate our criteria for no effect. It does not indicate statistical significance.
- A p value above or below a bar indicates statistical significance reported in the original study publication. If there is no p value with a bar, the outcome was not significant in the original study publication.
- BSI-18: Brief Symptom Inventory; STAI = State Trait Anxiety Inventory; CESD = Center for Epidemiologic Studies Depression Scale; PSS = Perceived Stress Scale; SCL90: Symptom Checklist-90.

Figure 16. Meta-analysis of the effects of meditation programs on negative affect



BSI-18: Brief Symptom Inventory; STAI = State Trait Anxiety Inventory; CESD = Center for Epidemiologic Studies Depression Scale; PSS = Perceived Stress Scale; MM=Mindfulness meditation; wks=weeks; MBSR =Mindfulness-based stress reduction

Figure 17. Relative difference between groups in the changes in measures of negative affect, in the mindfulness versus non-specific active control studies (sensitivity analysis)



1. **Relative difference between groups in the change score.** This is a relative percent difference, using the baseline mean in the meditation group as the denominator. For example, if the meditation group improves from a 10 to 19 on a mental health scale and the control group improves from 11 to 16 on the same scale, the relative difference between groups in the change score is: $((19-10)-(16-11))/10 \times 100 = 40\%$. The interpretation is that there is a 40% relative improvement on the mental health scale in the meditation group compared with the control group. See Appendix E for absolute difference in change score values. Improvement in all scales is indicated in the positive direction. A positive relative percent difference means that the score improved more in the intervention group than in the control group
2. NR / NS = Not Reported/Not significant. The trial measured this outcome and stated they were non-significant, and did not report actual results.
3. Black dotted lines from -5% to +5% indicate our criteria for no effect. It does not indicate statistical significance.
4. A p value above or below a bar indicates statistical significance reported in the original study publication. If there is no p value with a bar, the outcome was not significant in the original study publication.
5. BSI-18 = Brief Symptom Inventory, General Symptom Severity Subscale; STAI = State Trait Anxiety Inventory; PSS = Perceived Stress Scale; BAI = Beck Anxiety Index; SCL90-GSI = Symptom Checklist 90 Global Severity Index.

Mantra Meditation Programs versus Non-specific Active Control

Six trials compared mantra meditation programs with non-specific active controls, and evaluated a negative affect outcome. Five were transcendental meditation trials and one was other mantra meditation program. Five trials reported on anxiety and one on depression. Since only one nonsignificant depression outcome was added to the existing anxiety analysis, it did not change our conclusions on consistency of results from that of the anxiety analysis (Figure 19). A sensitivity analysis prioritizing stress/distress over anxiety was conducted, and the overall results did not change (Figure 20). The sensitivity analysis changed three anxiety outcomes to stress outcomes, and added to the inconsistency. A meta-analysis of the scales used in the sensitivity analysis suggested a small statistically significant improvement in negative affect (Figure 21). However, due to medium risk of bias, inconsistency seen on the difference in change analysis, and indirect measures of negative affect, this finding did not change our overall conclusion.

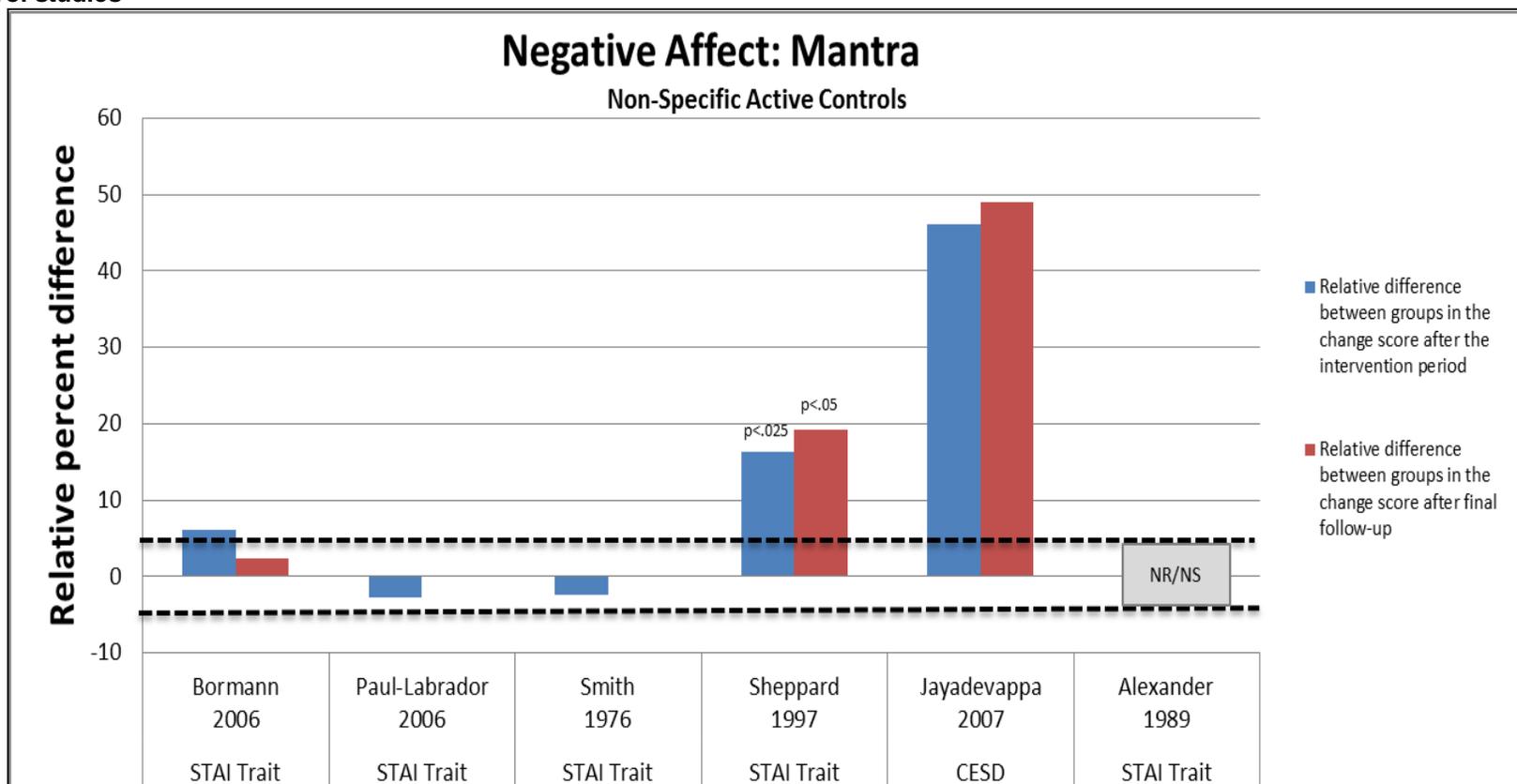
The strength of evidence is insufficient that mantra programs have an effect on negative affect among various clinical populations when compared with a non-specific active control. We based this rating on overall medium risk of bias, inconsistent results, indirect measures of negative affect, and imprecise estimates (Table 15).

Table 15. Grade of trials addressing the efficacy of mantra meditation programs on negative affect compared with non-specific active controls among diverse populations

Number of Trials; Subjects	Domains Pertaining to Strength of Evidence				Magnitude of Effect and Strength of Evidence
	Risk of Bias	Consistency	Directness	Precision	
Negative Affect					Insufficient SOE of an effect
6; 369	Medium	Inconsistent	Indirect	Precise	-2.8% to +46.1% improvement

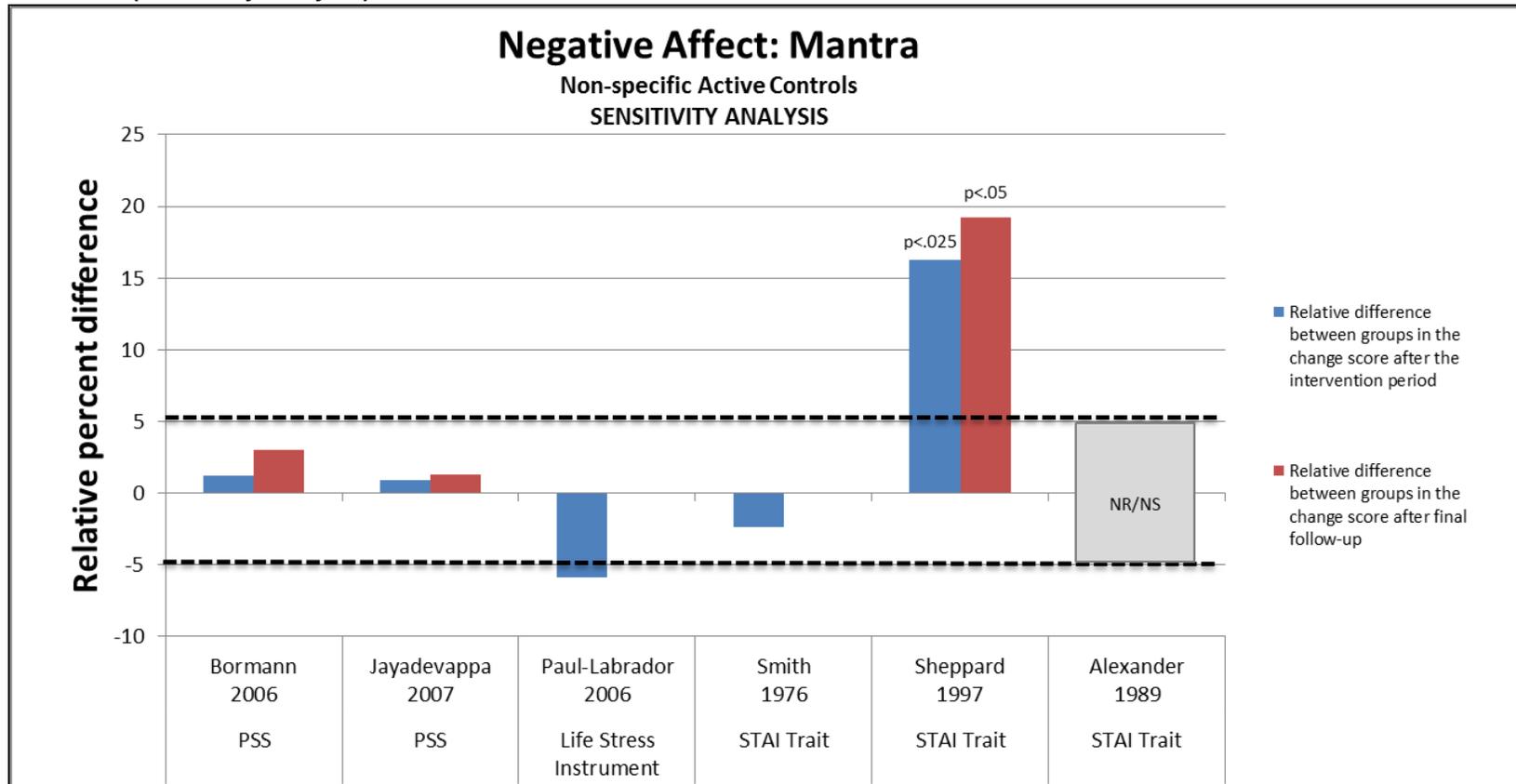
SOE = Strength of Evidence

Figure 19. Relative difference between groups in the changes in measures of negative affect, in the mantra versus non-specific active control studies



1. **Relative difference between groups in the change score.** This is a relative percent difference, using the baseline mean in the meditation group as the denominator. For example, if the meditation group improves from a 10 to 19 on a mental health scale and the control group improves from 11 to 16 on the same scale, the relative difference between groups in the change score is: $\frac{((19-10)-(16-11))}{10} \times 100 = 40\%$. The interpretation is that there is a 40% relative improvement on the mental health scale in the meditation group compared with the control group. See Appendix E for absolute difference in change score values. Improvement in all scales is indicated in the positive direction. A positive relative percent difference means that the score improved more in the intervention group than in the control group
2. NR / NS = Not Reported/Not significant. The trial measured this outcome and stated they were non-significant, and did not report actual results.
3. Black dotted lines from -5% to +5% indicate our criteria for no effect. It does not indicate statistical significance.
4. A p value above or below a bar indicates statistical significance reported in the original study publication. If there is no p value with a bar, the outcome was not significant in the original study publication.
5. STAI = State Trait Anxiety Inventory; CESD = Center for Epidemiologic Studies Depression Scale.

Figure 20. Relative difference between groups in the changes in measures of negative affect, in the mantra versus non-specific active control studies (sensitivity analysis)



1. **Relative difference between groups in the change score.** This is a relative percent difference, using the baseline mean in the meditation group as the denominator. For example, if the meditation group improves from a 10 to 19 on a mental health scale and the control group improves from 11 to 16 on the same scale, the relative difference between groups in the change score is: $\frac{((19-10)-(16-11))}{10} \times 100 = 40\%$. The interpretation is that there is a 40% relative improvement on the mental health scale in the meditation group compared with the control group. See Appendix E for absolute difference in change score values. Improvement in all scales is indicated in the positive direction. A positive relative percent difference means that the score improved more in the intervention group than in the control group
2. NR / NS = Not Reported/Not significant. The trial measured this outcome and stated they were non-significant, and did not report actual results.
3. Black dotted lines from -5% to +5% indicate our criteria for no effect. It does not indicate statistical significance.
4. A p value above or below a bar indicates statistical significance reported in the original study publication. If there is no p value with a bar, the outcome was not significant in the original study publication.
5. PSS = Perceived Stress Scale; STAI = State Trait Anxiety Inventory.

Positive Affect

Mindfulness Meditation Programs versus Non-specific Active Control

Two trials compared mindfulness meditation programs with non-specific active controls, and evaluated positive affect as an outcome. They used either a breast cancer or organ transplant population, were between 100 and 137 patients, and were both of medium risk of bias. One used the Sense of Coherence meaningfulness subscale, and the other used the short form 36 vitality subscale.

Henderson et al. randomized women with early-stage breast cancer (n=100) to MBSR or non-specific active control.⁵⁰ Subjective well-being was a secondary endpoint as measured by the Sense of Coherence Meaningfulness Subscale. At 4 months there was a statistically significant 6.8 percent improvement in mean Sense of Coherence Meaningfulness Subscale scores in the MBSR group as compared with the control group (p <0.05). However, this trial measured numerous outcomes and did not make any corrections for multiple comparisons. This trial had a medium risk of bias, provided 25 hours of training over 8 weeks, and did not specify whether it recommended home practice or not.

Gross et al. randomized solid organ transplant patients, post-surgery, (n=137) to MBSR versus health education.⁴⁷ The study used the short form-36 (SF-36) Vitality Score to measure improvement in positive mood as a secondary outcome. There were no differences between the groups at end of treatment. This trial provided 27 hours of training by a trained teacher, and unspecified amount of home practice over 8 weeks.

Overall, the difference in change graphs show a small inconsistent effect of the mindfulness meditation programs on positive mood with one trial showing a small significant effect that diminishes with time, and the other trial showing a null effect that improves over time but remains insignificant (Figures 22 -23).

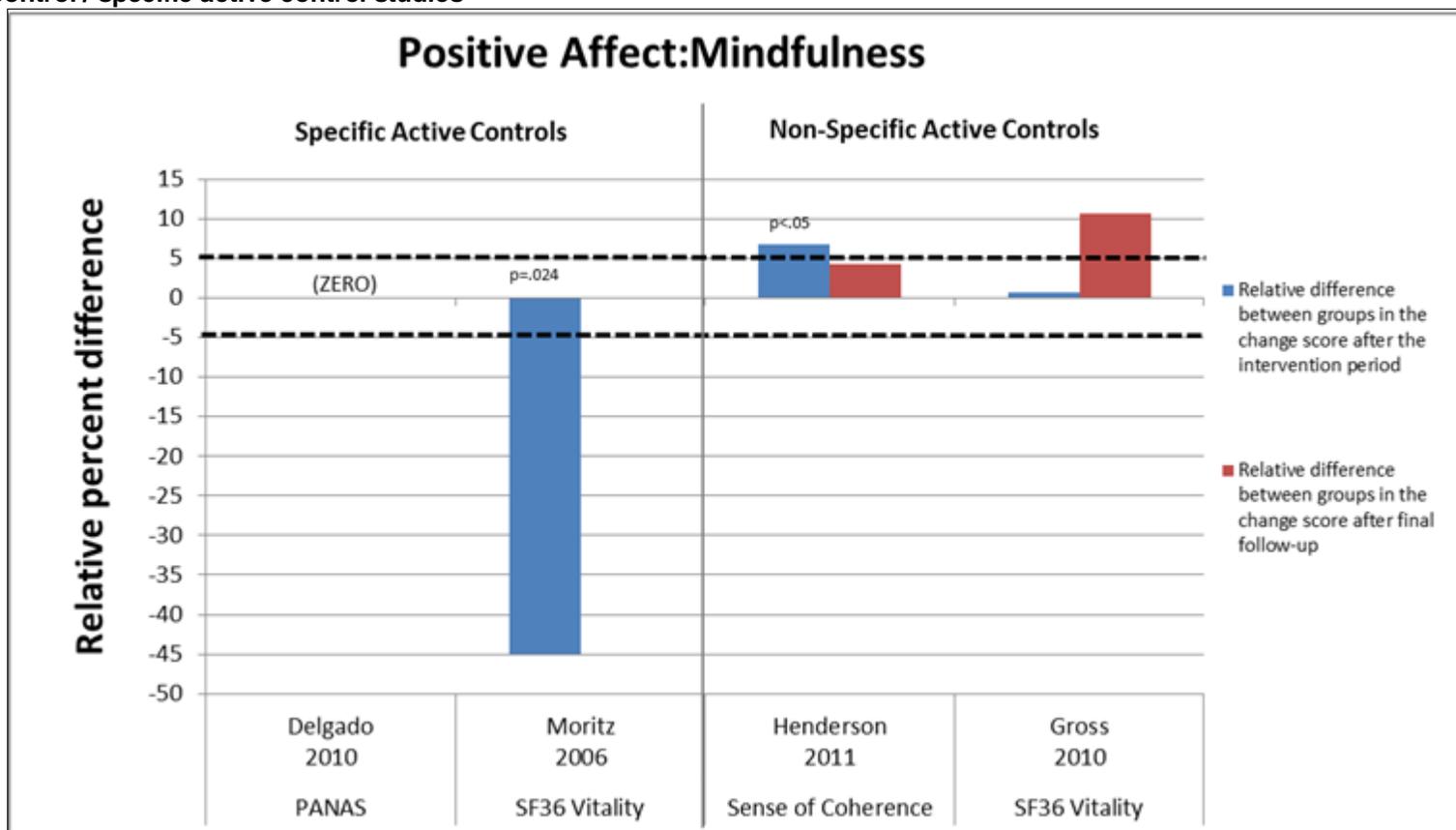
The strength of evidence is insufficient that mindfulness meditation program have an effect on positive affect when compared with a non-specific active control. We based this rating on medium risk of bias, inconsistent findings, indirect measures, and imprecise estimates (Table 16).

Table 16. Grade of trials addressing the efficacy of mindfulness meditation programs on positive affect compared with non-specific active controls among organ transplant recipients and breast cancer patients

Number of Trials; Subjects	Domains Pertaining to Strength of Evidence				Magnitude of Effect and Strength of Evidence
	Risk of Bias	Consistency	Directness	Precision	
Positive Affect					Insufficient SOE of an effect
2; 237	Medium	Inconsistent	Indirect	Imprecise	0.7% to 6.8% improvement

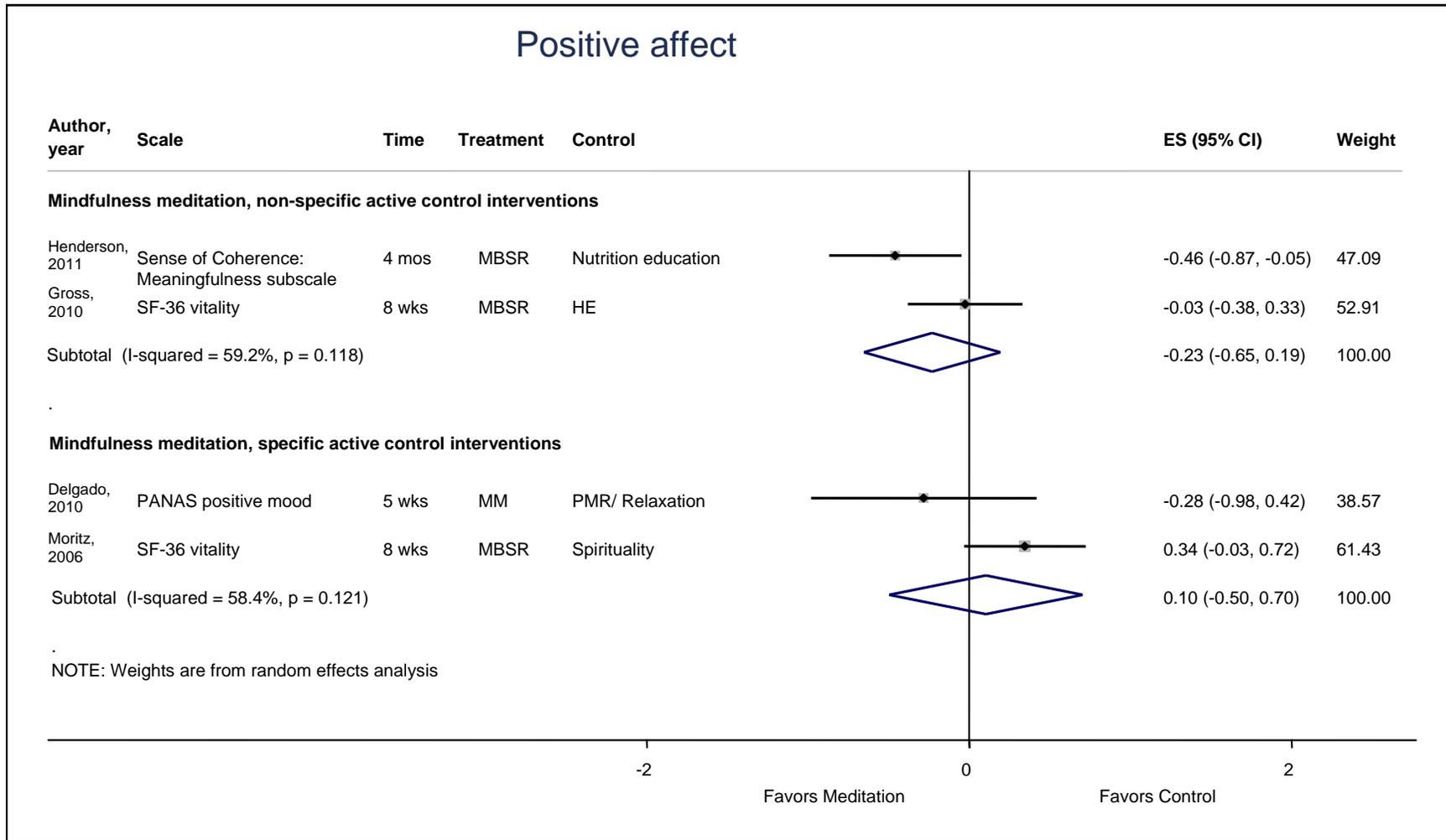
SOE = Strength of Evidence

Figure 22. Relative difference between groups in the changes in measures of positive affect, in the mindfulness versus non-specific active control / specific active control studies



1. **Relative difference between groups in the change score.** This is a relative percent difference, using the baseline mean in the meditation group as the denominator. For example, if the meditation group improves from a 10 to 19 on a mental health scale and the control group improves from 11 to 16 on the same scale, the relative difference between groups in the change score is: $\frac{((19-10)-(16-11))}{10} \times 100 = 40\%$. The interpretation is that there is a 40% relative improvement on the mental health scale in the meditation group compared with the control group. See appendix E for absolute difference in change score values. Improvement in all scales is indicated in the positive direction. A positive relative percent difference means that the score improved more in the intervention group than in the control group
2. NR / NS = Not Reported/Not significant. The trial measured this outcome and stated they were non-significant, and did not report actual results.
3. Black dotted lines from -5% to +5% indicate our criteria for no effect. It does not indicate statistical significance.
4. A p value above or below a bar indicates statistical significance reported in the original study publication. If there is no p value with a bar, the outcome was not significant in the original study publication.
5. PANAS = Positive and Negative Affect Scale; SF36 = Short Form-36.
6. Text describing results for comparisons with specific active controls for positive affect starts on page 87

Figure 23. Meta-analysis of the effects of meditation programs on positive affect with up to 4 months of followup



SF36 = Short Form-36; PANAS = Positive and Negative Affect Score.

Text describing results for comparisons with specific active controls for anxiety starts on page 87

Transcendental Meditation versus Non-specific Active Control

Jayadevappa et al. randomized congestive heart failure patients (n=23) to either 3 months of transcendental meditation or health education, assessing positive mood as a secondary outcome using the SF36 Vitality subscale.⁶⁹ With 100 percent trial completion and a 95 percent compliance rate among the originally randomized subjects, this trial found no differences at 3 and 6 months (Figure 24). This trial had a low risk of bias, and provided 22.5 hours of training over 6 months by trained and certified teachers. It recommended up to 90 hours of home practice during this time.

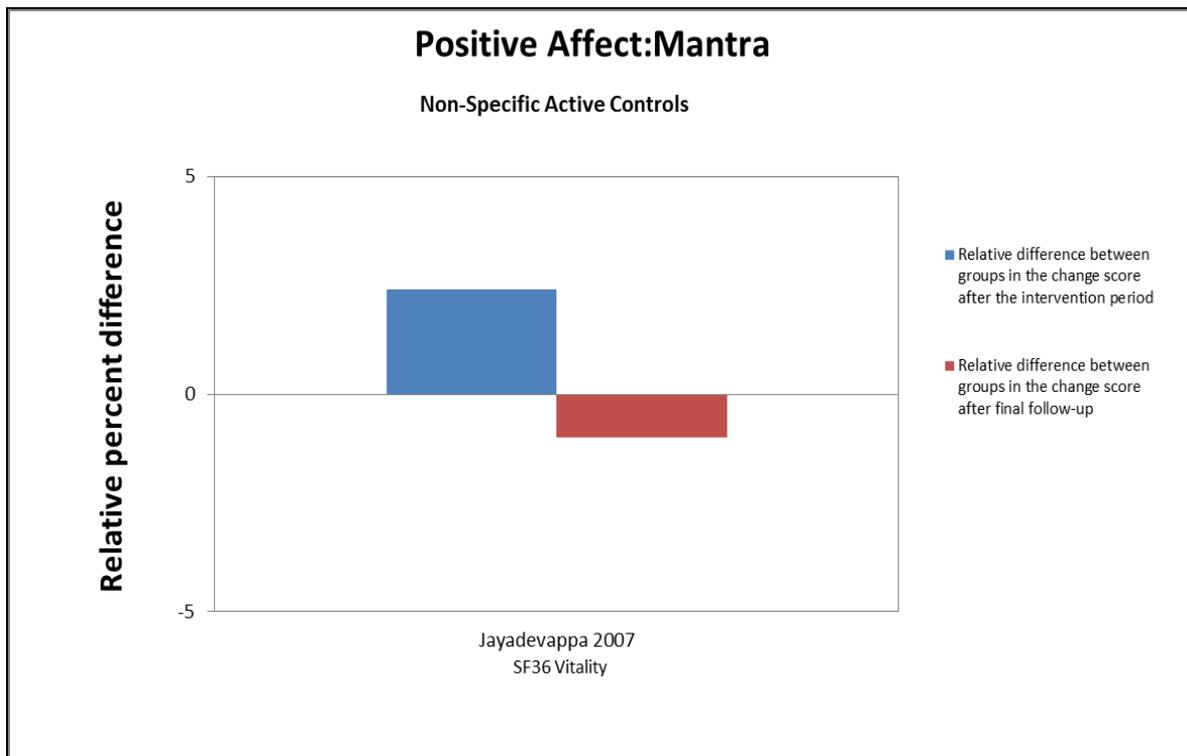
The strength of evidence is insufficient about the effects of transcendental meditation on positive affect when compared with a non-specific active control. We based this rating on a single low risk of bias study, unknown consistency, indirect measures, and imprecise estimates (Table 17).

Table 17. Grade of trials addressing the efficacy of transcendental meditation on positive affect compared with non-specific active controls among cardiac patients

Number of Trials; Subjects	Domains Pertaining to Strength of Evidence				Magnitude of Effect and Strength of Evidence
	Risk of Bias	Consistency	Directness	Precision	
Positive Affect					Insufficient SOE of an effect
1; 23	Low	Unknown	Indirect	Imprecise	+2.4%

SOE = Strength of Evidence; TM = Transcendental Meditation

Figure 24. Relative difference between groups in the changes in measures of positive affect, in the mantra versus non-specific active control studies



1. **Relative difference between groups in the change score.** This is a relative percent difference, using the baseline mean in the meditation group as the denominator. For example, if the meditation group improves from a 10 to 19 on a mental health scale and the control group improves from 11 to 16 on the same scale, the relative difference between groups in the change score is: $\frac{((19-10)-(16-11))}{10} \times 100 = 40\%$. The interpretation is that there is a 40% relative improvement on the mental health scale in the meditation group compared with the control group. See appendix E for absolute difference in change score values. Improvement in all scales is indicated in the positive direction. A positive relative percent difference means that the score improved more in the intervention group than in the control group
2. NR / NS = Not Reported/Not significant. The trial measured this outcome and stated they were non-significant, and did not report actual results.
3. Black dotted lines from -5% to +5% indicate our criteria for no effect. It does not indicate statistical significance.
4. A p value above or below a bar indicates statistical significance reported in the original study publication. If there is no p value with a bar, the outcome was not significant in the original study publication.
5. SF-36 = Short Form-36

Mental component of health-related quality of life

Mindfulness Meditation Programs versus Non-specific Active Control

Gross et al. randomized solid organ transplant patients, post-surgery, (n=137) to mindfulness-based stress reduction (MBSR) versus health education.⁴⁷ The trial used the SF-12 Mental Component Score to measure improvement in the mental component of health-related quality of life (QOL) as a secondary outcome. There were no differences between the groups at end of treatment (p=.29). This trial provided 27 hours of training by a trained teacher, and unspecified amount of home practice over 8 weeks. This trial had medium risk of bias.

Mularski et al. randomized elderly patients, predominantly men, with moderate to severe COPD (n=49) to a mindfulness-based breathing therapy or a support group.⁵⁶ The trial used the Short Form SF-36 for Veterans Mental Summary (VR-36) to measure quality of life (QOL) as a secondary outcome. There was a non-significant 8.3 percent improvement in the VR-36 Mental Summary scores in the mindfulness-based breathing therapy (MBBT) group after 2 months. This trial suffered from a 42 percent attrition rate and was rated as a high risk of bias.

The difference in change graphs suggested a small nonsignificant improvement for mindfulness meditation programs in the mental component of quality of life (QOL) when compared with nonspecific active controls (right side of Figure 25).

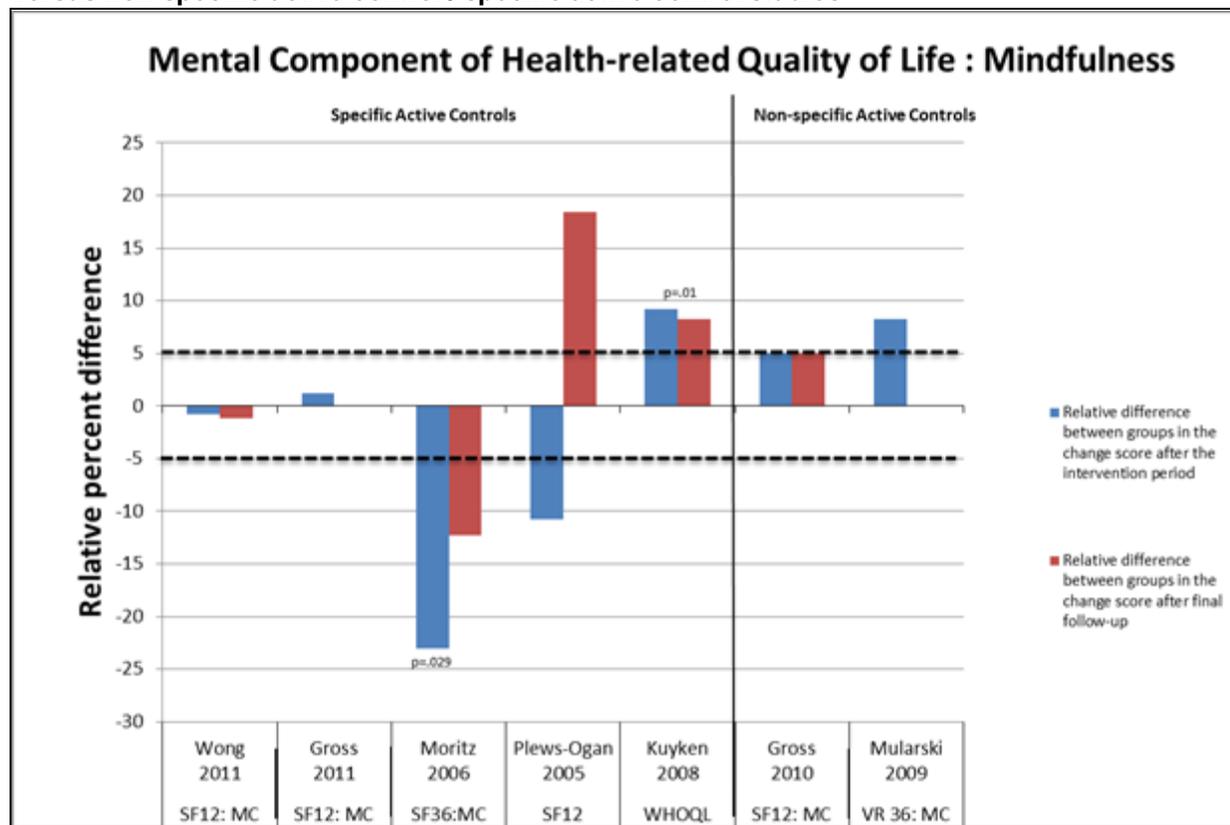
The strength of evidence is insufficient that mindfulness meditation programs have an effect on the mental component of health-related quality of life in organ transplant or COPD patients as compared with a non-specific active control. We based this rating on overall high risk of bias, consistent findings, direct measures, and imprecise estimates (Table 18).

Table 18. Grade of trials addressing the efficacy of mindfulness meditation programs on the mental component of health-related quality of life compared with non-specific active controls among organ transplant/chronic obstructive pulmonary disease patients

Number of Trials; Subjects	Domains Pertaining to Strength of Evidence				Magnitude of Effect and Strength of Evidence
	Risk of Bias	Consistency	Directness	Precision	
Mental health component of health-related QOL					Insufficient SOE of an effect
2; 186	High	Consistent	Direct	Imprecise	+5% to +8.3% improvement

SOE = Strength of Evidence; QOL = Quality of Life

Figure 25. Relative difference between groups in the changes in measures of studies mental component of health-related quality of life, in the mindfulness versus non-specific active control / specific active control studies



1. **Relative difference between groups in the change score.** This is a relative percent difference, using the baseline mean in the meditation group as the denominator. For example, if the meditation group improves from a 10 to 19 on a mental health scale and the control group improves from 11 to 16 on the same scale, the relative difference between groups in the change score is: $\frac{((19-10)-(16-11))}{10} \times 100 = 40\%$. The interpretation is that there is a 40% relative improvement on the mental health scale in the meditation group compared with the control group. See appendix E for absolute difference in change score values. Improvement in all scales is indicated in the positive direction. A positive relative percent difference means that the score improved more in the intervention group than in the control group
2. NR / NS = Not Reported/Not significant. The trial measured this outcome and stated they were non-significant, and did not report actual results.
3. Black dotted lines from -5% to +5% indicate our criteria for no effect. It does not indicate statistical significance.
4. A p value above or below a bar indicates statistical significance reported in the original study publication. If there is no p value with a bar, the outcome was not significant in the original study publication.
5. SF12:MC = Short Form-12: Mental Component Score of Health-related Quality of Life; SF36:MC = Short Form 36: Mental Component Score of Health-related Quality of Life; WHOQL = World Health Organization Quality of Life Assessment; VR36 = Veterans RAND 36 Item Health Survey.
6. Text describing results for comparisons with **specific** active controls for mental component of health-related quality of life starts on page 88

Comparisons with Specific Active Control

Anxiety

Mindfulness Meditation Programs versus Specific Active Control

Seven trials evaluated a mindfulness meditation program against a specific active control for the outcome of anxiety. Four trials used mindfulness-based stress reduction (MBSR), one mindfulness-based cognitive therapy (MBCT), and two mindfulness mediation. The control groups were heterogeneous including medications, spirituality interventions, and group therapies. Sample sizes ranged from 26 to 110. One trial was rated as high risk of bias, four medium risk of bias, and two low risk of bias.

Wong et al.⁶⁴ randomized Chinese-speaking participants with chronic pain (n=99) to an 8-week MBSR program or a multidisciplinary pain intervention. The trial saw non-significant changes at 2 and 6 months post-intervention in the state trait anxiety index (STAI) State or Trait scores. The profile of mood states (POMS) Tension difference-in-change score showed the greatest change (11.5 percent) favoring MBSR, but was also non-significant.

Gross et al. randomized adults with primary chronic insomnia (n=30) to an 8-week MBSR program or an 8-week course of pharmacotherapy with eszopiclone.⁴⁸ At 2 and 5 months post-intervention, there were no significant changes in STAI State scores in either group, but the directionality of difference-in-change point estimates favored the MBSR group.

Moritz et al. randomized people with mood disorders (n=165) recruited from primary care clinics to 8 weeks of either MBSR or an 8-week audio-taped spirituality home trial program.⁵⁴ This trial evaluated the superiority of a spirituality program to MBSR, as opposed to other trials, using a comparative effectiveness design. MBSR was used as the control. They utilized a profile of mood states score of 40 or greater as inclusion criteria, indicating a moderate degree of mood disturbance, and as a main outcome measure. Although groups appeared matched for amount of training (12 hours over 8 weeks), the spirituality group received up to 42 hours of home practice over that time and it is unclear whether the MBSR group received the same. At 8 weeks, the difference in the MBSR group from baseline was 39 percent lower than that in the spirituality group (p=0.007).

Koszycki et al.⁵¹ randomized patients with generalized social anxiety disorder (n=53) to an 8-week course of MBSR or a 12-week course of group cognitive behavior therapy. MBSR received a maximum of 27.5 hours of training and a maximum of 28 hours of home practice over 8 weeks. Outcome measures included four scales of social anxiety, which favored group cognitive behavior therapy over MBSR: Liebowitz Social Anxiety-Fear (p=.09), Liebowitz Social Anxiety-Avoidance (p=.009), Social Phobia Scale (p=.006), and Social Interaction Scale (p=.057). Although the groups cognitive behavior therapy group ran for 4 weeks longer than MBSR, the total dose was similar (27.5 hours of training for MBSR vs. 30 hours for group cognitive behavior therapy). It remains unclear if it was the effect of the training over a longer period of time in the group cognitive behavior therapy arm that accounted for the differences. The analysis appeared to compare post-treatment scores only, and it was unclear whether they accounted for baseline differences in the analysis, given that there were large baseline differences between the groups.

Philippot et al. randomized patients with tinnitus (n=30) to a 6-week modified MBCT program or progressive muscular relaxation training.⁵⁸ This trial used the STAI (unspecified) and found no statistically significant differences between-groups. It provided 13.5 hours of training and an unspecified amount of home practice. We rated it as medium risk of bias.

Delgado et al. randomized worriers (n=36) to 5 weeks of mindfulness meditation or progressive muscular relaxation, providing 10 hours of training and unspecified amount of home practice.⁴⁴ They found no significant differences in the STAI trait, and had a medium risk of bias. Piet et al. randomized 26 patients with social phobia to MBCT or group cognitive behavior therapy.⁵⁹ They provided 16 hours of training and up to 28 hours of home practice over an 8-week period. This trial found no difference between the groups on the beck anxiety index. However, the cognitive behavior therapy group was provided nearly double the amount of group training, 28 hours over 14 weeks, and this increased time and attention in the control group may not allow appropriate comparisons between the groups. This trial had a medium risk of bias.

The difference-in-change graphs showed inconsistent results(Figure 26) A meta-analysis of these trials showed a small nonsignificant effect slightly favoring the specific active control at end of treatment and end of study time points (Figures 5 and 6).

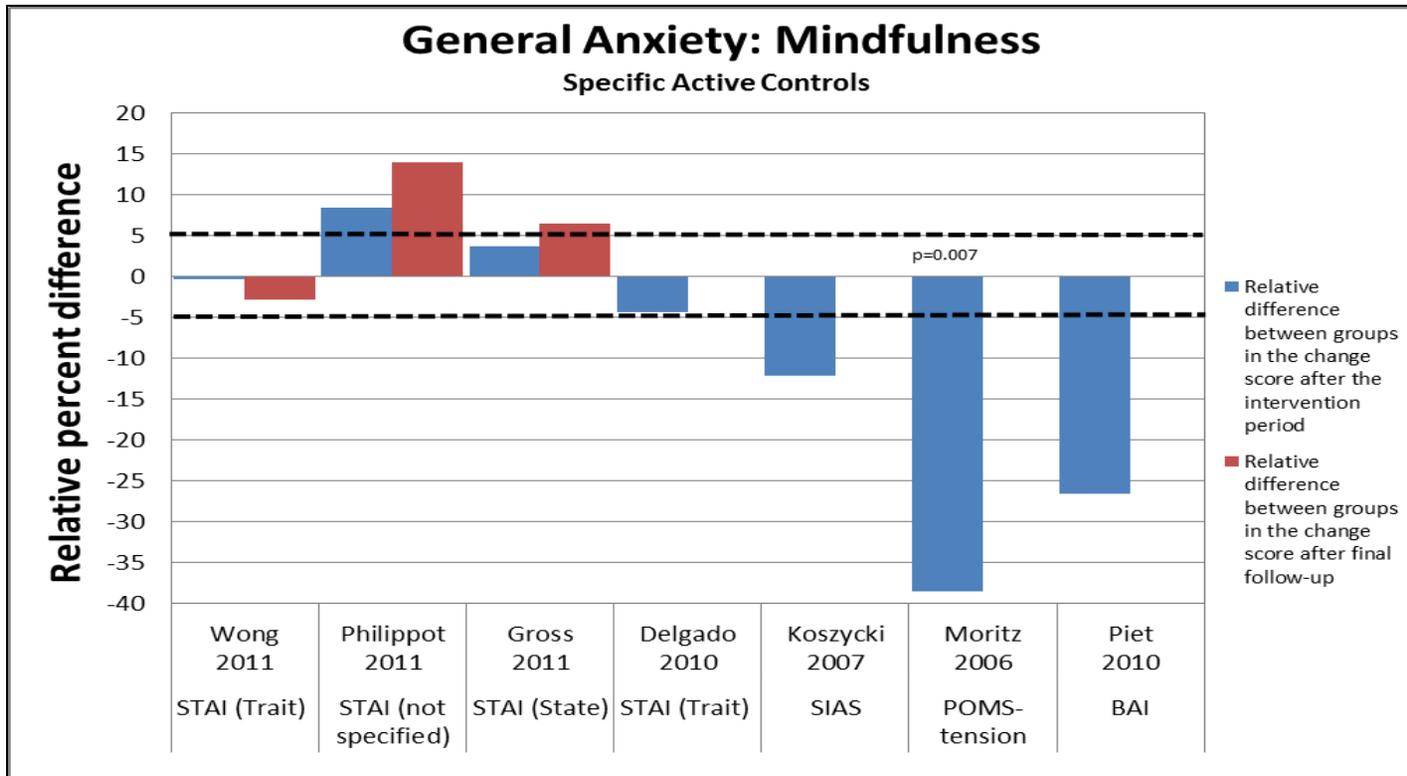
The strength of evidence is insufficient that mindfulness meditation programs have an effect on anxiety among various clinical populations when compared with a variety of specific active controls. We based this rating on overall medium risk of bias, inconsistent findings, directness of measures, and imprecise estimates (Table 19).

Table 19. Grade of trials addressing the efficacy of mindfulness meditation programs on anxiety compared with specific active controls among diverse populations

Number of Trials; Subjects	Domains Pertaining to Strength of Evidence				Magnitude of Effect and Strength of Evidence
	Risk of Bias	Consistency	Directness	Precision	
Anxiety					Insufficient SOE of an effect
7; 372	Medium	Inconsistent	Direct	Imprecise	-38.6 to +8.4%

SOE = Strength of Evidence

Figure 26. Relative difference between groups in the changes in measures of general anxiety, in the mindfulness versus specific active control studies



- Relative difference between groups in the change score.** This is a relative percent difference, using the baseline mean in the meditation group as the denominator. For example, if the meditation group improves from a 10 to 19 on a mental health scale and the control group improves from 11 to 16 on the same scale, the relative difference between groups in the change score is: $\frac{((19-10)-(16-11))}{10} \times 100 = 40\%$. The interpretation is that there is a 40% relative improvement on the mental health scale in the meditation group compared with the control group. Improvement in all scales is indicated in the positive direction. A positive relative percent difference means that the score improved more in the intervention group than in the control group.
- NR / NS = Not Reported/Not significant. The trial measured this outcome and stated they were non-significant, and did not report actual results.
- Black dotted lines from -5% to +5% indicate our criteria for no effect. It does not indicate statistical significance.
- A p value above or below a bar indicates statistical significance reported in the original study publication. If there is no p value with a bar, the outcome was not significant in the original study publication.
- STAI = State Trait Anxiety Index; SIAS = Social Interaction Scale; POMS = Profile of Mood States; BAI = Beck Anxiety Index.

Other Mantra Meditation versus Specific Active Control

Lehrer et al. assigned anxious participants to clinically standardized meditation (n=23) or progressive muscular relaxation (n=19).⁷⁰ The program provided 7.5 hours of training and unspecified amount of home practice over 5 weeks. Undergraduate and graduate students with 4 months of training in the technique and no prior teaching experience provided the training. Results on all four anxiety measures favored the progressive muscular relaxation group over the clinically standardized meditation group. For measures it used institute for personality and ability testing (IPAT) anxiety inventory, symptom checklist 90 anxiety subscale, and state trait anxiety index state and trait scales. At 6 weeks the differences were all non-significant, but ranged from 6 to 21 percent favoring the progressive muscular relaxation group (Figure 7).

The strength of evidence is insufficient about the effects of clinically standardized meditation on anxiety in an anxious population when compared with progressive muscular relaxation. We based this rating on a single study with medium risk of bias, unknown consistency, directness of measures, and imprecise estimates (Table 20).

Table 20. Grade of trials addressing the efficacy of clinically standardized meditation programs on anxiety compared with progressive muscle relaxation among anxious participants

Number of Trials; Subjects	Domains Pertaining to Strength of Evidence				Magnitude of Effect and Strength of Evidence at End of Intervention
	Risk of Bias	Consistency	Directness	Precision	
Anxiety					Insufficient SOE of an effect compared with PMR
1; 42	Medium	Unknown	Direct	Imprecise	-5.6% favoring PMR

SOE = Strength or Evidence; PMR = Progressive Muscle Relaxation

Depression

Mindfulness Meditation Programs versus Specific Active Control

Nine trials evaluated a mindfulness meditation programs against a specific active control for the outcome of depression. Four trials compared mindfulness-based stress reduction (MBSR) to various specific active controls in diverse populations. Three trials compared mindfulness-based cognitive therapy (MBCT) to either antidepressant among depressed patients or cognitive behavior therapy among anxious patients. Two trials compared a mindfulness meditation to progressive muscular relaxation.⁵⁸ Four trials had a low risk of bias, four had a medium risk of bias, and one had a high risk of bias. Sample sizes ranged from 25 to 123.

Wong et al. randomized patients with chronic pain (n=99) in Hong Kong to MBSR or a multidisciplinary pain intervention.⁶⁴ It used two scales to assess depression. It found a non-significant 10.7 percent improvement on the profile of mood states (POMS)-Depression at 2 months, which maintained to 6 months. However, it found no difference in the center for epidemiologic studies depression scale (CES-D) at 2 or 6 months. This trial had a low risk of bias, provided 27 hours of training and unspecified amount of home practice over 8 weeks. Its teachers were trained and had 5 years of experience teaching meditation.⁶⁴

Gross et al. randomized people with insomnia (n=27) to MBSR or eszopiclone.⁴⁸ They found a 25.4 percent change in CES-D favoring the drug at the end of 2 months, which increased to 42.2 percent at 5 months. Although these appeared to be large effects, the study reported the differences as not significant. This trial provided 26 hours of training and up to 36 hours of home practice over 8 weeks.

Koszyki et al. randomized patients with social anxiety disorder (n=53) to MBSR or group cognitive behavior therapy. The trial had high risk of bias. They found a non-significant 5.3 percent difference favoring the cognitive behavior therapy group on the beck depression inventory II.⁵¹

Moritz et al. randomized patients with mood disorders (n=110) to a spirituality program versus MBSR.⁵⁴ In this trial, MBSR was the active control for the spirituality intervention. The spirituality intervention included a meditative component. It provided about 12 hours of training in both interventions over an 8-week period, with unspecified amount of home practice in the MBSR group. It provided up to 42 hours of home practice in the spirituality group. There was no information on teacher qualifications for MBSR. There was a significant 31.7 percent improvement on the profile of mood states (POMS)-Depression scale in the spirituality program as compared with MBSR (p<0.013). This trial had a low risk of bias.

Segal et al. randomized depressed patients in acute remission to MBCT with tapering of antidepressant or maintenance antidepressant medication (n=53) to assess depression relapse. Relapse rates by 600 days were 46 percent for the antidepressant group and 38 percent for MBCT. This absolute 8 percent difference did not reach statistical significance. This trial had a low risk of bias, provided 23 hours of training by trained and certified teachers, and recommended an unspecified amount of home practice.⁶³

Kuyken et al. randomized patients with recurrent depression (n=123) who were in full or partial remission to either maintenance anti-depressant medication or MBCT with support to taper medication.⁵² After 15 months, 60 percent of the antidepressant group had relapsed as compared with 47 percent in the MBCT group. This 13 percent absolute difference did not reach statistical significance. They also measured the HAM-D scores, which were 31.7 percent lower in the MBCT group at 3 months and 26.7 percent lower at 15 months (p=.02). On a third measure, the beck depression inventory II, the MBCT group showed a 14.6 percent reduction at 3 months and 15 percent reduction at 15 months compared with the antidepressant group. These differences did not reach statistical significance. Of note, 75 percent of the MBCT had discontinued their antidepressant by 6 months. This was a low risk-of-bias trial that provided 24 hours of training and recommended up to 37.5 hours of home practice over an 8-week period. The teachers were trained and certified.

Piet et al. randomized young adults with social phobia (n=26) to either MBCT or group cognitive behavioral therapy in a crossover design with participants receiving both treatments.⁵⁹ We evaluated comparisons after the first intervention period only, before any crossover. They provided 16 hours of training and up to 28 hours of home practice over an 8-week period. This trial found a 24.3 percent non-significant change favoring the cognitive behavioral therapy group on the BDI-II. However, the cognitive behavioral therapy group received nearly doubles the amount of group training, 28 hours over 14 weeks, and this increased time and attention in the control group may not allow equivalent comparisons between the groups. This trial had a medium risk of bias.

Philippot et al. randomized patients with tinnitus (n=25) to a 6-week modified MBCT program or progressive relaxation training.⁵⁸ This trial used the beck depression inventory and

found an insignificant 8.7 percent differences between groups at 6 weeks favoring mindfulness meditation. At 18 weeks this effect disappeared. This trial had a medium risk of bias and provided 13.5 hours of training with an unspecified amount of home practice.

Delgado et al. randomized female university students (n=32) who were worriers to 5 weeks of mindfulness meditation or progressive muscular relaxation, providing 10 hours of training and unspecified amount of home practice.⁴⁴ The study found a non-significant 13.3 percent improvement in the beck depression inventory in the mindfulness meditation group as compared with progressive muscular relaxation. This trial had a medium risk of bias.

The difference in change graphs shows significant inconsistency (Figure 27). Two meta-analyses of results at the end of treatment and end of study show small nonsignificant effects slightly favoring meditation (Figures 9 and 10).

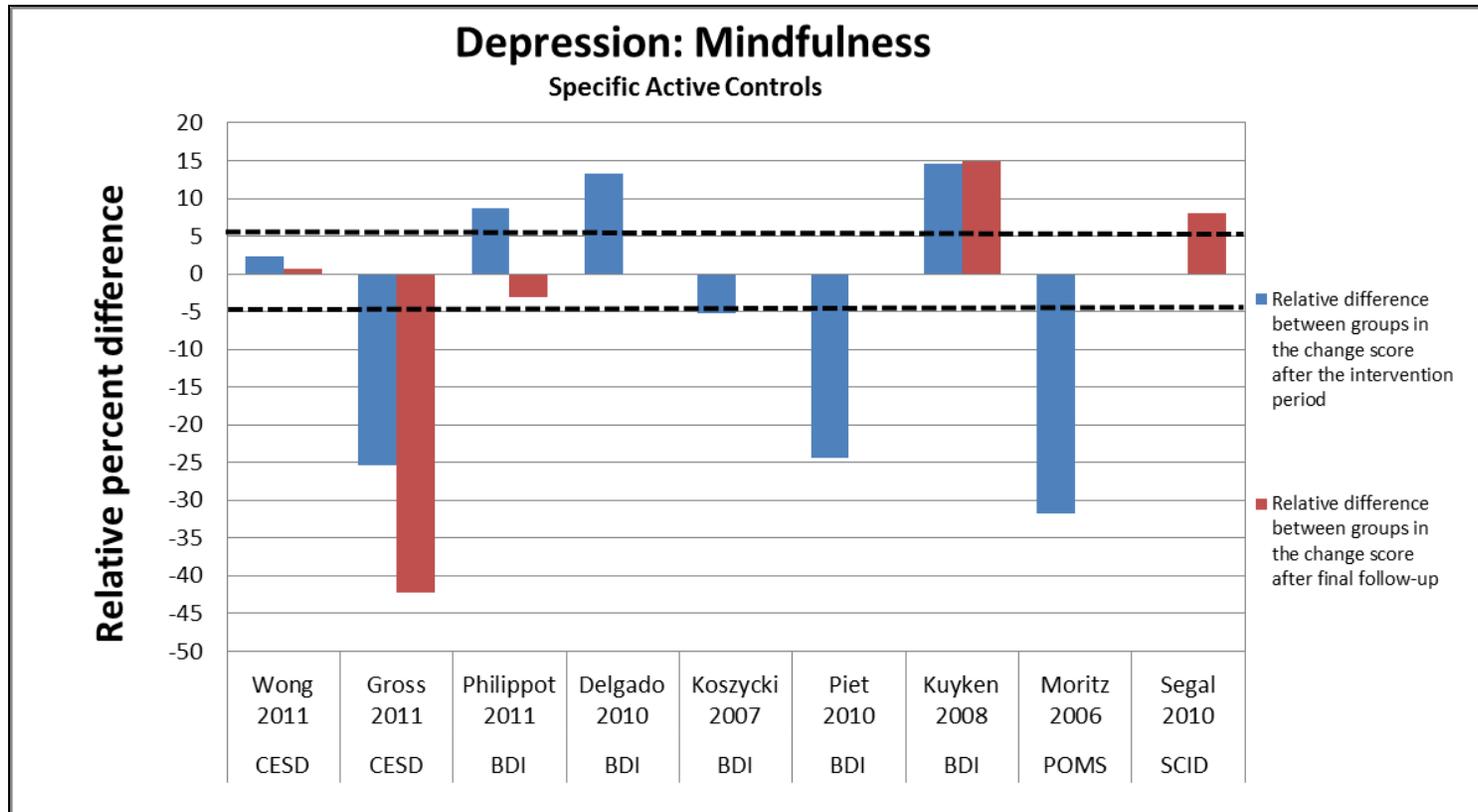
The strength of evidence is insufficient that mindfulness meditation programs have an effect on depressive symptoms among various clinical populations compared with a variety of specific active controls. We based this rating on overall medium risk of bias, inconsistent results, direct measures, and imprecise estimates (Table 21).

Table 21. Grade of trials addressing the efficacy of mindfulness meditation programs on depressive symptoms compared with specific active controls among diverse populations

Number of Trials; Subjects	Domains Pertaining to Strength of Evidence				Magnitude of Effect and Strength of Evidence
	Risk of Bias	Consistency	Directness	Precision	
Depressive Symptoms					Insufficient SOE of an effect
9; 579	Medium	Inconsistent	Direct	Imprecise	-31.7% to +14.6%

SOE = Strength of Evidence

Figure 27. Relative difference between groups in the changes in measures of depression, in the mindfulness versus specific active control studies



- Relative difference between groups in the change score.** This is a relative percent difference, using the baseline mean in the meditation group as the denominator. For example, if the meditation group improves from a 10 to 19 on a mental health scale and the control group improves from 11 to 16 on the same scale, the relative difference between groups in the change score is: $\frac{((19-10)-(16-11))}{10} \times 100 = 40\%$. The interpretation is that there is a 40% relative improvement on the mental health scale in the meditation group compared with the control group. See Appendix E for absolute difference in change score values. Improvement in all scales is indicated in the positive direction. A positive relative percent difference means that the score improved more in the intervention group than in the control group.
- NR / NS = Not Reported/Not significant. The trial measured this outcome and stated they were non-significant, and did not report actual results.
- Black dotted lines from -5% to +5% indicate our criteria for no effect. It does not indicate statistical significance.
- A p value above or below a bar indicates statistical significance reported in the original study publication. If there is no p value with a bar, the outcome was not significant in the original study publication.
- CESD = Center for Epidemiologic Studies Depression Scale; BDI = Beck Depression Inventory; POMS = Profile of Mood States; SCID = Structured Clinical Interview.

Other Mantra Meditation versus Specific Active Control

Lehrer et al. assigned anxious participants to clinically standardized meditation or progressive muscular relaxation (n=42).⁷⁰ The program provided 7.5 hours of training and unspecified amount of home practice over five weeks. The trainers were undergraduate and graduate students with 4 months of training in the technique and no prior teaching experience. SCL-90 depression scores favored the progressive muscular relaxation group over the clinically standardized meditation group. The difference-in-change scores were all non-significant, but ranged from 27.8 percent at 6 weeks to 7.8 percent at 6 months favoring the progressive muscular relaxation group (Figure 11).

The strength of evidence is insufficient that clinically standardized meditation has an effect on depressive symptoms in an anxious population compared with progressive muscular relaxation. We based this rating on a single study with medium risk of bias, unknown consistency, direct measures, and imprecise estimates (Table 22).

Table 22. Grade of trials addressing the efficacy of clinically standardized meditation programs on depression compared with progressive muscle relaxation among anxious participants

Number of Trials; Subjects	Domains Pertaining to Strength of Evidence				Magnitude of Effect and Strength of Evidence at End of Intervention
	Risk of Bias	Consistency	Directness	Precision	
Depressive Symptoms					Insufficient SOE of an effect
1; 42	Medium	Unknown	Direct	Imprecise	-27.8% favoring PMR

SOE = Strength of Evidence; PMR = Progressive Muscle Relaxation

Stress and Distress

Mindfulness Meditation Programs versus Specific Active Control

Three mindfulness trials evaluated distress as a secondary outcome among populations with some form of emotional distress. Delgado et al. randomized female university students (n=32) who had high scores on the PSWQ to 5 weeks of mindfulness meditation or progressive muscular relaxation, providing 10 hours of training and unspecified amount of home practice.⁴⁴ Scores on the positive and negative affect scale(PANAS)- Negative Mood were relatively unchanged at 5 weeks of intervention, and there was no difference between the two groups at the end of treatment. This trial had a medium risk of bias.

Moritz et al. randomized patients with mood disorders (n=110) to a spirituality program versus MBSR.⁵⁴ In this trial, MBSR was the active control. It provided about 12 hours of training in both interventions over an 8-week period. It provided up to 42 hours of home practice in the spirituality group and an unspecified amount of home practice in the MBSR group. There was no information on teacher qualifications for MBSR. This trial used two scales that assessed distress. They found a 23.8 percent change favoring spirituality at 8 weeks (p=.034) on the profile of mood states (POMS) total mood disturbance score, and a 22.4 percent change favoring spirituality at 8 weeks (p=.034) on the SF36 Mental Health subscale score. This trial had a low

risk of bias. It is notable that this intervention included a meditative component, as well as breathing exercises that may resemble features of MBSR.

Piet et al. randomized young adults with social phobia (n=26) to MBCT or group cognitive behavioral therapy in a crossover design with participants receiving both treatments.⁵⁹ We evaluated comparisons after the first intervention period only, before any crossover. They provided 16 hours of training and up to 28 hours of home practice over an 8-week period. This trial found a 13.2 percent non-significant change favoring the cognitive behavior therapy group on the symptom checklist 90 global severity index. However, the cognitive behavior therapy group received nearly twice the amount of group training, 28 hours over 14 weeks, and this increased time and attention in the control arm may not allow equivalent comparisons between the groups. This trial had a medium risk of bias.

The difference in change graphs showed consistent results favoring the specific active control (Figure 28). A meta-analysis suggested a nonsignificant null effect (Figure 13).

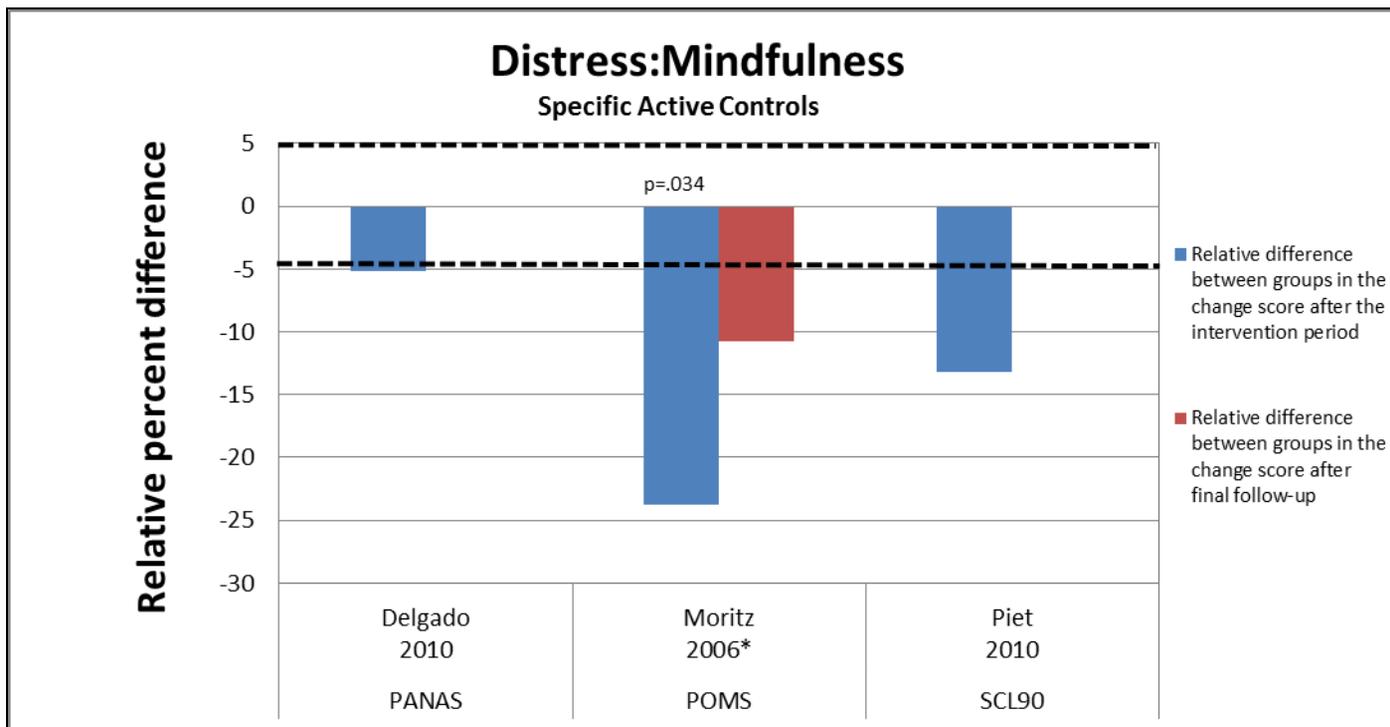
The strength of evidence is low that mindfulness meditation programs do not improve distress among those with mood disturbance or symptoms of anxiety compared with a variety of specific active controls. We based this rating on overall medium risk of bias, consist results, direct measures, and imprecise estimates (Table 23).

Table 23. Grade of trials addressing the efficacy of mindfulness meditation programs on distress compared with specific active controls among populations with emotional distress

Number of Trials; Subjects	Domains Pertaining to Strength of Evidence				Magnitude of Effect and Strength of Evidence
	Risk of Bias	Consistency	Directness	Precision	
Distress					Low SOE of no effect on distress
3; 168	Medium	Consistent	Direct	Imprecise	- 5.2% to- 23.8% (favoring control)

SOE = Strength of Evidence

Figure 28. Relative difference between groups in the changes in measures of distress, in the mindfulness versus specific active control studies



- Relative difference between groups in the change score.** This is a relative percent difference, using the baseline mean in the meditation group as the denominator. For example, if the meditation group improves from a 10 to 19 on a mental health scale and the control group improves from 11 to 16 on the same scale, the relative difference between groups in the change score is: $((19-10)-(16-11))/10 \times 100 = 40\%$. The interpretation is that there is a 40% relative improvement on the mental health scale in the meditation group compared with the control group. See Appendix E for absolute difference in change score values. Improvement in all scales is indicated in the positive direction. A positive relative percent difference means that the score improved more in the intervention group than in the control group
- NR / NS = Not Reported/Not significant. The trial measured this outcome and stated they were non-significant, and did not report actual results.
- Black dotted lines from -5% to +5% indicate our criteria for no effect. It does not indicate statistical significance.
- A p value above or below a bar indicates statistical significance reported in the original study publication. If there is no p value with a bar, the outcome was not significant in the original study publication.
- PANAS = Positive and Negative Affect Schedule; POMS = Profile of Mood States; SCL90 = Symptom Checklist 90.

Positive Affect

Mindfulness Meditation Programs versus Specific Active Control

Two mindfulness trials evaluated the effect compared with a specific active control on the outcome of positive affect. Delgado et al. randomized female students (n=32) with high scores on the Pittsburgh Sleep Quality Index (PSWQ) to 5 weeks of either mindfulness training or progressive muscle relaxation training, providing 10 hours of training and unspecified amount of home practice.⁴⁴ The trial did not detect any within or between-group effects on the PANAS positive affect scale. This trial had a medium risk of bias.

Moritz et al. randomized patients with mood disorders (n=110) to a spirituality program versus MBSR.⁵⁴ In this trial, MBSR was the active control for the spirituality intervention they were testing. The trial selected participants with high scores on the profile of mood states (POMS) scale. The spirituality program had meditative components in it. It provided about 12 hours of training in both interventions over an 8-week period, with unspecified amount of home practice in the MBSR group. It provided up to 42 hours of home practice in the spirituality group. There was no information on teacher qualifications for MBSR. The study used the SF-36 Vitality Score to measure improvement in positive affect as a secondary outcome. The SF-36 Vitality Scores were 45 percent greater for the spirituality group (p=.024). This trial had a low risk of bias.

The difference in change graphs showed inconsistent results (Figure 16). A meta-analysis showed a nonsignificant effect slightly favoring the control group (Figure 17).

The strength of evidence is insufficient that mindfulness meditation programs have an effect on positive affect among those with a mood disturbance or symptoms of anxiety when compared with a variety of specific active controls. We based this rating on overall medium risk of bias, inconsistent findings, direct measures, and imprecise estimates (Table 24).

Table 24. Grade of trials addressing the efficacy of mindfulness meditation programs on positive affect compared with progressive muscle relaxation or spirituality among patients with worry or mood disorders

Number of Trials; Subjects	Domains Pertaining to Strength of Evidence				Magnitude of Effect and Strength of Evidence
	Risk of Bias	Consistency	Directness	Precision	
Positive Affect					Insufficient SOE of an effect
2; 142	Medium	Inconsistent	Direct	Imprecise	-45% to 0% (favoring control)

SOE = Strength of Evidence; MM = Mindfulness Meditation

Mental Component of Health-Related Quality of Life

Mindfulness Meditation Programs versus Specific Active Control

Five trials of mindfulness meditation programs evaluated the effect compared with a specific active control on the outcome of the mental component of health-related quality of life. Four were mindfulness-based stress reduction (MBSR) trials and one and mindfulness-based cognitive therapy (MBCT) trial. Three trials were low risk of bias, one medium, and one high. They used a variety of patient populations and specific active controls. Sample sizes ranged from 15 to 123.

Wong et al. randomized chronic pain patients (n=99) to an 8-week program in MBSR or multidisciplinary pain intervention (MPI).⁶⁴ The study used the validated Chinese SF-12 mental component subscale to measure quality of life as a secondary outcome. There was no significant change in the scores between groups at 2 or 5 months. This trial had a low risk of bias, provided 27 hours of training and an unspecified amount of home practice over 8 weeks. Its teachers were trained and had 5 years of experience teaching meditation.⁶⁴

Gross et al. randomized people with insomnia (n=27) to 8 weeks of MBSR versus pharmacotherapy for sleep (eszopiclone).⁴⁸ The trial used the SF-12 mental summary score to measure quality of life as a secondary outcome. There was no significant change in SF-12 scores between the two groups. This trial provided 26 hours of training and up to 36 hours of home practice over 8 weeks. Its teachers were trained and certified.

Moritz et al. randomized patients with mood disorders (n=110) to a spirituality program versus MBSR.⁵⁴ In this trial, MBSR was the active control. It provided about 12 hours of training in both interventions over an 8-week period, with unspecified amount of home practice in the MBSR group. It provided up to 42 hours of home practice in the spirituality group. There was no information on teacher qualifications for MBSR. The trial used the SF-36 mental component survey to measure quality of life as a secondary outcome. They found a 23 percent change favoring spirituality at 8 weeks (p=.029). This trial had a low risk of bias. It is notable that this intervention included a meditative component, as well as breathing exercises that may resemble features of MBSR.

Plews-Ogan et al. randomized people with chronic musculoskeletal pain (n=15) to 8 weeks of MBSR training or weekly massage.⁶¹ The trial used the SF-12 Mental Health score to measure quality of life as a primary endpoint. The difference-in-change point estimates were 10.8 percent favoring massage at 8 weeks and 18.4 percent favoring MBSR at 12 weeks. The trial did not calculate significance for difference-in-change estimates. This trial provided 20 hours of training over 8 weeks, and unspecified amount of home practice. There was no information on teacher qualifications. It had a high risk of bias.

Kuyken et al. randomized depressed patients at risk for relapse (n=123) to 8 weeks of MBCT and antidepressant tapering or maintenance antidepressant therapy.⁵² The trials used the World Health Organization Quality of Life Instrument Psychological Subscale to measure quality of life as a secondary outcome. At 3 months it found a 9.2 percent improvement in the MBCT group, which maintained at 15 months (p=.01). This trial provided 24 hours of training over 8 weeks by trained and certified instructors, and recommended up to 37.5 hours of home practice during that time. This trial had a low risk of bias.

The difference in change graphs showed inconsistent results (Figure 15). Meta-analysis showed a small nonsignificant effect (Figure 29).

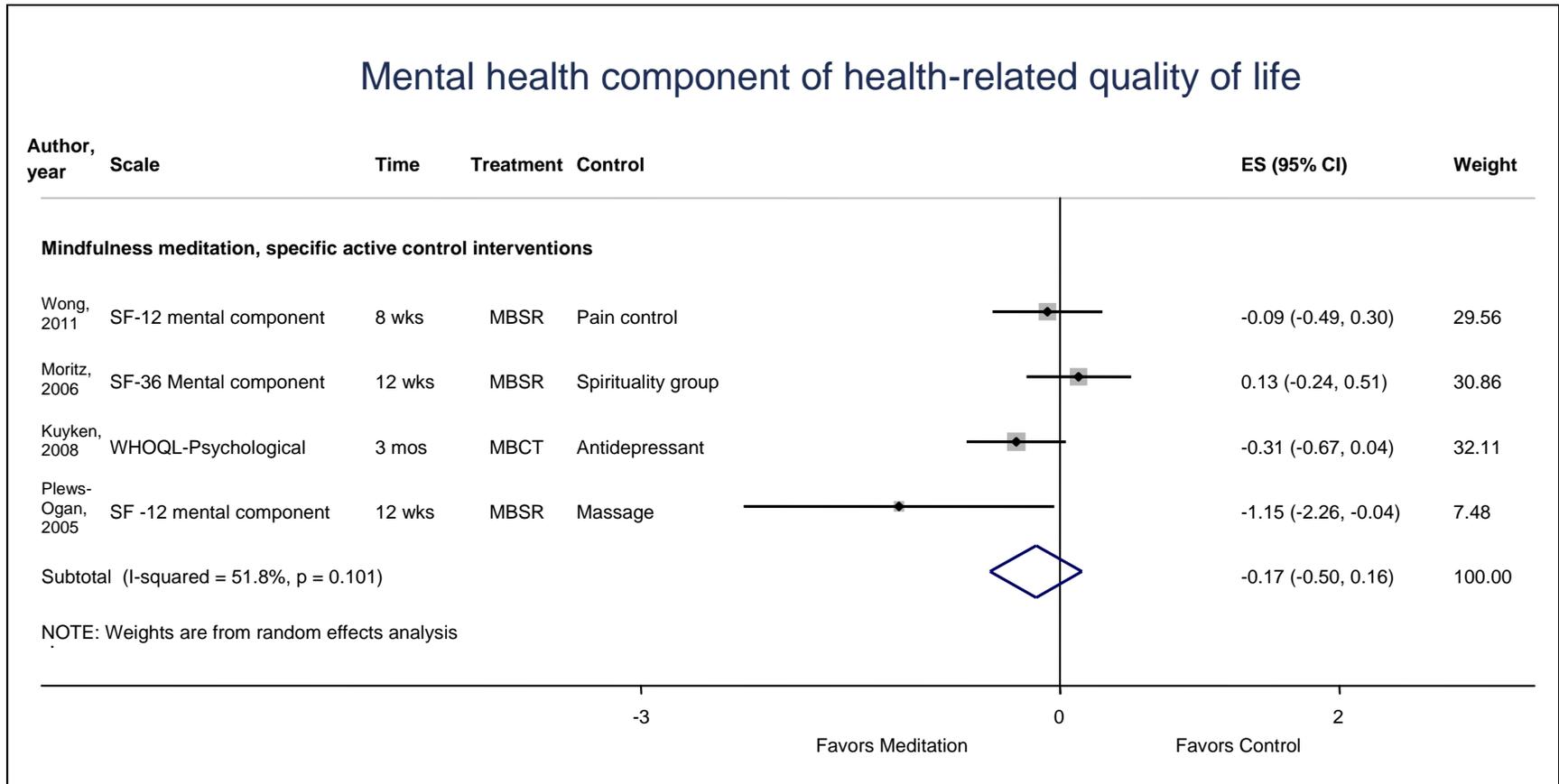
The strength of evidence is insufficient that mindfulness meditation program have an effect on the mental component of health related quality of life among various clinical populations when compared with a variety of specific active controls. We based this rating on overall medium risk of bias, inconsistent findings, direct measures, and imprecise estimates (Table 25).

Table 25. Grade of trials addressing the efficacy of mindfulness meditation programs on the mental component of health-related quality of life compared with specific active controls among various populations

Number of Trials; Subjects	Domains Pertaining to Strength of Evidence				Magnitude of Effect and Strength of Evidence
	Risk of Bias	Consistency	Directness	Precision	
Mental Component of Health-Related Quality of Life					Insufficient SOE of an effect
5;374	Medium	Inconsistent	Direct	Imprecise	-23% to +9.2%

SOE = Strength of Evidence; QOL = Quality of Life

Figure 29. Meta-analysis of the effects of meditation programs on the mental health component of health-related quality of life with up to 3 months of followup



SF12:MC = Short Form-12: Mental Component Score of Health-related Quality of Life; SF36:MC = Short Form-36: Mental Component Score of Health-related Quality of Life; WHOQL = World Health Organization Quality of Life Assessment.

Applicability

Most of the trials that we included for this key question took place in the U.S. or Europe; only two trials took place in Asia, and no trials took place on other continents. Most of the trials were in outpatient settings. Almost all the trials listed some exclusion criteria which would apply to a large number of patients in an everyday internal medicine or primary care practice, including substance abuse, psychiatric disorder, or various medical disorders.

Regarding the population characteristics of the trials for this key question, most of the trials did not specify the racial or ethnic characteristics of the included population. While 15 trials specified the educational characteristics of the study populations, the trials did not report other measures of socioeconomic status.

While a number of chronic medical conditions were addressed by some of the trials for this key question, including metabolic syndrome, chronic obstructive pulmonary disease, HIV, and congestive heart failure, the trials did not address a number of common medical conditions frequently found in medical practice, and often associated with anxiety, depression, stress, and distress, including diabetes, irritable bowel syndrome, and opiate dependence.

Thus, the findings for this key question would be least applicable to patients with substance abuse or other medical or psychiatric conditions excluded from the study populations. Given that the trials only substantially represented two continents, and the racial and ethnic makeup of the populations was not always specified, it is unlikely that these findings would be applicable to a diverse patient population.

Regarding the applicability of an intervention to a medical practice, the transcendental meditation trials involved daily training in their initial phases, which would be impractical in a typical outpatient setting. The weekly training in the mindfulness interventions might be generally applicable in such a context given sufficient personnel and resources.

Key Question 2. What are the efficacy and harms of meditation programs on attention among those with a clinical condition (medical or psychiatric)?

Key Points and Evidence Grades

- The strength of evidence is insufficient that mindfulness meditation programs have an effect on measures of attention among older caregivers compared with a non-specific active control due to medium risk of bias in a single trial, unknown consistency, directness of measures, and imprecise estimates.
- The strength of evidence is insufficient that transcendental meditation has an effect on measures of attention among an elderly population compared with non-specific active controls due to medium risk of bias in a single trial, unknown consistency, directness of measures, and imprecise estimates.

Harms

- We found no studies that reported on harms

Trial Characteristics

Two randomized controlled trials assessed the efficacy of meditation programs on attention as a component of their trials. Oken et al. assessed the effects of a 7-week mindfulness meditation program on stress among caregivers of close relatives with dementia.⁵⁷ Alexander et al. assessed the effects of a 12-week transcendental meditation program on cognitive function and longevity among the elderly.⁶⁵ Neither trial reported the specific period of recruitment. Both trials took place in the U.S. in outpatient settings among either stressed or very elderly populations. The mindfulness meditation trial included participants with a score greater than 9 on the PSS and excluded individuals who were medically unstable, had significant cognitive dysfunction, significant visual impairment, or previous experience with stress-reduction classes.⁵⁷ The transcendental meditation trial recruited elderly volunteers from retirement communities or nursing homes and stratified their randomization by the participants score on the Dementia Screening Test. It excluded anyone who was unable to remember instructions from day to day.⁶⁵ (Appendix E, Evidence Table 2)

Population Characteristics

The mindfulness meditation trial enrolled 31 dementia caregivers with a mean age range in the 60s.⁵⁷ The transcendental meditation trial enrolled 73 individuals from homes for the elderly with a mean age of 80.7 years.^{57 65} Participants were predominantly female in both trials. The mindfulness meditation trial reported racial characteristics, with a greater than 90 percent white trial population (Appendix E).

Intervention Characteristics

The mindfulness meditation trial included three arms: a composite intervention based on mindfulness-based stress reduction (MBSR)/ mindfulness-based cognitive therapy (MBCT), which was compared with education (non-specific active control), and to respite care.⁵⁷ The transcendental meditation trial included four arms: transcendental meditation compared with a guided attention technique and mental relaxation (both non-specific active controls) and usual care.⁶⁵ The trial delivered both meditation interventions in a group format. The maximal training dose for mindfulness meditation trial was 9 hours delivered over 7 weeks; the transcendental meditation trial did not specify dosing. Both trials used trained teachers but did not specify the amount of training or meditation experience. The mindfulness meditation trial recommended practice at home but did not specify the total duration. The transcendental meditation trial recommended 20 minutes twice daily for a maximal home practice dose of 56.3 hours over 12 weeks. Neither trial recorded actual amounts of training or home practice by the participants.⁵⁷ (Appendix E)

Outcomes

Two cognitive tasks, the Attentional Network Test and the Stroop Color-Word Interference Test, were used as the measures of attention in the two trials. The Attentional Network Test is a computerized task for assessing various attention networks. This test requires participants indicate the direction of a target arrow that is accompanied on each side by two additional arrows. Occasionally, the target arrow is preceded by cues. The mindfulness meditation trial used a shortened version of this test that included only two attention conditions: cued/noncued and

congruent/incongruent conditions, which present companion arrows in the same or opposite direction as the target arrow. The results included a conflict score, calculated as the reaction time difference between the incongruent and congruent conditions; and the alerting score, calculated as the reaction time difference between the noncued and cued conditions.

The transcendental meditation trial used the Stroop Color-Word Interference Test, a task of cognitive flexibility and selective attention in which participants are timed in several conditions: reading color names printed in black ink, naming colors, and naming the colors of words printed in a conflicting color. This trial used the interference score as an outcome, which is the additional time required to complete the third part of the task compared with the second part; a lower score indicates better performance.

Attention

Mindfulness Meditation Programs vs. Non-specific Active Control

In the mindfulness meditation trial among caregivers of elderly relatives with dementia (n=21), the Attentional Network Test alerting score for the meditation group was worse than for the education group at baseline. At 8 weeks post-intervention the meditation group improved its performance by doubling its score, resulting in an 81 percent increase from baseline compared with education.⁵⁷ This suggests an appropriate use of a cue by the meditation group to improve their performance from baseline to post-intervention. However, the data were highly skewed, and it is not apparent that the differences between meditation and education arms were statistically significant. There was a 15 percent non-significant difference among the groups on the Attentional Network Test conflict score favoring mindfulness meditation (p=0.14).⁵⁷

In summary, this trial had a medium risk of bias due to several factors including high attrition, allocation to groups was not concealed, and there was no intent-to-treat analysis. Overall, the strength of evidence is insufficient to comment on whether mindfulness meditation interventions improve attention among an older population compared with a non-specific active control due to medium risk of bias, unknown consistency, directness of measures, and imprecision.

Transcendental Meditation versus Non-specific Active Control

In a transcendental meditation trial of elderly individuals (n=62), there were no significant differences among groups post-intervention at 12 weeks on the Stroop Interference score. There was, however, a non-significant trend, with transcendental meditation performing better than a guided attention technique and mental relaxation by 20 percent (p<.10).⁶⁵

This trial had a medium risk of bias due to high attrition, no intent-to-treat analysis, and no description of withdrawals and dropouts. Overall, the strength of evidence is insufficient to comment on the effects of transcendental meditation on attention among an elderly population compared with non-specific active controls, due to medium risk of bias in a single trial, unknown consistency, directness of measures, and imprecision (Table 26).

None of the trials reported on harms.

Table 26. Grade of trials addressing the efficacy of meditation programs on measures of attention compared with a non-specific active control among elderly individuals

Condition; Number of Trials; Subjects	Domains Pertaining to Strength of Evidence				Magnitude of Effect and Strength of Evidence
	Risk of Bias	Consistency	Directness	Precision	
MM: Stressed Caregivers					Insufficient SOE of an effect on the Attention Network Score
1; 21	Medium	Unknown	Direct	Imprecise	15% to 81% favoring MM
TM: Elderly					Insufficient SOE of an effect on the Stroop Interference score
1;62	Medium	Unknown	Direct	Imprecise	20% favoring TM

SOE = Strength of Evidence; MM = Mindfulness Meditation; TM = Transcendental Meditation

Applicability

Both trials took place in the U.S. in outpatient settings with predominantly female participants. Only one trial reported on race and participants were predominantly white. Both trials studied older populations (dementia caregivers and individual from homes for the elderly) without direct complaints of cognitive difficulties (i.e., attention). Therefore, these findings may not be applicable to other clinical populations where cognitive function is a reported concern (e.g., Attention-deficit/Hyperactivity Disorder), and improvement (or lack thereof) on cognitive measures could provide more useful clinical information.

Key Question 3: What are the efficacy and harms of meditation programs on health-related behaviors affected by stress, specifically substance use, sleep, and eating, among those with a clinical condition (medical or psychiatric)?

Key Points and Evidence Grades

Comparisons with Non-specific Active Controls

- The strength of evidence is insufficient about the effects of mindfulness meditation programs on sleep among a variety of populations when compared with a non-specific active control. We based this rating on overall medium risk of bias, inconsistent findings, direct measures, and imprecise estimates.

Comparisons with Specific Active Controls

- The strength of evidence is insufficient about the effects of mindfulness meditation programs on health-related behaviors affected by stress (substance use, sleep, or eating) among various populations when compared with a variety of specific active controls. We based this rating on overall high risk of bias, inconsistent findings, direct measures, and imprecise estimates.
- The strength of evidence is low that mantra meditation programs do not reduce alcohol use among alcohol abusing populations when compared with intensive running or biofeedback. We based this rating on overall medium risk of bias, consistent findings, direct measures, and imprecise estimates.

Harms

- Four trials reported that they evaluated harms; none found any adverse events.

Trial Characteristics

Of the nine trials that we included for this KQ,^{42 43 45 47-49 57 62 67 71 75} eight took place in the U.S., while the other took place in Germany. Seven of these trials took place exclusively in an outpatient setting, two took place in an inpatient setting, and the remaining two trials had multiple locations. Only two of these trials explicitly reported the year of recruitment, and none of the trials reported the time period of recruitment.

All but two of these trials explicitly stated the length of treatment and timing of subsequent followup. Treatment ranged from 4 to 15 weeks, and followup ranged from none (i.e. treatment assessed at its end) to 18 months.

All nine trials reported inclusion and exclusion criteria. One trial excluded individuals with chronic substance dependence. Five trials excluded subjects if they had unstable medical conditions. Five other trials excluded patients due to psychiatric criteria. Two trials excluded due to severe cognitive dysfunction.

Four of the nine trials that we included in this review evaluated the effects of meditation on substance use: one related to cigarette smoking,^{43 67} and three related to alcohol and drug use.^{42 71 75 42 45 75} One trial considered the effect of meditation on eating behaviors.⁴⁹ The remaining four of the nine included trials examined the effect of meditation programs on sleep.^{47 48 57 62} (Appendix E)

Population Characteristics

Four trials took place in populations with chronic medical conditions;^{47-49 62 67} four trials took place in populations with substance abuse;^{42 43 45 71 75} and one trial targeted a population of caregivers under stress.⁵⁷ The percentage of female subjects totaled 30 percent or greater in six of the nine trials,^{43 47-49 57 62} with two of the nine trials including female subjects exclusively.^{49 49 57 62} The mean age of trial participants ranged from 24 to 67 years. Two of the nine trials exhibited significant racial diversity in the subject populations.^{43 45 75} Seven of the nine trials provided information on the level of education completed by trial participants (Appendix E).

Intervention Characteristics

Of the four trials assessing the effects of meditation on substance use, two used mindfulness meditation based on mindfulness based relapse prevention, with 9 to 12 hours of training over four to nine weeks. Reporting of training and experience in mindfulness instruction ranged from 12 years to greater than 13 years of mindfulness experience and social work training, although there was no explicit mention of centralized training or certification. Another trial used clinically standardized meditation, a mantra-based concentrative meditation intervention taught by “experienced meditators,” after which the group meditated together 3 times per week for the 8-week intervention.⁷¹ One trial used a transcendental meditation intervention taught by a certified instructor. Instruction occurred using a seven-step process, followed by group meditations.⁷⁵ For the substance-use trials, comparisons included cognitive behavioral therapy treatment,⁴² biofeedback,⁷⁵ smoking-cessation education,^{43 67} and exercise.⁷¹

Hebert’s trial assessing eating in breast cancer patients compared a nutrition education program with a mindfulness-based program adapted from MBSR, both consisting of 14 weekly 2.5-hour classes and a day-long retreat.⁴⁹ Masters-level psychologists with extensive training in yoga and mindfulness taught the mindfulness intervention.

All four trials evaluating meditation for sleep evaluated MBSR^{47 48 62} or mindfulness-based stress reduction (MBSR)/ mindfulness-based cognitive therapy MBCT⁵⁷ composite programs. The MBSR programs consisted of eight weekly 2.5-hour classes and one day-long retreat, led by instructors trained in MBSR at the University of Massachusetts Center for Mindfulness. The MBSR/MBCT composite program consisted of six weekly 90-minute classes and did not report MBSR instructor training. Comparison treatment included pharmacotherapy for sleep⁴⁸ programs in relaxation,⁶² or health education matched for time and attention.^{47 57}

Only three of the nine trials investigating stress-related behaviors measured adherence to home meditation practice.^{43 47 48} (Appendix E)

Outcomes

Sleep

Mindfulness Meditation Programs versus Non-specific Active Control

Three trials compared a mindfulness meditation programs with a non-specific active control on the outcome of sleep quality. All three used the Pittsburgh Sleep Quality Index (PSQI), and had a medium risk of bias. Schmidt et al. randomized women with fibromyalgia (n=109) to 8 weeks of mindfulness-based stress reduction (MBSR) or a non-specific active control.⁶² The study used the PSQI to measure sleep as a secondary endpoint and showed no difference between the arms. This trial provided 27 hours of training over 8 weeks by trained and certified teachers, and recommended up to 42 hours of home practice. It had a medium risk of bias.

Oken et al. randomized people who take care of elderly relatives with dementia (n=19) to 6 weeks of mindfulness meditation or a non-specific active control.⁵⁷ The trial used the PSQI and Epworth Sleepiness Scale (ESS) to measure sleep as a secondary outcome. This trial showed a 12.8 percent change on the ESS and a 3.4 percent change on the Pittsburgh Sleep Quality Index, both were non-significant and favored the control group. This trial had a medium risk of bias and provided 9 hours of training over 7 weeks by a trained teacher and an unspecified amount of home practice.

Gross et al. randomized solid organ transplant recipients, post-surgery, (n=137) to either 8 weeks of MBSR or non-specific active control.⁴⁷ The trial used the PSQI to measure sleep quality as a primary outcome. In a difference-in-change analysis, the MBSR group showed a 24.1 percent improvement in PSQI at 8 weeks, which further improved to 30.1 percent at 1 year (p=.02). This trial had a medium risk of bias, and provided 27 hours of training by a trained teacher and an unspecified amount of home practice over 8 weeks.

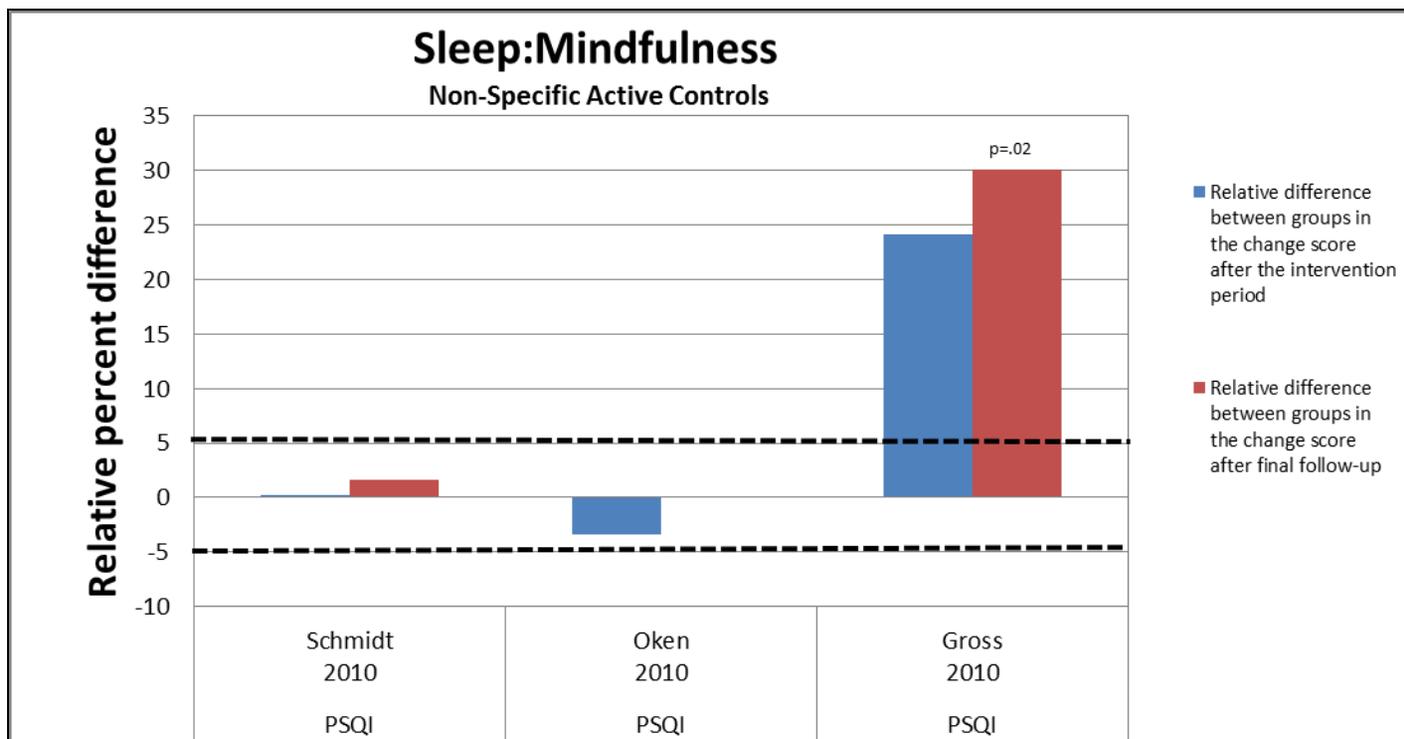
The difference in change graphs showed inconsistent results (Figure 30). A meta-analysis showed a small nonsignificant effect slightly favoring mindfulness (Figure 31). The strength of evidence is insufficient that mindfulness meditation programs have an effect on sleep among a variety of populations when compared with a non-specific active control. We based this rating on trials of medium bias, inconsistent findings, direct measures, and imprecise estimates (Table 27).

Table 27. Grade of trials addressing the efficacy of mindfulness meditation program on sleep quality among various populations compared with a non-specific active control

Number of Trials; Subjects	Domains Pertaining to Strength of Evidence				Magnitude of Effect and Strength of Evidence
	Risk of Bias	Consistency	Directness	Precision	
Sleep Quality					Insufficient SOE of an effect
3; 265	Medium	Inconsistent	Direct	Imprecise	-3.4% to 24.1%

SOE = Strength of Evidence;

Figure 30. Relative difference between groups in the changes in measures of sleep, in the mindfulness versus non-specific active control studies



- Relative difference between groups in the change score.** This is a relative percent difference, using the baseline mean in the meditation group as the denominator. For example, if the meditation group improves from a 10 to 19 on a mental health scale and the control group improves from 11 to 16 on the same scale, the relative difference between groups in the change score is: $((19-10)-(16-11))/10 \times 100 = 40\%$. The interpretation is that there is a 40% relative improvement on the mental health scale in the meditation group compared with the control group. Improvement in all scales is indicated in the positive direction. A positive relative percent difference means that the score improved more in the intervention group than in the control group
- NR / NS = Not Reported/Not significant. The trial measured this outcome and stated they were non-significant, and did not report actual results.
- Black dotted lines from -5% to +5% indicate our criteria for no effect. It does not indicate statistical significance.
- A p value above or below a bar indicates statistical significance reported in the original study publication. If there is no p value with a bar, the outcome was not significant in the original study publication.
- PSQI = Pittsburgh Sleep Quality Index.

Mindfulness Meditation Programs versus Specific Active Control

Sleep, Substance Use, and Eating

Four trials evaluated the effects of mindfulness meditation programs against a specific active control on the outcomes in the domain of^{42 45 67 75} health-related behaviors affected by stress.^{42 43 48 49} One trial assessed effects on smoking, one on alcohol, one on sleep, and one on eating. Two trials had high risk of bias, and two had medium risk of bias. They used a variety of specific active controls.

Brewer et al. randomized smokers (N=71) to an 8-session, 4-week program of mindfulness meditation compared with a specific active control, the American Lung Association's freedom from smoking (FFS) program.⁴³ The mindfulness meditation program is based on mindfulness-based relapse prevention and MBSR, and provided up to of 12 hours of meditation training by a single therapist with 13 years of experience with mindfulness meditation. While the FFS group reduced their cigarette use by 12 cigarettes/day, mindfulness meditation participants smoked 4.2 cigarettes/day less than the FFS program in a difference-in-change calculation ($p=.008$) at the end of the 4-week program. Mindfulness meditation participants had 21 percent higher levels of 1-week point-prevalence abstinence from smoking at 4 weeks ($p=.06$) and 25 percent higher abstinence at 17-week followup ($p=0.012$). Additionally, within the mindfulness meditation group, both formal ($p=0.019$) and informal ($p=0.01$) mindfulness practice resulted in less cigarette use. This trial had a high risk of bias.⁴³ Overall, the strength of evidence is low to conclude that a 4-week mindfulness meditation program has an effect on smoking compared with a FFS program among smokers, due to high risk of bias, unknown consistency, directness of measures, and precise results.

Brewer et al. conducted a separate trial in which they randomized individuals with alcohol and/or cocaine abuse who were seeking outpatient treatment ($n=24$) to mindfulness meditation that consisted of mindfulness-based relapse prevention with cognitive behavioral therapy.⁴² Following the treatment programs, there were no statistically significant differences in alcohol ($p=.17$) or cocaine ($p=.09$) use between groups. This trial provided 9 hours of training over 9 weeks by a teacher with 12 years of meditation experience, and did not report on whether it recommended any home practice. It had a 61 percent attrition rate and had a high risk of bias.

Gross et al. randomized people with insomnia ($n=27$) to MBSR or eszopiclone.⁴⁸ Sleep was a primary outcome. The study measured sleep time by wrist actigraphy. It measured overall sleep quality by the Pittsburgh Sleep Quality Index (PSQI) and Insomnia Severity Index. Total sleep time and wake after sleep onset were not different between the groups, although it favored the eszopiclone group. The PSQI indicated a 14.7 percent improvement favoring the MBSR group, while the Insomnia Severity Index showed a 15.5 percent improvement favoring the eszopiclone group. Both were non-significant. This trial provided 26 hours of training and up to 36 hours of home practice over 8 weeks. It had a medium risk of bias.

Hebert et al. evaluated the effects of MBSR compared with a nutrition education program among women with stage I or II breast cancer ($n=106$).⁴⁹ Ninety-five percent of the participants had complete diary data post-intervention (at 4 months) and 93 percent at 1 year. Women in the nutrition group had a significant 19.1 percent reduction in fat consumption at 4 months ($p<.05$) and 11.3 percent reduction at 1 year ($p<.05$) compared with MBSR. There were no differences in

overall caloric consumption between groups at 4 months or 1 year. This trial had a medium risk of bias.

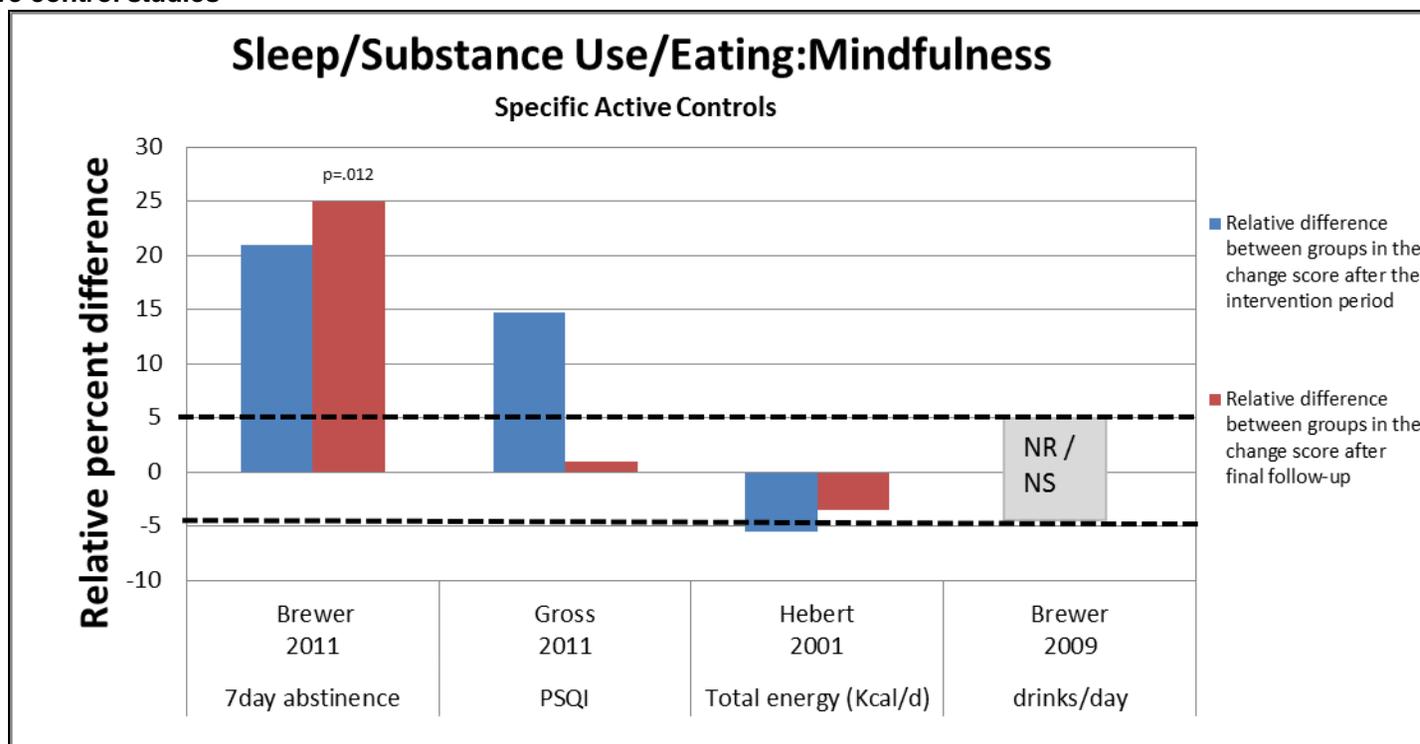
The differences in change graphs showed inconsistent results (Figure 32). The strength of evidence is insufficient that mindfulness meditation programs have an effect on health-related behaviors affected by stress (substance use, sleep, or eating) among various populations when compared with a variety of specific active controls. We based this rating on overall high risk of bias, inconsistent findings, direct measures, and imprecise estimates (Table 28).

Table 28. Grade of trials addressing the efficacy of mindfulness meditation programs on health-related behaviors affected by stress (substance use, sleep, eating) compared with specific active controls in various populations

Number of Trials; Subjects	Domains Pertaining to Strength of Evidence				Magnitude of Effect and Strength of Evidence
	Risk of Bias	Consistency	Directness	Precision	
Health related behaviors affected by stress (substance use, sleep, eating)					Insufficient SOE of an effect
4; 228	High	Inconsistent	Direct	Imprecise	-5.5% to +21%

SOE = Strength of Evidence.

Figure 32. Relative difference between groups in the changes in measures of sleep/substance use/ eating, in the mindfulness versus specific active control studies



- Relative difference between groups in the change score.** This is a relative percent difference, using the baseline mean in the meditation group as the denominator. For example, if the meditation group improves from a 10 to 19 on a mental health scale and the control group improves from 11 to 16 on the same scale, the relative difference between groups in the change score is: $((19-10)-(16-11))/10 \times 100 = 40\%$. The interpretation is that there is a 40% relative improvement on the mental health scale in the meditation group compared with the control group. Improvement in all scales is indicated in the positive direction. A positive relative percent difference means that the score improved more in the intervention group than in the control group.
- NR / NS = Not Reported/Not significant. The trial measured this outcome and stated they were non-significant, and did not report actual results.
- Black dotted lines from -5% to +5% indicate our criteria for no effect. It does not indicate statistical significance.
- A p value above or below a bar indicates statistical significance reported in the original study publication. If there is no p value with a bar, the outcome was not significant in the original study publication.
- PSQI = Pittsburgh Sleep Quality Index; Kcal/d = Kilocalorie per day.

Mantra Meditation Programs versus Specific Active Control

Two trials used a mantra meditation programs to assess the effects on alcohol consumption against either an intensive running program among college students or biofeedback among recovering alcoholics.^{71 75} Murphy et al. randomized male college students who were heavy social drinkers (n= 27) to an 8-week treatment programs in clinically standardized meditation or running.⁷¹ The running group consumed 99.3mL of ethanol less than the meditation group (p=.35). The meditation group received 8 hours of training over eight weeks by a teacher with some experience in meditation, and up to 37.5 hour of home practice. The running group received 28 hours of training. This trial had a high risk of bias.

Taub et al. randomized alcoholics (n=87) in residential treatment program to transcendental meditation or two different specific active control arms: biofeedback or neurotherapy. There was no difference in the percent of days abstinent from alcohol between the transcendental meditation group and biofeedback. The transcendental meditation group provided up to 19 hours of training over 4 weeks by certified teachers, and did not specify whether it recommended any amount of home practice. This trial had medium risk of bias.⁷⁵

The difference in change graphs showed consistent results favoring control (Figure 33). The strength of evidence is low that mantra meditation programs do not reduce alcohol use among alcohol abusing populations when compared with intensive running or biofeedback. We based this rating on overall medium risk of bias, consistent findings, direct measures, and imprecise estimates (Table 29).

Table 29. Grade of trials addressing the efficacy and harms of mantra meditation programs on alcohol use among heavy alcohol drinkers compared with intensive running program or biofeedback

Number of Trials; Subjects	Domains Pertaining to Strength of Evidence				Magnitude of Effect and Strength of Evidence
	Risk of Bias	Consistency	Directness	Precision	
Alcohol use					Low SOE that alcohol use is not reduced
2; 145	Medium	consistent	Direct	Imprecise	-4.6% abstinence to -36.1% reduced consumption (both favoring control)

SOE = Strength of Evidence; CSM = Clinically Standardized Meditation; TM = Transcendental Meditation

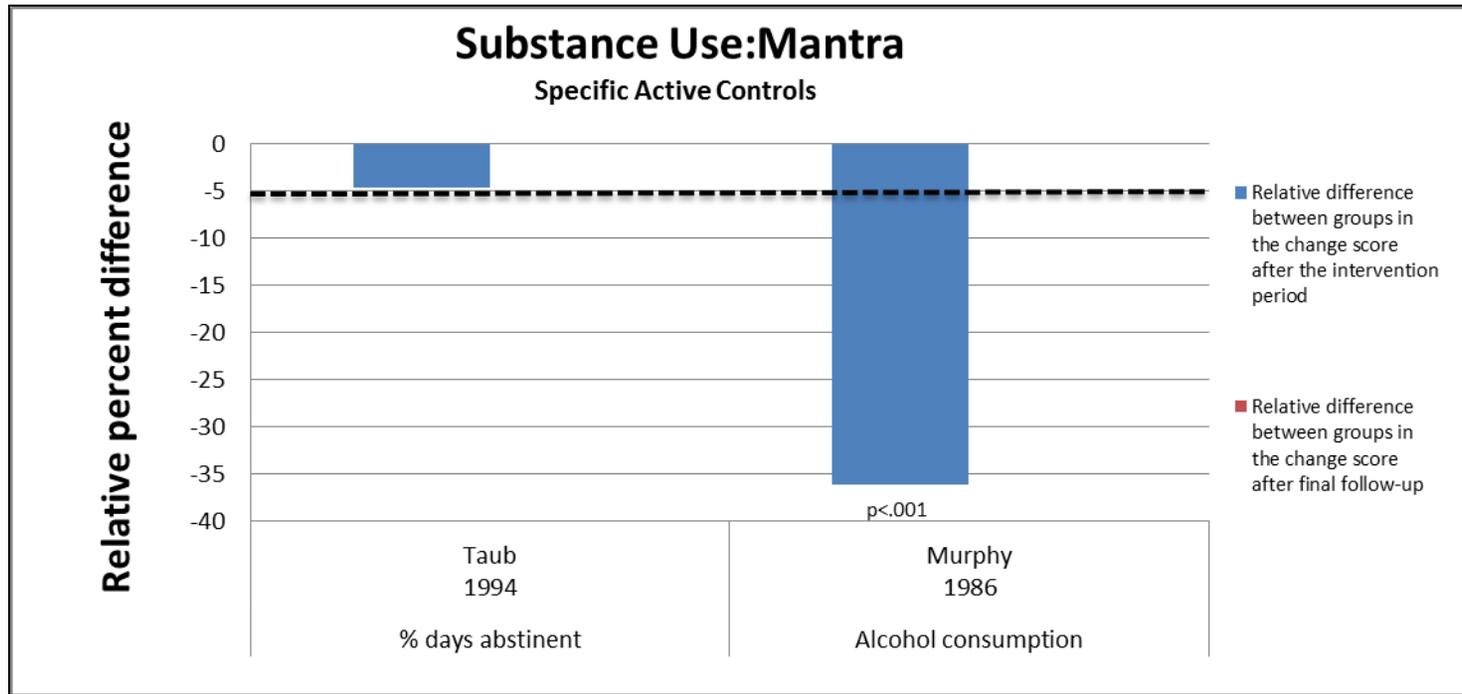
Applicability

Eight of nine trials took place in the U.S.; other regions might not find these findings applicable. Most of the trials took place in outpatient settings, so applicability to the inpatient setting is limited.

Regarding the population characteristics of the trials for this key question, only two of nine trials exhibited significant racial diversity in the study populations. Most of the trials excluded subjects from groups who might commonly be found in a medical practice, including those with unstable medical conditions and psychiatric disorders.

Characteristics of the interventions represented in this key question were diverse, making it difficult to foresee how these findings would be applicable to a similarly wide array of mindfulness practices under everyday clinical situations. For example, the trials did not specify the certification and training of instructors, and only a few trials specified the time spent in home training.

Figure 33. Relative difference between groups in the changes in measures of substance use, in the mantra versus specific active control studies



1. **Relative difference between groups in the change score.** This is a relative percent difference, using the baseline mean in the meditation group as the denominator. For example, if the meditation group improves from a 10 to 19 on a mental health scale and the control group improves from 11 to 16 on the same scale, the relative difference between groups in the change score is: $\frac{((19-10)-(16-11))}{10} \times 100 = 40\%$. The interpretation is that there is a 40% relative improvement on the mental health scale in the meditation group compared with the control group. See Appendix E for absolute difference in change score values. Improvement in all scales is indicated in the positive direction. A positive relative percent difference means that the score improved more in the intervention group than in the control group
2. NR / NS = Not Reported/Not significant. The trial measured this outcome and stated they were non-significant, and did not report actual results.
3. Black dotted lines from -5% to +5% indicate our criteria for no effect. It does not indicate statistical significance.
4. A p value above or below a bar indicates statistical significance reported in the original study publication. If there is no p value with a bar, the outcome was not significant in the original study publication.

Key Question 4. What are the efficacy and harms of meditation programs on pain and weight among those with a clinical condition (medical or psychiatric)?

Key Points and Evidence Grades

Comparisons with Non-specific Active Controls

- The strength of evidence is moderate that mindfulness meditation programs have a small improvement in pain severity among a variety of populations when compared with a non-specific active control. We based this rating on trials of medium bias, consistent findings for a small positive effect, direct measures, and precise estimates.
- The strength of evidence is low that mantra meditation programs have no effect on pain severity among those with congestive heart failure when compared with a non-specific active control. We based this rating on a single trial of low risk of bias, unknown consistency, direct measures, and imprecise estimates.
- The strength of evidence is insufficient that mindfulness meditation programs have an effect on weight among breast cancer patients when compared with a non-specific active control. We based this rating on a single medium risk of bias study, unknown consistency, directness of measures, and imprecise estimates.
- The strength of evidence is insufficient that mantra meditation programs have an effect on weight among diabetics and hypertensive when compared with a non-specific active control. We based this rating on overall high risk of bias, consistent null findings, directness of measures, and imprecise estimates.

Comparisons with Specific Active Controls

- The strength of evidence is low that mindfulness-based stress reduction has no effect on pain severity among those with chronic musculoskeletal pain or mood disturbance, compared with a specific active control. We based this rating on overall medium risk of bias, consistent null results, direct measures of pain, and imprecise estimates.

Harms

- Four trials reported that they evaluated harms; none found any adverse events.

Trial Characteristics

We found 11 randomized control trials (RCTs) on this key question. Eight RCTs took place in the U.S., one in Canada, one in Germany, and one in Hong Kong. All involved outpatients. Four trials did not report recruitment periods, the others were between 2000 and 2009. Trial duration ranged from 3 months to 1 year. Inclusion criteria were adults for all trials. Two recruited only females.^{46 62}(Appendix E)

Population Characteristics

Five of the trials recruited participants who reported a chronic pain condition^{46 55 61 62 64} while three used non-pain populations.^{47 54 69} Two trials used general chronic pain patients of whom more than 95 percent had musculoskeletal pain,^{61 64} while the other three used women with IBS (visceral pain), women with fibromyalgia (musculoskeletal pain), and patients with low back pain (also musculoskeletal pain). Trials using a pain population ranged in sample size from 30-177. Two included only women.^{46 62} Mean age was around 45-50 for these trials except for a trial that studied elderly low-back-pain patients⁵⁵ who were, on average, 75 years old. Only one trial reported ethnicity,⁴⁶ in which 72 percent were white, 17 percent black, and the remaining were “other.” Three trials reported education level. The percent that had completed high school ranged from 11 to 53 percent.^{46 62 64} The majority of participants in the IBS trial had a college or graduate level education.⁴⁶ Among the non-pain population trials, participants were either solid organ transplant recipients,⁴⁷ patients, post-surgery, with psychological distress,⁵⁴ or African Americans with CHF.⁶⁹ Sample sizes ranged from 23-165 including 30-80 percent women (Appendix Evidence Table 3).

Intervention Characteristics

Five trials used mindfulness-based stress reduction (MBSR),^{47 54 61 62 64} two were a mindfulness meditation program,^{46 55} and one utilized transcendental meditation.⁶⁹ While all trials used active controls, two of the MBSR trials used a specific active control such as a multidisciplinary pain management program or massage. All others used a non-specific active control to control for time, attention, and expectation, such as a health education group. The mindfulness programs were typically conducted weekly for 1.5 to 2.5 hours over 8 weeks, and ranged from 12 to 27 in total hours of training. Although all of the trials indicated, in some form, that they recommended daily practice, only two of the trials specified the amount, recommending 45 minutes daily.^{55 62} None of the trials reported on the actual amount of home practice participants experienced in the meditation arm. Reports on instructor qualifications were lacking for most trials. Five of seven mindfulness trials indicated that instructors had some training^{46 47 55 62 64} but only two gave enough information to suggest that the instructors had some kind of certification.^{55 62} Only one trial reported on the personal meditation experience of the instructors⁵⁵ and three trials reported an instructor’s level of teaching experience.^{62 64}

The transcendental meditation trial included 1.5 daily sessions for seven consecutive days, and followup refresher meetings twice monthly for the first 3 months and then once monthly for the next 3 months. The trial did not give details of the followup meetings, but we estimated the duration at approximately 22.5 hours over a 6-month period, assuming the meetings were also 1.5 hours in length (an amount roughly similar to the mindfulness trials). They recommended approximately half-hour daily home practice for 6 months, which calculates to approximately 90 hours of home practice over 6 months. This trial reported a certified trainer without giving details of years of meditation or teaching experience.

Three trials measured weight changes.^{68 49 67} Two were transcendental meditation^{68 67} and one used mindfulness meditation.⁴⁹ None of these trials reported details of hours of training, although we estimated the mindfulness meditation trial trained participants for 45 hours over a 15 week period. It gave no details on instructor qualifications or whether the participants performed home practice. Both transcendental meditation trials indicated their teachers were either trained or certified, and recommended between 30-40 min of daily meditation for a 6-month period,

amounting to a total expected home practice dose of 90-120 hours. None of the trials reported actual amounts of meditation (Appendix E).

Outcomes

Ascertainment of Outcomes (Scales)

Studies measured pain severity using the 11-point Numerical Rating Scale for pain intensity or unpleasantness, Perceived Pain Scale Affective and Sensory subscales, SF 36 Bodily Pain subscale, McGill Pain Questionnaire, and IBS Abdominal Pain Severity subscale. Studies measured pain interference using the Fibromyalgia Impact Questionnaire and the Roland Morris Disability Scale. Studies measured weight in either pounds or kilograms (Table 3).

Pain Severity

Mindfulness meditation program versus a Non-specific Active Control

Four trials evaluated mindfulness-based stress reduction (MBSR) against a non-specific active control and assessed the outcome of pain severity.^{46 47 55 62} One trial evaluated visceral pain while the other three evaluated musculoskeletal pain. One trial had a low risk of bias, the remaining three had a medium risk of bias.

Gaylord et al. randomized women with IBS (n=75) to MBSR versus support program for women with irritable bowel syndrome.⁴⁶ This was the only trial to assess visceral pain, and found a 30.6 percent reduction in abdominal pain severity in the MBSR group compared with control at 8 weeks; this maintained at 6 months (p=.015). This was a medium risk of bias trial that provided 23 hours of training and unspecified amount of home practice over 8 weeks.

Schmidt et al. randomized women with fibromyalgia (n=109) to 8 weeks of MBSR or a non-specific active control.⁶² The trial used PPS to measure pain severity as a secondary outcome. The Pain Perception (Sensory) (PPS) has affective and sensory subscales; the affective dimension measures the unpleasantness of the pain experience, whereas the sensory dimension measures the intensity of sensory qualities of the pain experience. There were no significant differences between the MBSR and control on either of the subscales (p=.18 for affective subscale, p=.60 for sensory subscale), although the meditation arm was favored by 5.7% for the sensory subscale. This trial provided 27 hours of training over 8 weeks by trained and certified teachers, and recommended up to 42 hours of home practice. It had a medium risk of bias.

Gross et al. randomized solid organ transplant patients, post-surgery, (n=137) to MBSR versus health education.⁴⁷ They found no change in the SF36 Bodily Pain subscale within groups or between groups at two months or one year, although the meditation arm was favored by 5.1%. This trial provided 27 hours of training by a trained teacher, and unspecified amount of home practice over 8 weeks. This trial had medium risk of bias.

Morone et al. randomized older adults with chronic low back of moderate intensity (n=35) to MBSR or a health education program for 8 weeks.⁵⁵ They used two scales to assess pain severity: SF36 pain subscale and McGill Pain Questionnaire Current Pain score. The MBSR group showed a non-significant 8.6 percent improvement in the SF36 pain subscale at 8 weeks compared with control, but these differences disappeared at 6 months. There were no effects seen in the McGill Pain Questionnaire in a differences-in-change analysis. This trial provided 12

hours of training over 8 weeks by a teacher with 25 years of meditation experience and some teaching experience. The trial recommended up to 42 hours of home practice over the 8 weeks. This trial had a low risk of bias.

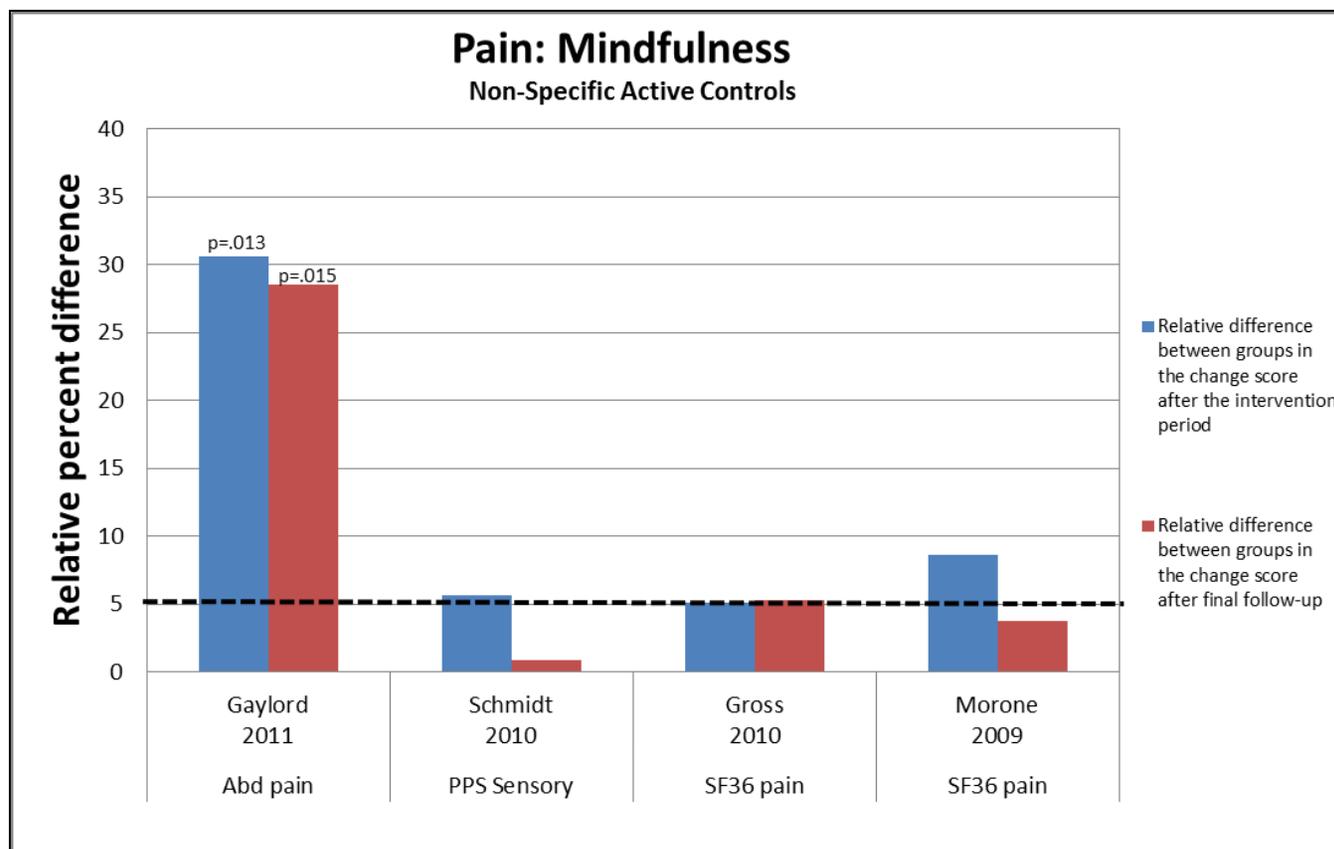
The difference in change graphs showed consistent small positive effects on pain severity (Figure 34). A meta-analysis showed a small statistically significant effect size favoring mindfulness meditation programs (Figure 35). The strength of evidence is moderate that mindfulness meditation programs have a small improvement in pain severity among a variety of populations when compared with a non-specific active control. We based this rating on trials of medium bias, consistent findings for a small positive effect, direct measures, and precise estimates (Table 30).

Table 30. Grade of trials addressing the efficacy of mindfulness-based stress reduction on pain severity compared with non-specific active controls among visceral pain, musculoskeletal pain, and organ transplant patients

Number of Trials; Subjects	Domains Pertaining to Strength of Evidence				Magnitude of Effect and Strength of Evidence
	Risk of bias	Consistency	Directness	Precision	
Pain Severity					Moderate SOE of an effect on pain severity
4; 341	Medium	Consistent	Direct	Precise	5.1% to 30.6% reduction in pain severity favoring MBSR

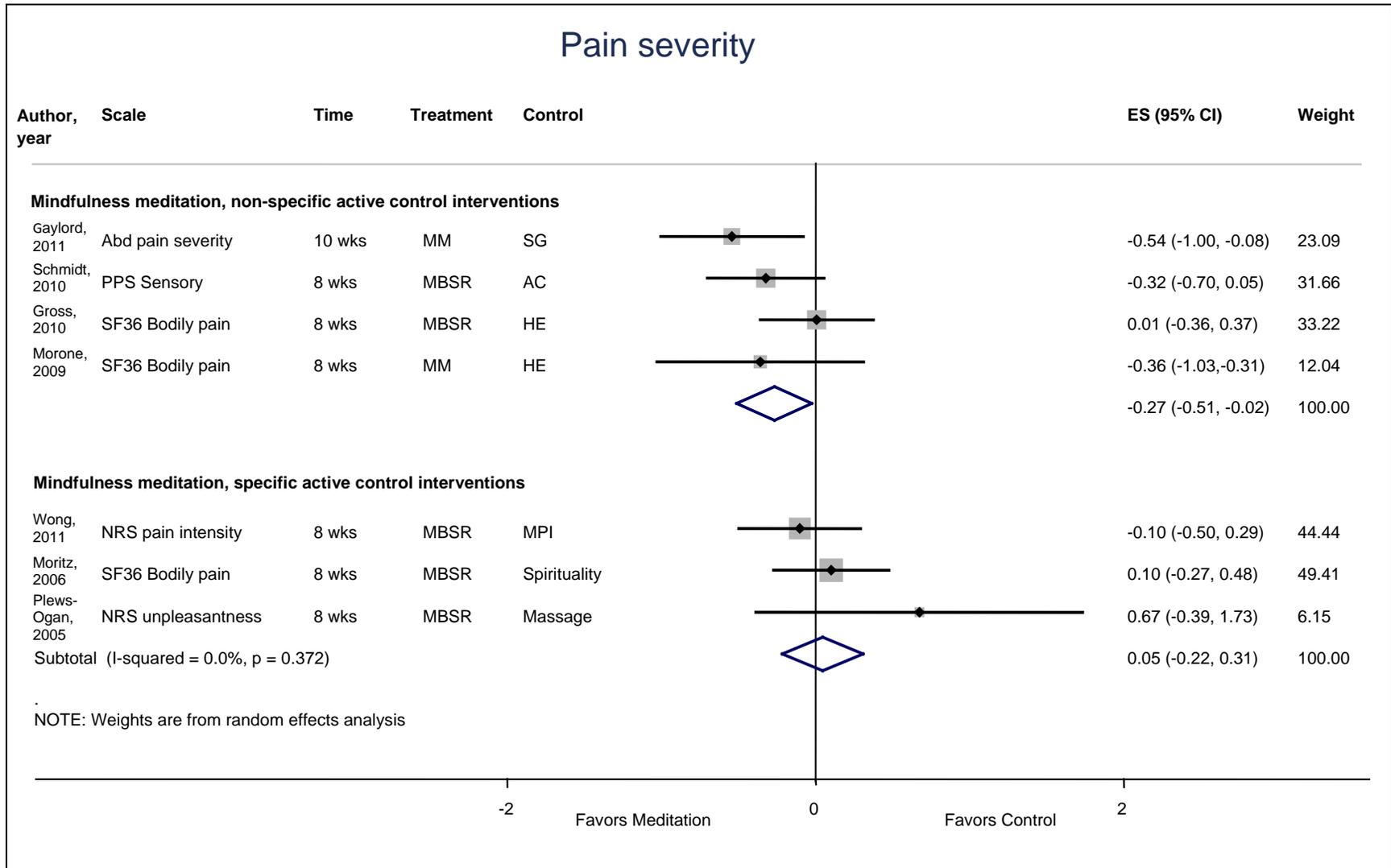
SOE = Strength of Evidence; MBSR = Mindfulness-based Stress Reduction

Figure 34. Relative difference between groups in the changes in measures of pain, in the mindfulness versus non-specific active control studies



1. **Relative difference between groups in the change score.** This is a relative percent difference, using the baseline mean in the meditation group as the denominator. For example, if the meditation group improves from a 10 to 19 on a mental health scale and the control group improves from 11 to 16 on the same scale, the relative difference between groups in the change score is: $\frac{(19-10)-(16-11)}{10} \times 100 = 40\%$. The interpretation is that there is a 40% relative improvement on the mental health scale in the meditation group compared with the control group. See Appendix E for absolute difference in change score values. Improvement in all scales is indicated in the positive direction. A positive relative percent difference means that the score improved more in the intervention group than in the control group.
2. NR / NS = Not Reported/Not significant. The trial measured this outcome and stated they were non-significant, and did not report actual results.
3. Black dotted lines from -5% to +5% indicate our criteria for no effect. It does not indicate statistical significance.
4. A p value above or below a bar indicates statistical significance reported in the original study publication. If there is no p value with a bar, the outcome was not significant in the original study publication.
5. Abd = Abdomen; PPS = Pain Perception (Sensory); SF36 = Short Form-36.

Figure 35. Meta-analysis of the effects of meditation programs on pain severity with 8 to 10 weeks of followup



Abd = Abdomen; PPS = Pain Perception (Sensory); SF36 = Short Form-36; NRS = Numeric Rating Scale.

Transcendental Meditation versus Non-specific Active Control

One transcendental meditation trial on African Americans with congestive heart failure assessed pain as a secondary outcome using the SF 36 pain subscale (n=23).⁶⁹ With 100 percent trial completion and 95 percent compliance rate among the originally randomized subjects, there were no differences in the pain scores in both groups at 3 months. However, at 6 months the transcendental meditation group showed an 18.4 percent improvement over health education (p=.08). This trial had a low risk of bias, and provided 22.5 hours of training over 6 months by trained and certified teachers. It recommended up to 90 hours of home practice during this time.

The strength of evidence is low that mantra meditation programs have no effect on pain severity among those with congestive heart failure when compared with a non-specific active control. We based this rating on a single trial of low risk of bias, unknown consistency, direct measures, and imprecise estimates (Table 31).

Table 31. Grade of trials addressing the efficacy of transcendental meditation on pain severity compared with non-specific active controls among cardiac patients

Number of Trials; Subjects	Domains Pertaining to Strength of Evidence				Magnitude of Effect and Strength of Evidence
	Risk of Bias	Consistency	Directness	Precision	
Pain Severity					Low SOE of no effect on pain severity
1; 23	Low	Unknown	Direct	Imprecise	-2.1% reduction in pain (favoring control)

SOE = Strength Of Evidence

Mindfulness Meditation Programs versus a Specific Active Control

Three trials assessed mindfulness-based stress reduction (MBSR) against a specific active control for the outcome of pain severity. Two trials were conducted in chronic pain populations, one in a mood disturbed population.

Wong et al. randomized patients with chronic pain (n=99) in Hong Kong to MBSR or a multidisciplinary pain intervention.⁶⁴ The trial included participants who reported greater than or equal to 4/10 pain on the numerical rating scale. The multidisciplinary pain intervention group specifically excluded teaching of any mind-body techniques that might have overlapped with MBSR. Researchers powered this trial to detect a 1-point difference in the numerical rating scale between the two groups. The trial found no statistically significant difference between interventions. Both interventions reduced pain by approximately 0.5 points post treatment and 1 point at 6 months. This trial had a low risk of bias, provided 27 hours of training and unspecified amount of home practice over 8 weeks. Teachers were trained and had 5 years of experience teaching meditation.⁶⁴

Plews-Ogan et al. randomized people with chronic musculoskeletal pain (n=15) to 8 weeks of MBSR training or weekly massage.⁶¹ The study used the 11-point numerical rating scale for pain unpleasantness to measure pain as one of two primary endpoints. It found that the massage group improved 2.9 points while the MBSR group improved by 0.7 points at 2 months. The trial did not calculate significance for difference-in-change estimates. This trial provided 20 hours of training

over 8 weeks, and unspecified amount of home practice. There was no information on teacher qualifications. It had a high risk of bias.

Moritz et al. randomized patients with mood disorders (n=110) to a spirituality program versus MBSR.⁵⁴ In this trial, MBSR was the active control. The spirituality intervention included a meditative component. It used the SF 36 bodily pain scale as a secondary outcome. In a difference-in-change estimate it found a non-significant 5.8 percent improvement in the spirituality group compared with the MBSR group. This trial provided about 12 hours of training in both interventions over an 8-week period, with unspecified amount of home practice in the MBSR group. It provided up to 42 hours of home practice in the spirituality group. There was no information on teacher qualifications for MBSR. This trial had a low risk of bias.

The difference in change graphs showed inconsistent results favoring a null effect or the control (Figure 36). A meta-analysis suggested a null effect (Figure 35).

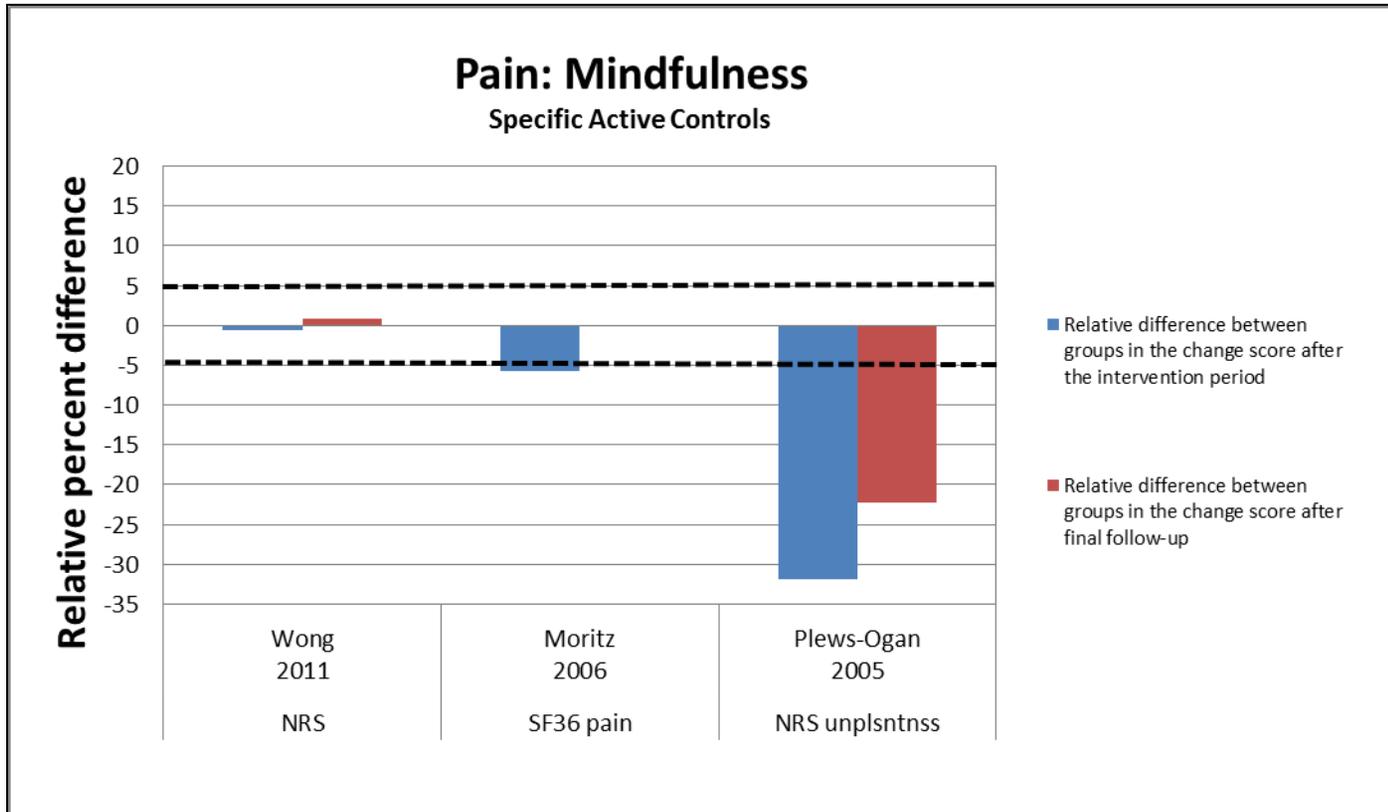
The strength of evidence is low that MBSR has no effect on pain severity among those with chronic musculoskeletal pain or mood disturbance, compared with a specific active control. We based this rating on overall medium risk of bias, consistent null results, direct measures of pain, and imprecise estimates (Table 32).

Table 32. Grade of trials addressing the efficacy of mindfulness-based stress reduction on pain severity compared with specific active controls among chronic pain and mood disturbance patients

Number of Trials; Subjects	Domains Pertaining to Strength of Evidence				Magnitude of Effect and Strength of Evidence
	Risk of Bias	Consistency	Directness	Precision	
Pain Severity					Low SOE of no effect on pain severity
3; 234	Medium	Consistent	Direct	Imprecise	-0.6% to -5.8% favoring control

SOE = Strength of Evidence

Figure 36. Relative difference between groups in the changes in measures of pain, in the mindfulness versus specific active control studies



1. **Relative difference between groups in the change score.** This is a relative percent difference, using the baseline mean in the meditation group as the denominator. For example, if the meditation group improves from a 10 to 19 on a mental health scale and the control group improves from 11 to 16 on the same scale, the relative difference between groups in the change score is: $\frac{((19-10)-(16-11))}{10} \times 100 = 40\%$. The interpretation is that there is a 40% relative improvement on the mental health scale in the meditation group compared with the control group. See Appendix E for absolute difference in change score values. Improvement in all scales is indicated in the positive direction. A positive relative percent difference means that the score improved more in the intervention group than in the control group.
2. NR / NS = Not Reported/Not significant. The trial measured this outcome and stated they were non-significant, and did not report actual results.
3. Black dotted lines from -5% to +5% indicate our criteria for no effect. It does not indicate statistical significance.
4. A p value above or below a bar indicates statistical significance reported in the original study publication. If there is no p value with a bar, the outcome was not significant in the original study publication.
5. NRS = Numeric Rating Scale; SF36 = Short Form-36; unplsntnss = unpleasantness.

Weight

Mindfulness Meditation Programs versus a Specific Active Control

Hebert et al. randomized women with early stage breast cancer (n=99) to mindfulness-based stress reduction (MBSR) versus nutrition education for 15 weeks.⁴⁹ This trial found no difference in weight between the three groups at 4 or 12 months. This trial provided approximately 45 hours of training over 15 weeks, did not report on any teacher qualifications and did not specify whether they recommended any home practice. This trial had a medium risk of bias.

The strength of evidence is insufficient that mindfulness meditation programs have an effect on weight among breast cancer patients when compared with a specific active control. We based this rating on a single medium risk of bias study, unknown consistency, directness of measures, and imprecise estimates (Table 33).

Table 33. Grade of trials addressing the efficacy of mindfulness-based stress reduction on weight among breast cancer patients compared with a specific active control

Number of Trials; Subjects	Domains Pertaining to Strength of Evidence				Magnitude of Effect and Strength of Evidence
	Risk of Bias	Consistency	Directness	Precision	
Weight					Insufficient evidence of an effect
1; 99	Medium	Unknown	Direct	Imprecise	1.7% weight gain in MBSR group

SOE = Strength of Evidence; MBSR = Mindfulness-based Stress Reduction

Transcendental Meditation versus a Non-specific Active Control

Two trials of transcendental meditation evaluated weight as an outcome. Elder et al. randomized adults with elevated HgA1c (n=54) to a transcendental meditation program versus diabetes education classes⁶⁸. There were no differences between the groups in weight loss (p=.26). This trial did not report on the amount of training provided or the duration of the training. It did specify it recommended about 90 hours of home practice over 6 months. The teachers were trained teachers of transcendental meditation. This trial had a medium risk of bias.

Castillo-Richmond et al. conducted a trial of transcendental meditation using a subsample from a larger randomized trial of transcendental meditation on cardiovascular outcomes (n=60 of 170 from the original trial).⁶⁷ This trial found no difference in weight after 7 months between the groups (p=.48). This trial did not specify the amount of training provided, but did specify it recommended up to 120.6 hours of home practice over 7 months. The teachers were trained and certified in the transcendental meditation tradition. This trial had a high risk of bias, due largely to uncertain sampling methods from the primary trial.

The difference in change graphs showed a consistent null effect on weight. The strength of evidence is insufficient that mantra meditation programs have an effect on weight among diabetics and hypertensive when compared with a non-specific active control. We based this rating on overall high risk of bias, consistent null findings, directness of measures, and imprecise estimates (Table 34).

Table 34. Grade of trials addressing the efficacy of meditation programs on weight among those with a clinical condition

Number of Trials; Subjects	Domains Pertaining to Strength of Evidence				Magnitude of Effect and Strength of Evidence
	Risk of Bias	Consistency	Directness	Precision	
Weight					Insufficient evidence of an effect
2; 114	High	Consistent	Direct	Imprecise	-1.8% to + 1.2% change in weight in TM group

SOE = Strength of Evidence;

Assessment of Potential Publication Bias

We could not conduct any reliable quantitative tests for publication bias since few studies were available for most outcomes, and we were unable to include all eligible studies in the meta-analysis due to missing data. Consequently, funnel plots were unlikely to provide much useful information regarding the possibility of publication bias. Our review of clinicaltrials.gov registration database did not provide sufficient information on the scales trials used to measure outcomes, or on the types of controls they used. This did not allow us to verify whether a potentially applicable outcome could have been included in our review. While examining for selective outcome reporting, we found one trial that selectively reported on positive outcomes.⁵⁰ Among 101 outcomes in 34 trials, trials did not give enough information to calculate a relative difference in the change score (our primary analysis) for seven outcomes due to statistically insignificant findings. These are represented as solid grey boxes in the figures. Trials did not give enough information to conduct a meta-analysis on thirty outcomes. Our findings from the primary analysis are therefore less likely to be affected by publication bias than the meta-analysis.

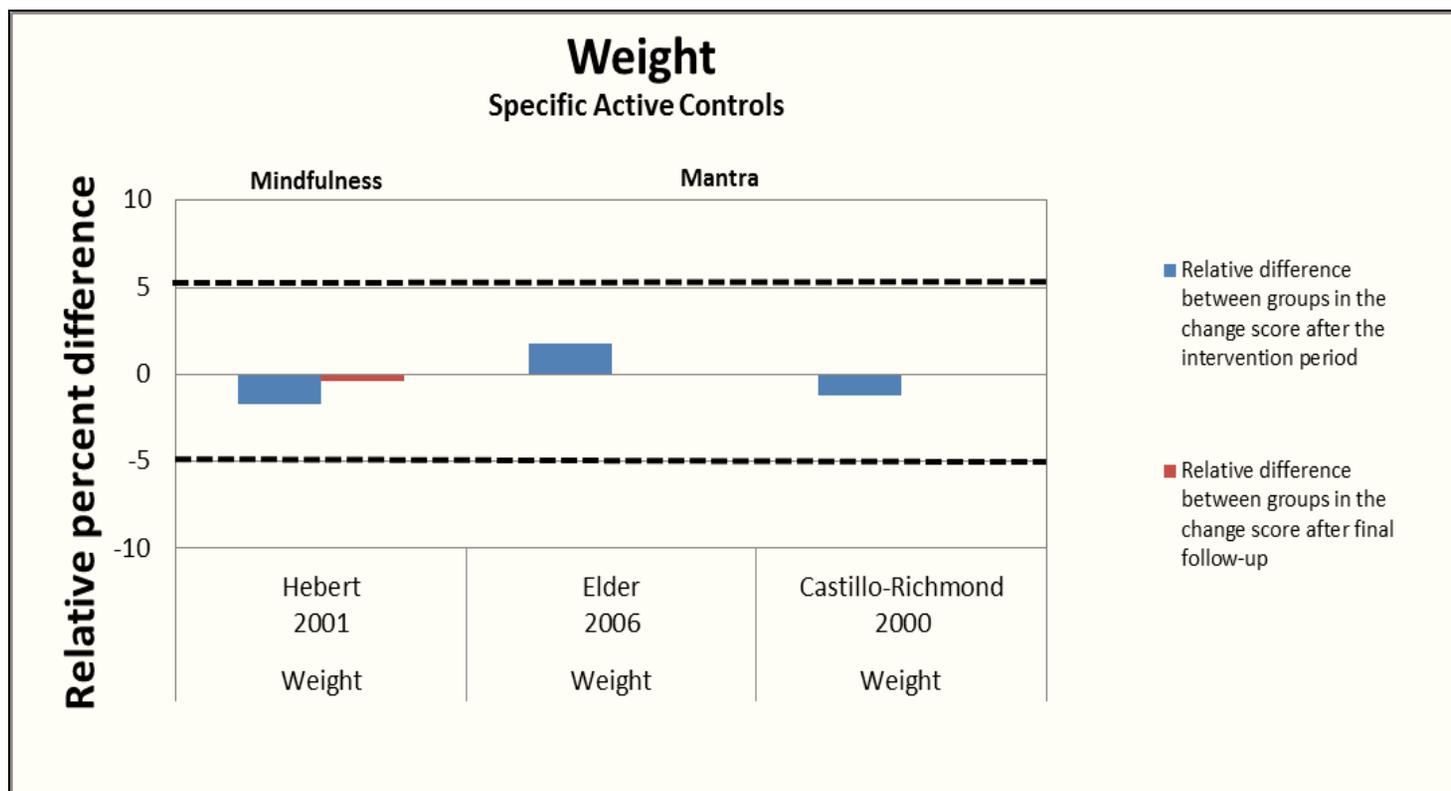
Applicability

Eight of 11 trials took place in the U.S., the remainders took place in Canada, Germany, and Hong Kong, so that these findings might be inapplicable to patients or settings in other regions. All of the trials took place in outpatient settings, so these findings would not be applicable to the inpatient setting.

Regarding the population characteristics of the trials for this key question, only one trial reported the racial or ethnic characteristics of its study population. In addition, these trials under represent younger patients (less than 45) and older patients (age greater than 80), making these findings less applicable to those groups. The most important proviso regarding the population characteristics is that the trials for this key question were of two different kinds: those in populations with chronic pain, and those predominantly with another condition. Thus, the populations in these trials were heterogeneous as a group, making it difficult to identify the clinical populations to which these findings would be most applicable.

Characteristics of the interventions represented in this key question were diverse, making it difficult to foresee how these findings would be applicable to a similarly wide array of mindfulness practices under everyday clinical situations. For example, only a few trials specified the certification and training of instructors or the time spent in home training.

Figure 37. Relative difference between groups in the changes in measures of weight, in the mindfulness /mantra versus specific active control studies



- Relative difference between groups in the change score.** This is a relative percent difference, using the baseline mean in the meditation group as the denominator. For example, if the meditation group improves from a 10 to 19 on a mental health scale and the control group improves from 11 to 16 on the same scale, the relative difference between groups in the change score is: $\frac{((19-10)-(16-11))}{10} \times 100 = 40\%$. The interpretation is that there is a 40% relative improvement on the mental health scale in the meditation group compared with the control group. See Appendix E for absolute difference in change score values. Improvement in all scales is indicated in the positive direction. A positive relative percent difference means that the score improved more in the intervention group than in the control group
- NR / NS = Not Reported/Not significant. The trial measured this outcome and stated they were non-significant, and did not report actual results.
- Black dotted lines from -5% to +5% indicate our criteria for no effect. It does not indicate statistical significance.
- A p value above or below a bar indicates statistical significance reported in the original study publication. If there is no p value with a bar, the outcome was not significant in the original study publication.
- Units of weight: kilograms (Hebert, 2001) and pounds (Elder, 2006; Castillo-Richmond, 2000).

Discussion

Thirty-four randomized controlled trials (RCTs) reported in this review assessed the effects of different types of meditation programs.

Key Question 1. What are the efficacy and harms of meditation programs on negative affect (e.g. anxiety, stress) and positive affect (e.g. well-being) among those with a clinical condition (medical or psychiatric)?

We found 26 trials for this Key Question. Our review reports a number of findings with low strength of evidence, and the majority of findings with insufficient strength of evidence. The findings with low strength of evidence are of clinical relevance, albeit with some caveats attached. In general, mindfulness meditation programs had low strength of evidence to improve any dimension of negative affect that we reviewed including anxiety, depression, and perceived stress/general distress. Mantra meditation programs had low strength of evidence to improve anxiety but had insufficient evidence for an effect on depressive symptoms and low strength of evidence that it did not improve perceived stress. There was insufficient strength of evidence to suggest any effect on positive affect for mindfulness meditation program and low strength of evidence that mantra meditation programs had no effect on positive affect, but this was largely limited by a paucity of studies reporting on this outcome. Some of the differences may also be due to the type of populations studied, and whether they had high levels of a particular negative affect to begin with.

In the outcome of anxiety, we found mindfulness meditation program had low strength of evidence to improve anxiety. These trials used mostly female populations. However, the two trials with mostly men^{47 53} appeared to show as much consistency as those which used mostly or all women.^{46 50 60 62} When using specific active controls, MBSR did not have a clear effect on general anxiety. All of these trials except one⁵³ used anxiety as a secondary outcome, and did not use an anxious population. One study of MBSR enrolled people with social anxiety but found no effect compared with group cognitive behavioral therapy.⁵⁹ In general, among non-clinically anxious populations, mindfulness programs may hold some benefit, but the strength of evidence is low. There was one Korean meditation program that used an anxious population and had large effect sizes for anxiety. This warrants further investigation.

Four trials of transcendental meditation and one trial of other mantra (OM) evaluated anxiety as an outcome. Only one trial showed a statistically significant effect⁷³ while the remaining four trials showed a null effect. The trial by Smith et.al. was the only trial conducted in an anxious population, but was rated as high risk of bias and also showed null results.⁷⁴ Of note, the mantra trials in general tended to have longer follow up periods for their first outcome assessment than mindfulness trials. Mindfulness trials tended to collect their first outcome assessment at 8 weeks, whereas the transcendental meditation trials tended to do this at 3-6 months. It is unclear if this time difference in collection may influence the results.

Our review included only two trials of mindfulness-based cognitive therapy (MBCT) on anxiety, and neither found an effect.^{58 59} Two previous reviews have assessed the role of MBCT on anxiety.¹² One study conducted a meta-analytic review on mindfulness-based therapies for

anxiety and depression in a variety of clinical populations and concluded that MBCT is an effective intervention for reducing anxiety.¹³ Chiesa et al. (2010) stated that there is limited evidence that MBCT could provide some improvement in residual anxiety symptoms in some populations. However, both of these reviews included both RCTs and non-RCTs. Bohlmeijer (2010) evaluated RCTs of MBSR only, mostly compared with wait-list controls, and found a small effect size for anxiety among the higher quality studies it evaluated.⁸ This is generally in line with our findings. However, a strength of our review is the focus on randomized trials with non-specific active controls. Despite the low strength of evidence of a benefit, our results should give us greater confidence that the reported benefits are not due to having a flawed comparison group.

In the outcome of depression, we find low strength of evidence that mindfulness meditation program reduce depressive symptoms compared with a non-specific active control. None of these trials were conducted in depressed populations. While the mindfulness trials that used a specific active control showed great inconsistency in results, it is notable that two trials of MBCT were conducted among patients in full or partial remission from a major depressive episode and showed improvements in depressive symptoms and relapse rates. These two trials^{63,52} used a clinically important outcome of relapse rate among a depression population, compared mindfulness-based cognitive therapy with tapering of antidepressant medication to maintenance antidepressant medication, and found consistent absolute 8% to 13% reductions in relapse rates. Both trials were rated as having low risk of bias. These findings warrant further investigation, and are generally consistent with prior reviews. Piet et al. (2011) conducted a review evaluating the effect of MBCT for prevention of relapse or recurrence among patients with recurrent major depressive disorder in remission.¹⁷ This review included both of the trials we listed in our review and four other trials that used a usual-care control. This review found a moderate and statistically significant effect for MBCT. Chiesa et al. (2010) conducted a review on MBCT for psychiatric disorders and found that MBCT plus gradual discontinuation of maintenance antidepressants was not significantly different from the effects of continuing current antidepressant pharmacologic treatment, suggesting that MBCT was a potentially effective alternative.¹² Bohlmeijer (2010) evaluated RCTs of MBSR only, mostly compared with wait-list controls, and found a small effect size for depression.⁸

Surprisingly, very few trials reported on perceived stress. We found low strength of evidence that mindfulness meditation program result in small improvements in stress and distress when compared with non-specific active controls. In a prior review, Chiesa et al. (2009) found that MBSR had a “significant positive effect” when compared with an inactive control on reducing stress.¹⁰ We found no RCTs with an active control that assessed stress as an outcome utilizing MBSR specifically. Among three mantra trials, two were low risk of bias transcendental meditation trials among cardiac patients. The effect for all three trials was consistently null. Although it would appear that mantra meditation programs do not have an effect on stress, it is unclear if cardiac patients have the level of stress that can be affected by these programs. The number of studies was extremely limited.

Well-being and positive mood are positive dimensions of mental health. Meditation programs seek not only to reduce negative symptomatology, but also to improve the positive dimensions of health. The available evidence did not show any effects on these dimensions, but very few studies reported on these positive affect outcomes.

Mindfulness meditation programs similarly did not affect the overall mental component of health-related quality of life. However, there were very few trials addressing this outcome.

Key Question 2. What are the efficacy and harms of meditation programs on attention among those with a clinical condition (medical or psychiatric)?

Two RCTs compared meditation programs to active controls on the outcome of attention. There were no statistically significant differences between groups on any components of the two measures of attention included in the two trials (the Attentional Network Test and the Stroop Color Word Interference Test). There were trends suggesting that meditation programs performed better than non-specific active controls on these measures, although these did not reach statistical significance. Overall, there is insufficient strength of evidence to comment on whether meditation programs improve attention among an older population compared with active controls. This is largely due to the small number of trials that assessed the outcome of attention, both of which had a medium risk of bias; a limited number of measures; and limited diversity in the populations, which were older, predominantly women, and white.

Of note, three previous reviews assessed the role of meditation programs on attention. A Cochrane review by Krisanaprakornkit et al,⁷⁷ on meditation therapies for attention-deficit/hyperactivity disorder that included two mantra meditation trials, could not make any conclusions regarding the effectiveness of meditation programs for attention-deficit/hyperactivity disorder due to high risk of bias and small sample sizes. That review is not directly comparable to the current review as the trial population is different (the previous review included children with attention-deficit/hyperactivity disorder), and each used different measures of attention. In addition, the previous review included four RCTs, two of which focused on yoga as the primary intervention which was not included in the current review. Two additional systematic reviews assessed the effect of transcendental meditation (Canter et al, 2003)²⁴ and mindfulness meditation programs (Chiesa 2010) on cognitive functioning, including the domain of attention. While the review by Canter et al. (2003) did not specify results pertaining to attention, the authors concluded that evidence does not support that transcendental meditation has “a specific and cumulative effect on cognitive function.” The review by Chiesa included 23 trials but only six RCTs, with the majority of the RCTs (4 of 6) conducted in healthy populations. Of note, the two trials on clinical populations did not include active controls and were, therefore, not included in the present review. The authors preliminarily concluded that mindfulness meditation programs were associated with improvements in attention, although the authors noted that limitations and variability in the trials requires further assessment. In conjunction with the current review, these findings further reiterate the need for more comprehensive trials with a variety of clinical populations (e.g., disorders where attention may be compromised) to provide a clearer understanding of the impact of meditation programs on attention.

Key Question 3. What are the efficacy and harms of meditation programs on health-related behaviors affected by stress, specifically substance use, sleep, and eating, among those with a clinical condition (medical or psychiatric)?

We included nine trials for this KQ, four trials evaluating the effect of meditation on substance use,^{42 43 45 67 71 75} one trial evaluating eating,⁴⁹ and four trials with sleep disorders.^{47 48 57} Overall, there is insufficient evidence to support that the existing meditation trials alter health-related behaviors affected by stress.

Among the four trials evaluating substance use, all four were conducted in substance using populations. Taken together, the trials of mindfulness and mantra meditation failed to provide sufficient evidence of benefit in reducing use of cigarettes, alcohol, or cocaine. One trial of MBSR among breast cancer patients failed to show an effect on reducing calorie consumption.⁴⁹ Among the four trials in which sleep was an outcome, only one used an insomnia population⁴⁸, but failed to provide evidence of an effect on sleep time or quality. Three other trials, which assessed sleep as a secondary outcome among various clinical populations, had inconsistent results on sleep quality.

Our findings are consistent with systematic reviews in this area, which have found insufficient evidence for the effects of meditation programs on health-related behaviors affected by stress among controlled studies. Zgierska et al. conducted a systematic review, which included trials of a mindfulness-based intervention in patients with substance abuse.²⁰ It found no significant effect. Regarding eating disorders, Warden (2011) conducted a systematic review, which included articles considering mindfulness therapy as a treatment for eating disorders.¹⁸ The authors stated that they found evidence of the effectiveness of mindfulness-based interventions for eating disorders. However, this review consisted of largely uncontrolled studies with an N of 1. The literature in this area is still in a preliminary state with regards to quality.

Winbush et al. evaluated seven trials on sleep, four of them uncontrolled, and concluded that the uncontrolled trials found an effect on sleep disturbance while the controlled trials did not find an effect.¹⁹ This is also in line with the findings of this review.

Key Question 4. What are the efficacy and harms of meditation programs on pain and weight among those with a clinical condition (medical or psychiatric)?

We included 11 RCTs for this key question. We found moderate strength of evidence that mindfulness-based stress reduction (MBSR) reduces pain severity to a small degree when compared with a non-specific active control. We also found low strength of evidence that when MBSR was compared with various specific active controls including massage, MBSR was not superior in reducing pain severity. One transcendental meditation trial did not find any improvement in pain severity, but was conducted in 23 patients with CHF and pain was a secondary outcome.

Among the trials evaluating pain, most evaluated musculoskeletal pain. Based on one study with large significant findings, there is a suggestion that MBSR may be useful for visceral pain.

Gaylord et al. evaluated 75 women with irritable bowel syndrome and found a statistically significant 30 percent reduction in abdominal pain severity at 2 months that maintained at six months. Previous systematic reviews by Veehof et. al. of trials for pain concluded an effect size of .37 for pain for MBSR and acceptance and commitment therapy, suggesting they were good alternatives to cognitive behavior therapy.⁷⁸ A review by Bernardy et al. combined MBSR with a number of cognitive behavior therapy used on fibromyalgia patients and found that this group of interventions had no significant effects on pain among fibromyalgia patients.²¹ Both included control and uncontrolled trials.

There were very few trials evaluating weight as an outcome, and it was not a primary outcome for any. There was insufficient strength of evidence to suggest that transcendental meditation or MBSR have an effect on weight

Limitations of the Primary Studies

Although we collected information on amount of training, the trials did not provide enough information to make use of that data. The studies generally did not provide enough information to allow us to draw any conclusions about how the effects of the interventions differed among subpopulations, such as racial-ethnic groups, elderly patients, or patients with specific medical or psychiatric conditions. The limited number of trials using diverse comparators among diverse populations also made using the available information on “dose” of meditation difficult. In addition, we could not rule out selective outcomes reporting and publication bias.

It may be that specific scales may be more relevant for a particular form of meditation. In many cases only certain measures were assessed and the scales may have been limited in their ability to detect an effect. For example, in gauging attention, trials only used two measures of attention, and it is possible that these were not sensitive measures for the populations assessed.

We intended to evaluate the effects of meditation programs on a broad range of medical and psychiatric conditions since stress outcomes are not limited to any particular medical or psychiatric condition. Despite our focus on a subset of meditation programs tested in active controlled RCTs, we were largely unable to detect a specific effect of meditation on most outcomes, with the majority of our grades being insufficient or low. This was mostly driven by two important evaluation criteria: the risk of bias and the inconsistencies in the body of evidence. The specific reasons for such inconsistencies may have included the differences in the particular clinical conditions, as well as the type of control groups used. When a study compared a meditation program to a specific active control, we could not easily compare these trials with those that used a non-specific active control. We therefore separated these comparisons to be able to evaluate the effects against a relatively homogenous nonspecific active control group. Comparing trials that used one specific active control to another specific active control in general led to large inconsistencies that could be explained by differences in the control groups (Figures 22, 25-28). The variations in sensitivities of scales that trials used to detect changes from the intervention and the paucity of trials within each outcome domain may have also contributed to the inconsistent findings. Another possibility is that there is no real effect of the programs on many of the outcomes that had inconsistent findings. While some of the outcomes were primary outcomes, many were secondary outcomes and the studies may not have been appropriately powered to detect changes.

Limitations of the Review

An important decision in setting up this review was the choice to examine only studies that randomized participants to a meditation program or an active control. We chose not to include observational studies or trials with non-active controls because there remain questions as to the specific effects of meditation on clinical outcomes, and such studies would have too high of a risk of bias to be able to answer those questions. Observational studies have a particularly high risk of bias in this area of research because of problems such as self-selection of interventions (people are more likely to enroll in a meditation program if they believe in its benefits or have prior experience with meditation) and the use of outcome measures that can be easily biased by participants' beliefs in the benefits of meditation. In making this decision, we restricted our ability to examine longer-term outcomes, including potential harms of meditation. This is an intriguing issue in the literature, as various experts believe that the benefits of meditation increase with practice and may require years for meaningful, clinically relevant changes to occur. Also, because meditation requires behavior change and skill development, it is very likely that participants in observational studies are self-selected for personal characteristics that may not generalize to the larger population. This type of longitudinal observational study could be informative once the clinical efficacy of an intervention is established. Since the clinical efficacy of meditation programs remains in question, the validity of longitudinal observational studies remains limited.

We generally rated all self-reported outcomes as being direct except for measures of craving or submeasures of negative or positive affect. Some may consider the measures we rated as direct to be indirect, which would further lower the strength of evidence for such ratings. Our assessment of the risk of bias of these trials needs to be interpreted in the light of unique risk of bias issues for non-pharmacologic interventions where blinding of intervention is not possible. We did not rate the strength of evidence on publication bias. Our review of clinicaltrials.gov registration database did not provide sufficient information on the scales trials used to measure outcomes, or on the types of controls they used. This did not allow us to verify whether a potentially applicable outcome could have been included in our review.

Our assessment of a 5 percent difference in the outcome change scores as being potentially clinically significant needs to be interpreted in the context of heterogeneous scales reporting on various measures. The literature does not clearly define the appropriate threshold for what is clinically significant on these scales, and it is likely that there is variability among the measures. Some may consider a higher or lower threshold as being relevant. Another limitation is that our method of displaying the relative difference between groups in the change scores from different measurement scales did not take into consideration how the scales varied in the range of scores that were possible. However, we thought this simple method of displaying the data would make it easier for readers to understand the data. Whenever possible, we also displayed the results using a meta-analysis of standardized mean differences that did account for differences between the measurement scales.

The personal characteristics of individuals (e.g. personality, spirituality, education, etc.) may influence their understanding and skill in performing meditation. Although trials appeared to recruit individuals with diverse conditions, we are unable to comment on whether this may have affected any results. We were limited in our ability to determine the overall applicability of the body of evidence to the broad population of patients that could benefit from mindfulness meditation because the studies varied so much in many ways other than just the specific targeted population (i.e., varied in characteristics of the intervention, comparator, outcomes, timing, and

setting). Also, the studies generally did not provide enough information to be able to determine whether the effectiveness of mindfulness meditation varied by race, ethnicity, or education.

While this review sought to assess the effectiveness of meditation programs above and beyond the non-specific effects of expectation and attention, it did not assess the preferences of patients. For many patients, even though one therapy may not be better than another, they may still prefer it for personal or philosophical reasons. Further, by balancing expectations, we rule out the possibility of an intervention which cultivates high expectations to have a useful effect, particularly when it comes with few to no harms and fits within a person's philosophical mindset.

Future Directions

Further research in meditation would benefit from several considerations.

First, since meditation is a skill, more training with an expert and practice in daily life should lead to greater competency in the skill. Greater competency would presumably lead to better outcomes. When compared with other skills that require training, the amount of training afforded in the current paradigm is quite low. Consideration should be given to placing a greater emphasis on developing the skill. In order to facilitate this, better measurement tools are needed. The currently available mindfulness scales have not been well validated and do not appear to distinguish different forms of meditation. Thus, further work on the operationalization and measurement of mindfulness or the particular meditative skill is needed.

Second, trials should document the amount of training clinicians provide and patients receive, along with the amount of home practice patients complete. This gives an indication of how effective the program is at delivering training, how adherent participants were with accepting the intervention, and, in turn, the likelihood these skills will actually be learned and developed by participants.

Third, studies should place emphasis on teacher qualifications. A highly-experienced teacher could have a very different effect than an inexperienced teacher. Given the numerous uncertainties and difficulties around definitions and measurement of skill in meditation programs, quantifying teacher experience and competence adds yet another level of uncertainty. However, the range of experience in meditation and competence as a teacher of this skill likely plays a role in outcomes.

Fourth, the use of non-specific active control allows one to infer on the effect of meditation compared with such a control arm when they are matched for time, attention, and expectancy. When using a specific active control, if one finds no statistically significant superiority over the control, one is left with the issue of whether the meditation is equivalent to or not inferior to the control, or whether the trial was just underpowered to detect any difference. Conducting comparative effectiveness trials require prior specification of the hypothesis (superiority, equivalence, non-inferiority), appropriate determination of the margins of clinical significance, and minimum importance difference.⁷⁹ In the case of equivalence and non-inferiority trials, trials also need to have appropriate assay sensitivity. None of the trials showed statistically significant effects against a specific active control, nor did they appear adequately powered to assess non-inferiority or equivalence. This leaves a lot of uncertainty in such trial designs.

Fifth, positive outcomes are a key focus of meditative practices. However, positive outcomes were not included as primary or even secondary outcomes for most trials. The few exceptions that we reviewed included measures of positive affect, sense of coherence, and vitality. Future

studies should expand upon these domains. There are other domains such as self efficacy, which we did not review, that may also be important outcomes.

Future trials should appropriately report key design characteristics to enable the assessment of risk of bias. Future trials should register the trial on a national register, standardize training using trainers who meet specified criteria, specify primary and secondary outcomes *a priori*, power the trial based on the primary outcomes, use CONSORT recommendations for reporting results, and operationalize and measure the practice of meditation by study participants. However, an important part of the process of creating standardized meditation programs, when there is uncertainty around the effect or conceptualization of a particular program, is the innovation and testing of small changes to the existing programs in various contexts. We see this being done in the mindfulness trials and to a smaller degree in the mantra trials. While this adds a layer of complexity in synthesizing the results of these various programs, it should not hinder the innovation of meditation researchers.

Conclusions

Our review shows that there is moderate strength of evidence that mindfulness meditation programs are beneficial for reducing pain severity, and there is low strength of evidence that meditation programs, mindfulness in particular, may lead to improvement in dimensions of negative affect, including anxiety, depression, and perceived stress/general distress. Otherwise, much of the evidence was insufficient to address the comparisons for most of the questions. There may be many reasons for this general lack of evidence.

First, while we sought to review the highest standards of behavioral randomized controlled trials, there was wide variation in risk of bias among these. Of 34 randomized controlled trials, we only rated seven as low risk of bias. However, for studies where there is mostly a medium to high risk of bias, one might expect to see more positive results. We did not see this.

Second, many if not most studies appeared to be underpowered to find an effect, as we rated most of the studies as imprecise. While this is critical for the individual study, it may not matter as much for a systematic review in which we are also concerned with the directionality of effect among numerous studies, irrespective of their statistical significance. We did not see a convincing effect for many of these outcomes, although there were a number of mental health outcomes that had low strength of evidence.

Third, we attempted to analyze the effect meditation programs have on certain domains of mental, emotional, and physical health that are affected by stress. These domains are heterogeneous and studies often report them on different scales, which make it more complicated to analyze. However, for an intervention that focuses on reducing stress, we would expect to find some consistency in improvement on more than one mental health domain. We found low strength of evidence for an effect in most domains for one form of meditation or another. However, we did not see an effect on the mental component of health-related quality of life, or for positive affect. Due to the limited number of trials we reported, one should view these conclusions cautiously within the context of the particular population studied, type of meditation program used, and type of comparison used.

Fourth, for many outcomes, there was a dearth of adequate studies to draw detailed conclusions. For example, nearly all of the studies assessing pain focused on musculoskeletal pain populations. None assessed neuropathic pain, and only one assessed a visceral pain. We need further studies that better define what outcome is responsive to a particular meditation program.

Fifth, the reasons for a lack of a significant reduction of stress-related outcomes may have to do with the way the research community conceptualizes meditation programs, the difficulties of acquiring such skills, and the limited duration of randomized controlled trials. Historically, the general public did not conceptualize meditation as a quick fix toward anything. It was a skill one learns and practices over time to increase one's awareness, and through this awareness gains insight and understanding into the various subtleties of their existence. Trials of short duration and training may be insufficient to develop the meditative skills necessary to affect stress related outcomes.

Reference List

1. The National Center for Complementary and Alternative Medicine (NCCAM). Available at: <http://nccam.nih.gov/>
2. Barnes PM, Bloom B, Nahin RL. Complementary and alternative medicine use among adults and children: United States, 2007. Natl Health Stat Report 2008; (12):1-23.
3. Goyal M, Haythornthwaite J, Levine D *et al.* Intensive meditation for refractory pain and symptoms. J Altern Complement Med 2010; 16(6):627-31.
4. Chiesa A, Malinowski P. Mindfulness-based approaches: are they all the same? J Clin Psychol 2011; 67(4):404-24.
5. Walach H. Review of "Effectiveness of Meditation in Healthcare." Available at: <http://www.mum.edu/inmp/walach.html>. Accessed February 17, 2012. [Web Page].
6. Orme-Johnson DW. Commentary on the AHRQ report on research on meditation practices in health. J Altern Complement Med 2008; 14(10):1215-21.
7. Patient Reported Outcomes Measurement Information System (PROMIS®). Available at: <http://www.nihpromis.org/>. Accessed August 10, 2011. [Web Page].
8. Bohlmeijer E, Prenger R, Taal E, Cuijpers P. The effects of mindfulness-based stress reduction therapy on mental health of adults with a chronic medical disease: a meta-analysis. J Psychosom Res 2010; 68(6):539-44.
9. Chambers R, Gullone E, Allen NB. Mindful emotion regulation: An integrative review. Clin Psychol Rev 2009; 29(6):560-72.
10. Chiesa A, Serretti A. Mindfulness-based stress reduction for stress management in healthy people: a review and meta-analysis. J Altern Complement Med 2009; 15(5):593-600.
11. Chiesa A, Calati R, Serretti A. Does mindfulness training improve cognitive abilities? A systematic review of neuropsychological findings. Clin Psychol Rev 2011; 31(3):449-64.
12. Chiesa A, Serretti A. Mindfulness based cognitive therapy for psychiatric disorders: a systematic review and meta-analysis. Psychiatry Res 2011; 187(3):441-53.
13. Hofmann SG, Sawyer AT, Witt AA, Oh D. The effect of mindfulness-based therapy on anxiety and depression: A meta-analytic review. J Consult Clin Psychol 2010; 78(2):169-83.
14. Krisanaprakornkit T, Ngamjarus C, Witoonchart C, Piyavhatkul N. Meditation therapies for attention-deficit/hyperactivity disorder (ADHD). Cochrane Database Syst Rev 2010; (6):CD006507.
15. Ledesma D, Kumano H. Mindfulness-based stress reduction and cancer: a meta-analysis. Psychooncology 2009; 18(6):571-9.
16. Matchim Y, Armer JM, Stewart BR. Mindfulness-based stress reduction among breast cancer survivors: a literature review and discussion. Oncol Nurs Forum 2011; 38(2):E61-71.
17. Piet J, Hougaard E. The effect of mindfulness-based cognitive therapy for prevention of relapse in recurrent major depressive disorder: a systematic review and meta-analysis. Clin Psychol Rev 2011; 31(6):1032-40.
18. Wanden-Berghe RG, Sanz-Valero J, Wanden-Berghe C. The application of mindfulness to eating disorders treatment: a systematic review. Eat Disord 2011; 19(1):34-48.
19. Winbush NY, Gross CR, Kreitzer MJ. The effects of mindfulness-based stress reduction on sleep disturbance: a systematic review. Explore (NY) 2007; 3(6):585-91.
20. Zgierska A, Rabago D, Chawla N, Kushner K, Koehler R, Marlatt A. Mindfulness meditation for substance use disorders: a systematic review. Subst Abus 2009; 30(4):266-94.
21. Bernardy K, Fuber N, Kollner V, Hauser W. Efficacy of cognitive-behavioral therapies in fibromyalgia syndrome - a systematic review and metaanalysis of randomized controlled trials. J Rheumatol 2010; 37(10):1991-2005.
22. Rainforth MV, Schneider RH, Nidich SI, Gaylord-King C, Salerno JW, Anderson JW. Stress reduction programs in patients with

- elevated blood pressure: a systematic review and meta-analysis. *Curr Hypertens Rep* 2007; 9(6):520-8.
23. Anderson JW, Liu C, Kryscio RJ. Blood pressure response to transcendental meditation: a meta-analysis. *Am J Hypertens* 2008; 21(3):310-6.
 24. Canter PH, Ernst E. The cumulative effects of Transcendental Meditation on cognitive function--a systematic review of randomised controlled trials. *Wien Klin Wochenschr* 2003; 115(21-22):758-66.
 25. So K.T., Orme-Johnson D. W. Three randomized experiments on the longitudinal effects of the Transcendental Meditation technique on cognition. *Intelligence* 2001; 419-40.
 26. Travis F GS, Stixrud W. ADHD, Brain Functioning, and Transcendental Meditation Practice. *Mind & Brain, The Journal of Psychiatry* 2011; 73-81.
 27. Chen KW, Berger CC, Manheimer E et al.. Meditative therapies for reducing anxiety: a systematic review and meta-analysis of randomized controlled trials. *Depress Anxiety* 2012; 29(7):545-62.
 28. Chambless DL, Hollon SD. Defining empirically supported therapies. *J Consult Clin Psychol* 1998; 66(1):7-18.
 29. Hollon SD, Ponniah K. A review of empirically supported psychological therapies for mood disorders in adults. *Depress Anxiety* 2010; 27(10):891-932.
 30. Rappay L, Bystrisky A. Classical mindfulness: an introduction to its theory and practice for clinical application. *Ann N Y Acad Sci* 2009; 1172:148-62.
 31. Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med* 6(7): e1000097. 2009.
 32. Meditation Programs for Stress and Well-being - Research protocol. http://effectivehealthcare.ahrq.gov/ehc/products/375/981/Meditation-for-Stress_ProtocolAmendment_20121017.pdf
 33. Bhogal SK, Teasell RW, Foley NC, Speechley MR. The PEDro scale provides a more comprehensive measure of methodological quality than the Jadad scale in stroke rehabilitation literature. *J Clin Epidemiol* 2005; 58(7):668-73.
 34. Chambless DL, Ollendick TH. Empirically supported psychological interventions: controversies and evidence. *Annu Rev Psychol* 2001; 52:685-716.
 35. Cohen J. Statistical power analysis for the behavioral sciences. Hillsdale, NJ: L. Erlbaum Associates; 1988.
 36. Lyubomirsky S, King L, Diener E. The benefits of frequent positive affect: does happiness lead to success? *Psychol Bull* 2005; 131(6):803-55.
 37. Clark LA, Watson D. Tripartite model of anxiety and depression: psychometric evidence and taxonomic implications. *J Abnorm Psychol* 1991; 100(3):316-36.
 38. Methods Guide for Conducting Comparative Effectiveness Reviews. Rockville, MD: Agency for Healthcare Research and Quality; August 2007. AHRQ Publication No. 10(11)-EHC063-EF.
 39. Higgins JP, Altman DG, Gotzsche PC *et al.* The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011; 343:d5928.
 40. Higgins JPT, Green S, eds. Cochrane handbook for systematic reviews of Interventions Version 5.1.0. London: The Cochrane Collaboration; Updated March 2011. Available at: <http://www.cochrane.org/training/cochrane-handbook>. Accessed February 17, 2012.
 41. Owens DK LKADeal. AHRQ series paper 5: grading the strength of a body of evidence when comparing medical interventions--agency for healthcare research and quality and the effective health-care program. *J Clin Epidemiol* 2010; 63(5):513-23..
 42. Brewer JA, Sinha R, Chen JA *et al.* Mindfulness training and stress reactivity in substance abuse: results from a randomized, controlled stage I pilot study. *Subst Abus* 2009; 30(4):306-17.
 43. Brewer JA, Mallik S, Babuscio TA *et al.* Mindfulness training for smoking cessation:

- Results from a randomized controlled trial. *Drug Alcohol Depend* 2011.
44. Delgado LC, Guerra P, Perakakis P, Vera MN, Reyes del Paso G, Vila J. Treating chronic worry: Psychological and physiological effects of a training programme based on mindfulness. *Behav Res Ther* 2010; 48(9):873-82.
 45. Garland EL, Gaylord SA, Boettiger CA, Howard MO. Mindfulness training modifies cognitive, affective, and physiological mechanisms implicated in alcohol dependence: results of a randomized controlled pilot trial. *J Psychoactive Drugs* 2010; 42(2):177-92.
 46. Gaylord SA, Palsson OS, Garland EL *et al.* Mindfulness training reduces the severity of irritable bowel syndrome in women: results of a randomized controlled trial. *Am J Gastroenterol* 2011; 106(9):1678-88.
 47. Gross CR, Kreitzer MJ, Thomas W *et al.* Mindfulness-based stress reduction for solid organ transplant recipients: a randomized controlled trial. *Altern Ther Health Med* 2010; 16(5):30-8.
 48. Gross CR, Kreitzer MJ, Reilly-Spong M *et al.* Mindfulness-based stress reduction versus pharmacotherapy for chronic primary insomnia: a randomized controlled clinical trial. *Explore (NY)* 2011; 7(2):76-87.
 49. Hebert JR, Ebbeling CB, Olendzki BC *et al.* Change in women's diet and body mass following intensive intervention for early-stage breast cancer. *J Am Diet Assoc* 2001; 101(4):421-31.
 50. Henderson VP, Clemow L, Massion AO, Hurley TG, Druker S, Hebert JR. The effects of mindfulness-based stress reduction on psychosocial outcomes and quality of life in early-stage breast cancer patients: a randomized trial. *Breast Cancer Res Treat* 2011.
 51. Koszycki D, Benger M, Shlik J, Bradwejn J. Randomized trial of a meditation-based stress reduction program and cognitive behavior therapy in generalized social anxiety disorder. *Behav Res Ther* 2007; 45(10):2518-26.
 52. Kuyken W, Byford S, Taylor RS *et al.* Mindfulness-based cognitive therapy to prevent relapse in recurrent depression. *J Consult Clin Psychol* 2008; 76(6):966-78.
 53. Lee SH, Ahn SC, Lee YJ, Choi TK, Yook KH, Suh SY. Effectiveness of a meditation-based stress management program as an adjunct to pharmacotherapy in patients with anxiety disorder. *J Psychosom Res* 2007; 62(2):189-95.
 54. Moritz S, Quan H, Rickhi B *et al.* A home study-based spirituality education program decreases emotional distress and increases quality of life--a randomized, controlled trial. *Altern Ther Health Med* 2006; 12(6):26-35.
 55. Morone NE, Rollman BL, Moore CG, Li Q, Weiner DK. A mind-body program for older adults with chronic low back pain: results of a pilot study. *Pain Med* 2009; 10(8):1395-407.
 56. Mularski RA, Munjas BA, Lorenz KA *et al.* Randomized controlled trial of mindfulness-based therapy for dyspnea in chronic obstructive lung disease. *J Altern Complement Med* 2009; 15(10):1083-90.
 57. Oken BS, Fonareva I, Haas M *et al.* Pilot controlled trial of mindfulness meditation and education for dementia caregivers. *J Altern Complement Med* 2010; 16(10):1031-8.
 58. Philippot P, Nef F, Clauw L, Romree M, Segal Z. A Randomized Controlled Trial of Mindfulness-Based Cognitive Therapy for Treating Tinnitus. *Clin Psychol Psychother* 2011.
 59. Piet J, Hougaard E, Hecksher MS, Rosenberg NK. A randomized pilot study of mindfulness-based cognitive therapy and group cognitive-behavioral therapy for young adults with social phobia. *Scand J Psychol* 2010; 51(5):403-10.
 60. Pipe TB, Bortz JJ, Dueck A, Pendergast D, Buchda V, Summers J. Nurse leader mindfulness meditation program for stress management: a randomized controlled trial. *J Nurs Adm* 2009; 39(3):130-7.
 61. Plews-Ogan M, Owens JE, Goodman M, Wolfe P, Schorling J. A pilot study evaluating mindfulness-based stress reduction and massage for the management of chronic pain. *J Gen Intern Med* 2005; 20(12):1136-8.
 62. Schmidt S, Grossman P, Schwarzer B, Jena S, Naumann J, Walach H. Treating fibromyalgia with mindfulness-based stress reduction: results from a 3-armed randomized controlled trial. *Pain*

- 2011; 152(2):361-9.
63. Segal ZV, Bieling P, Young T *et al.* Antidepressant monotherapy vs sequential pharmacotherapy and mindfulness-based cognitive therapy, or placebo, for relapse prophylaxis in recurrent depression. *Arch Gen Psychiatry* 2010; 67(12):1256-64.
 64. Wong SY, Chan FW, Wong RL *et al.* Comparing the Effectiveness of Mindfulness-based Stress Reduction and Multidisciplinary Intervention Programs for Chronic Pain: A Randomized Comparative Trial. *Clin J Pain* 2011; 27(8):724-34.
 65. Alexander CN, Langer EJ, Newman RI, Chandler HM, Davies JL. Transcendental meditation, mindfulness, and longevity: an experimental study with the elderly. *J Pers Soc Psychol* 1989; 57(6):950-64.
 66. Bormann JE, Gifford AL, Shively M *et al.* Effects of spiritual mantram repetition on HIV outcomes: a randomized controlled trial. *J Behav Med* 2006; 29(4):359-76.
 67. Castillo-Richmond A, Schneider RH, Alexander CN *et al.* Effects of stress reduction on carotid atherosclerosis in hypertensive African Americans. *Stroke* 2000; 31(3):568-73.
 68. Elder C, Aickin M, Bauer V, Cairns J, Vuckovic N. Randomized trial of a whole-system ayurvedic protocol for type 2 diabetes. *Altern Ther Health Med* 2006; 12(5):24-30.
 69. Jayadevappa R, Johnson JC, Bloom BS *et al.* Effectiveness of transcendental meditation on functional capacity and quality of life of African Americans with congestive heart failure: a randomized control study *Ethn Dis.* 2007 Summer;17(3):595. *Ethnicity & Disease* 2007; 17(1):72-7.
 70. Lehrer PM. Progressive relaxation and meditation: A study of psychophysiological and therapeutic differences between two techniques. *Behav Res Ther* 1983; 21(6):651-62.
 71. Murphy TJ, Pagano RR, Marlatt GA. Lifestyle modification with heavy alcohol drinkers: effects of aerobic exercise and meditation. *Addict Behav* 1986; 11(2):175-86.
 72. Paul-Labrador M, Polk D, Dwyer JH *et al.* Effects of a randomized controlled trial of transcendental meditation on components of the metabolic syndrome in subjects with coronary heart disease. *Arch Intern Med* 2006; 166(11):1218-24.
 73. Sheppard II WD, Staggers Jr. FJ, John L. The effects of a stress management program in a high security government agency. 1997; 10(4):341-50.
 74. Smith JC. Psychotherapeutic effects of transcendental meditation with controls for expectation of relief and daily sitting. *J Consult Clin Psychol* 1976; 44(4):630-7.
 75. Taub E, Steiner SS, Weingarten E, Walton KG. Effectiveness of broad spectrum approaches to relapse prevention in severe alcoholism: A long-term, randomized, controlled trial of Transcendental Meditation, EMG biofeedback and electronic neurotherapy. *Alcoholism Treatment Quarterly* 1994; 11(1-2):187-220.
 76. Easwaran, E. (2001). *The mantram handbook*. 4th ed. Nilgiri press, Tomales, CA
 77. Krisanaparakornkit T, Krisanaparakornkit W, Piyavhatkul N, Laopaiboon M. Meditation therapy for anxiety disorders. *Cochrane Database Syst Rev* 2006; (1):CD004998.
 78. Veehof MM, Oskam MJ, Schreurs KM, Bohlmeijer ET. Acceptance-based interventions for the treatment of chronic pain: a systematic review and meta-analysis. *Pain* 2011; 152(3):533-42.
 79. Treadwell JR, Singh S, Talati R, et al. A Framework for "Best Evidence" Approaches in Systematic Reviews. *Methods Research Report* (Prepared by the ECRI Institute Evidence-based Practice Center under Contract No. HHS A 290-2007-10063-I). Rockville, MD: Agency for Healthcare Research and Quality; June 2011. AHRQ Publication No. 11-EHC046-EF.