Original Investigation

Meditation Programs for Psychological Stress and Well-being
A Systematic Review and Meta-analysis

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IMPORTANCE Many people meditate to reduce psychological stress and stress-related health problems. To counsel people appropriately, clinicians need to know what the evidence says about the health benefits of meditation.

OBJECTIVE To determine the efficacy of meditation programs in improving stress-related outcomes (anxiety, depression, stress/distress, positive mood, mental health–related quality of life, attention, substance use, eating habits, sleep, pain, and weight) in diverse adult clinical populations.

EVIDENCE REVIEW We identified randomized clinical trials with active controls for placebo effects through November 2012 from MEDLINE, PsycINFO, EMBASE, PsycArticles, Scopus, CINAHL, AMED, the Cochrane Library, and hand searches. Two independent reviewers screened citations and extracted data. We graded the strength of evidence using 4 domains (risk of bias, precision, directness, and consistency) and determined the magnitude and direction of effect by calculating the relative difference between groups in change from baseline. When possible, we conducted meta-analyses using standardized mean differences to obtain aggregate estimates of effect size with 95% confidence intervals.

FINDINGS After reviewing 18 753 citations, we included 47 trials with 3515 participants. Mindfulness meditation programs had moderate evidence of improved anxiety (effect size, 0.38 [95% CI, 0.12-0.64] at 8 weeks and 0.22 [0.02-0.43] at 3-6 months), depression (0.30 [0.00-0.59] at 8 weeks and 0.23 [0.05-0.42] at 3-6 months), and pain (0.33 [0.03- 0.62]) and low evidence of improved stress/distress and mental health–related quality of life. We found low evidence of no effect or insufficient evidence of any effect of meditation programs on positive mood, attention, substance use, eating habits, sleep, and weight. We found no evidence that meditation programs were better than any active treatment (ie, drugs, exercise, and other behavioral therapies).

CONCLUSIONS AND RELEVANCE Clinicians should be aware that meditation programs can result in small to moderate reductions of multiple negative dimensions of psychological stress. Thus, clinicians should be prepared to talk with their patients about the role that a meditation program could have in addressing psychological stress. Stronger study designs are needed to determine the effects of meditation programs in improving the positive dimensions of mental health and stress-related behavior.

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Many people use meditation to treat stress and stress-related conditions and to promote general health.[1,2] To counsel patients appropriately, clinicians need to know more about meditation programs and how they can affect health outcomes. Meditation training programs vary in several ways, including the type of mental activity promoted, the amount of training recommended, the use and qualifications of an instructor, and the degree of emphasis on religion or spirituality. Some meditative techniques are integrated into a broader alternative approach that includes dietary and/or movement therapies (eg, ayurveda or yoga).

Meditative techniques are categorized as emphasizing mindfulness, concentration, and automatic self-transcendence. Popular techniques, such as transcendental meditation, emphasize the use of a mantra in such a way that it transcends one to an effortless state where focused attention is absent.[3-5] Other popular techniques, such as mindfulness-based stress reduction, emphasize training in present-focused awareness or mindfulness. Uncertainty remains about what these distinctions mean and the extent to which these distinctions actually influence psychosocial stress outcomes.[5,6]

Reviews to date report a small to moderate effect of mindfulness and mantra meditation techniques in reducing emotional symptoms (eg, anxiety, depression, and stress) and improving physical symptoms (eg, pain).[7-26] These reviews have largely included uncontrolled and controlled studies, and many of the controlled studies did not adequately control for placebo effects (eg, waiting list– or usual care–controlled studies). Observational studies have a high risk of bias owing 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 report that they benefited from one) and use of outcome measures that can be easily biased by participants' beliefs in the benefits of meditation. Clinicians need to know whether meditation training has beneficial effects beyond self-selection biases and the nonspecific effects of time, attention, and expectations for improvement.[27,28]

An informative analogy is the use of placebos in pharmaceutical trials. A placebo is typically designed to match nonspecific aspects of the "active" intervention and thereby elicit the same expectations of benefit on the part of the provider and patient in the absence of the active ingredient. Office visits and patient-provider interactions, all of which influence expectations for outcome, are particularly important to control when the evaluation of outcome relies on patient reporting. In the situation when double-blinding has not been feasible, the challenge to execute studies that are not biased by these nonspecific factors is more pressing.[28] To develop evidence-based guidance on the use of meditation programs, we need to examine the specific effects of meditation in randomized clinical trials (RCTs) in which the nonspecific aspects of the intervention are controlled.

The objective of this systematic review is to evaluate the effects of meditation programs on negative affect (eg, anxiety, stress), positive affect (eg, well-being), the mental component of health-related quality of life, attention, health-related behaviors affected by stress (eg, substance use, sleep, eating habits), pain, and weight among persons with a clinical condition. We include only RCTs that used 1 or more control groups in which the amount of time and attention provided by the control intervention was comparable to that of the meditation program.

Methods

Study Selection

We searched the following databases for primary studies: MEDLINE, PsycINFO, EMBASE, PsycArticles, Scopus, CINAHL, AMED, and the Cochrane Library through June 2013. We developed a MEDLINE search strategy using PubMed medical subject heading terms and the 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 to identify articles missed in the database searches. We did not impose any limits based on language or date of publication. The protocol for this systematic review is publicly available.[29]

Two trained investigators independently screened titles and abstracts, excluding those that both investigators agreed met at least 1 of the exclusion criteria (**Table 1**). For those studies included after the first review, a second dual independent review of the full-text article occurred, and differences regarding article inclusion were resolved through consensus.

We included RCTs in which the control group was matched in time and attention to the intervention group. We also required that studies include participants with a clinical condition. We defined a clinical condition broadly to include mental health/psychiatric conditions (eg, anxiety or stress) and physical conditions (eg, lower back pain, heart disease, or advanced age). In addition, because stress is of particular interest in meditation studies, we also included trials that studied stressed populations, although they may not have had a defined medical or psychiatric diagnosis.

Data Abstraction and Data Management

We used systemic review software (DistillerSR, 2010; Evidence Partners) to manage the screening process. For each meditation program, we extracted information on measures of intervention fidelity, including dose, training, and receipt of intervention. We recorded the duration and maximal hours of structured training in meditation, the amount of home practice recommended, description of instructor qualifications, and description of participant adherence, if any. Because numerous scales measured negative or positive affect, we chose scales that were common to the other trials and the most clinically relevant to make comparisons more meaningful.

To display outcome data, we calculated the relative difference in change scores (ie, the change from baseline in the treatment group minus the change from baseline in the control group, divided by the baseline score in the treatment group). We used the relative difference in change scores to estimate the direction and approximate magnitude of effect for all outcomes. We were unable to calculate a relative differ-

Table 1. Study Inclusion and Exclusion Criteria

	Inclusion Criteria	Exclusion Criteria[a]
Population and condition of interest	Adult populations (≥18 y); clinical (medical or psychiatric) diagnosis, defined as any condition (eg, high blood pressure, anxiety) including a stressor	Studies of children (type and nature of meditation received may be significantly different from that of adults); studies of otherwise healthy individuals
Interventions	Structured meditation programs (any systematic or protocol meditation programs that follow predetermined curricula) consisting of, at a minimum, ≥4 h of training with instructions to practice outside the training session, including mindfulness-based programs (ie, MBSR, MBCT, vipassana, Zen, and other mindfulness meditation), mantra-based programs (ie, TM, other mantra meditation), and other meditation programs	Meditation programs in which the meditation is not the foundation and most of the intervention, including DBT; ACT; any of the movement-based meditations, such as yoga (eg, 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	Active control is 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 with the intervention; nonspecific active control only matches time and attention and is not a known therapy); specific active control compares the intervention with another known therapy, such as progressive muscle relaxation	Studies that only evaluate a waiting list or usual care control or do not include a comparison group
Study design	RCTs with an active control	Nonrandomized designs, such as observational studies
Timing and setting	Longitudinal studies that occur in general and clinical settings	None

Abbreviations: ACT, acceptance and commitment therapy; DBT, dialectical behavioral therapy; MBCT, mindfulness-based cognitive therapy; MBSR, mindfulness-based stress reduction; RCTs, randomized clinical trials; TM, transcendental meditation.

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

ence in change score for 6 outcomes owing to incompletely reported data for statistically insignificant findings. We considered a 5% relative difference in change score to be potentially clinically significant because these studies examined short-term interventions and relatively low doses of meditation.

For the purpose of generating an aggregate quantitative estimate of the effect of an intervention and the associated 95% confidence interval, we performed random-effects meta-analyses using standardized mean differences (effect size [ES]; Cohen *d*). We also used these analyses to assess the precision of individual studies, which we factored into the overall strength of evidence. For each outcome, ES estimates are displayed according to the type of control group and the duration of follow-up. Trials did not give enough information to conduct a meta-analysis on 16 outcomes. We display the relative difference in change scores along with the ES estimates from the meta-analysis so that readers can see the full extent of the available data (**Figure 1** and Supplement [eFigures 1 to 34]).

We classified the type of control group as a nonspecific active or specific active control (Table 1). The nonspecific active comparison conditions (eg, education or attention control) control for the nonspecific effects of time, attention, and expectation. Comparisons against these controls allow for assessments of the specific effectiveness of the meditation program beyond the nonspecific effects of time, attention, and expectation. This comparison is similar to a comparison against a placebo pill in a drug trial. Specific active controls are therapies (eg, exercise or progressive muscle relaxation) known or expected to change clinical outcomes. Comparisons against these controls allow for assessments of comparative effectiveness similar to those of drug trials that compare one drug against another known drug. Because these study designs are expected to yield different conclusions (efficacy vs comparative effectiveness), we separated them in our analyses.

Strength of the Body of Evidence

We assessed the quality of the trials independently and in duplicate based on the recommendations in the *Methods Guide for Conducting Comparative Effectiveness Reviews*.[30] We supplemented these tools with additional assessment questions based on the Cochrane Collaboration's risk-of-bias tool.[31,32] Two reviewers graded the strength of evidence for each outcome using the grading scheme recommended by the Methods Guide for Conducting Comparative Effectiveness Reviews.[33] This grading was followed by a discussion to review and achieve consensus on the assigned grades. In assigning evidence grades, we considered the following 4 domains: risk of bias, directness, consistency, and precision. We classified evidence into the following 4 basic categories: (1) high grade (indicating high confidence that the evidence reflects the true effect and that 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 that 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 that 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 that evidence is unavailable or inadequate to draw a conclusion).

Results

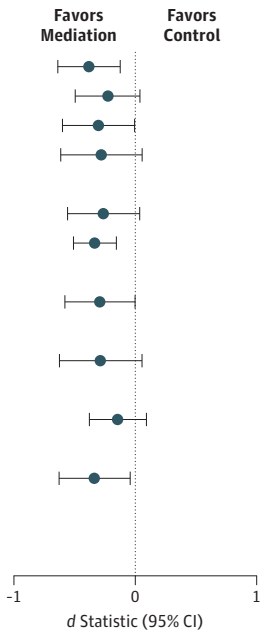
We screened 18 753 unique citations (**Figure 2**) and 1651 full-text articles. Forty seven trials met our inclusion criteria.[34-80]

Most trials were short-term but ranged from 3 weeks to 5.4 years in duration (**Table 2**). Not all trials reported the amount

Figure 1. Strength of Evidence on the Trial Outcomes

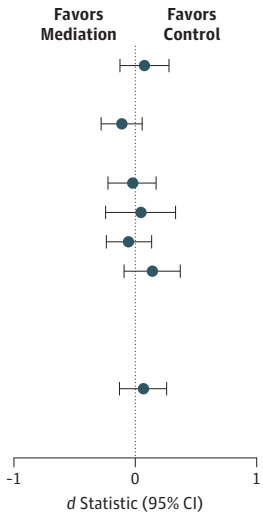
A Comparisons of Meditation Programs With Nonspecific Active Controls (Efficacy)

Outcome	Meditation Program	Clinical Population	No. of Trials, Total (PO); PA (MA)	Direction (Magnitude) of Effect	Strength of Evidence
Anxiety	Mindfulness	Various (n = 647)	8 (3); 7 (7)	↑(0% to +44%)	Moderate for improvement
	Mantra	Various (n = 237)	3 (2); 3 (3)	Ø (-3% to +6%)	Low for no effect
Depression	Mindfulness	Various (n = 806)	10 (4); 9 (8)	↑(-5% to +52%)	Moderate for improvement
	Mantra	Various (n = 440)	5 (1); 5 (3)	↑↓(-19% to +46%)	Insufficient
Stress/Distress	Mindfulness	Various (n = 735)[a]	9 (4); 8 (7)	↑(+1% to +21%)	Low for improvement
	Mantra	Select (n = 239)	4 (2); 4 (2)	Ø (-6% to +1%)	Low for no effect
Negative Affect	Mindfulness	Various (n = 1140)[b]	14 (5); 12 (11)	↑(-1% to +44%)	Low for improvement
	Mantra	Various (n = 438)[c]	5 (2); 5 (0)	↑↓(-3% to +46%)	Insufficient
Positive Affect	Mindfulness	Various (n = 293)	4 (0); 4 (4)	↑(+1% to +55%)	Insufficient
	TM (mantra)	CHF (n = 23)	1 (0); 1 (0)	Ø (+2%)	Insufficient
Quality of Life	Mindfulness	Various (n = 346)	4 (2); 4 (3)	↑(+5% to +28%)	Low for improvement
Attention	Mindfulness	Caregivers (n = 21)	1 (0); 1 (0)	↑(+15% to +81%)	Insufficient
Sleep	Mindfulness	Various (n = 578)	6 (2); 4 (4)	↑↓(-3% to +24%)	Insufficient
Substance Use	TM	CAD (n = 201)	1 (0); 0 (0)	Ø	Insufficient
Pain	Mindfulness	Select (n = 341)	4 (2); 4 (4)	↑(+5% to +31%)	Moderate for improvement
	TM (mantra)	CHF (n = 23)	1 (0); 1 (0)	Ø (-2%)	Low for no effect
Weight	TM (mantra)	Select (n = 297)	3 (0); 2 (0)	Ø (-1% to +2%)	Low for no effect



B Comparisons of Meditation Programs With Specific Active Controls (Comparative Effectiveness)

Outcome	Meditation Program	Clinical Population	No. of Trials, Total (PO); PA (MA)	Direction (Magnitude) of Effect	Strength of Evidence
Anxiety	Mindfulness	Various (n = 691)	11 (6); 11 (10)	↑↓(-39% to +8%)	Insufficient
	CSM (mantra)	Anxiety (n = 42)	1 (1); 1 (0)	↓(-6%)	Insufficient
Depression	Mindfulness	Various (n = 986)	13 (6); 13 (11)	↑↓(-32% to +23%)	Insufficient
	CSM (mantra)	Anxiety (n = 42)	1 (1); 1 (0)	↓(-28%)	Insufficient
Stress/Distress	Mindfulness	Various (n = 523)	7 (5); 7 (6)	↑↓(-24% to +18%)	Insufficient
Positive Affect	Mindfulness	Various (n = 297)	4 (2); 4 (4)	↑↓(-45% to +10%)	Insufficient
Quality of Life	Mindfulness	Various (n = 472)	6 (1); 6 (5)	↑↓(-23% to +9%)	Insufficient
Sleep	Mindfulness	Various (n = 311)	3 (1); 3 (2)	↑↓(-2% to +15%)	Insufficient
Eating	Mindfulness	Select (n = 158)	2 (1); 2 (0)	↓(-6% to -15%)	Insufficient
Smoking/Alcohol	Mindfulness	Substance abuse (n = 95)	2 (2); 1 (0)	↑(Ø to +21%)	Insufficient
Alcohol only	Mantra	Alcoholic (n = 145)	2 (2); 2 (0)	Ø (-5% to -36%)	Low for no effect
Pain	Mindfulness	Select (n = 410)	4 (2); 4 (4)	Ø (-1% to -32%)	Low for no effect
Weight	Mindfulness	Select (n = 151)	2 (2); 2 (0)	Ø (-2% to +1%)	Low for no effect



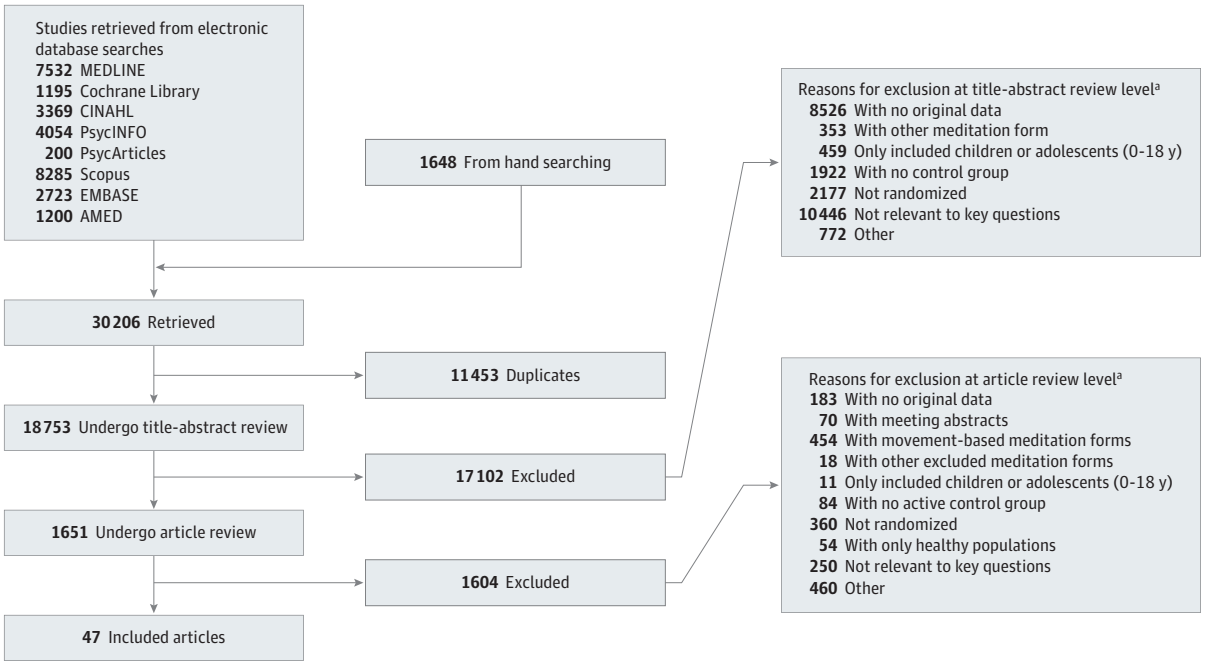
Summary across measurement domains of comparisons of meditation programs with nonspecific active controls (efficacy analysis) (A) and specific active controls (comparative effectiveness analysis) (B). CAD indicates coronary artery disease; CHF, congestive heart failure; CSM, clinically standardized meditation (a mantra meditation program); MA, meta-analysis; PA, primary analysis; PO, number of trials in which this was a primary outcome for the trial; and TM, transcendental meditation (a mantra meditation program). Direction is based on the relative difference in change analysis. ↑ Indicates the meditation group improved relative to the control group (with a relative difference generally ≥5% across trials); ↓, the meditation group worsened relative to the control group (with a relative difference generally ±5% across trials); Ø, a null effect (with a relative difference generally <5% across trials); and ↑↓, inconsistent findings (some trials reported improvement with meditation [relative to control], whereas others showed no improvement or improvement in the control group [relative to meditation]). Magnitude is based on the relative difference in the change score, a relative percent difference, using the baseline mean in the meditation group as the denominator. For example, if the meditation group improves from 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} × 100 = 40%. The interpretation 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. The meta-analysis figure (far right) shows the Cohen *d* statistic with the 95% CI.

[a]Summary effect size is not shown owing to concern about publication bias for this outcome.

[b]Negative affect combines the outcomes of anxiety, depression, and stress/distress and is thus duplicative of those outcomes.

[c]We did not perform an MA on this outcome because it would duplicate the anxiety MA for mantra. Anxiety and depression are indirect measures of negative affect and therefore resulted in a lower strength of evidence than that for the outcome of mantra on anxiety.

Figure 2. Summary of the Literature Search



[a]Total exceeds the number in the exclusion box because reviewers were allowed to mark more than 1 reason for exclusion.

of training or home practice recommended. Mindfulness-based stress reduction programs typically provided 20 to 27.5 hours of training during 8 weeks. The other mindfulness meditation trials provided about half this amount. Transcendental meditation trials were estimated to provide 16 to 39 hours in 3 to 12 months, whereas other mantra meditation programs provided about half this amount. Only 5 of the trials reported the trainers' actual meditation experience (ranging from 4 months to 25 years), and 6 reported the trainers' actual teaching experience (ranging from 0-15.7 years). Fifteen trials studied psychiatric populations, including those with anxiety, depression, stress, chronic worry, and insomnia. Five trials studied smokers and alcoholics, 5 studied populations with chronic pain, and 16 studied populations with diverse medical problems, including those with heart disease, lung disease, breast cancer, diabetes mellitus, hypertension, and human immunodeficiency virus infection.

The strength of evidence concerning the outcomes is shown in Figure 1. We found it difficult to draw comparative effectiveness conclusions owing to the large heterogeneity of type and strength of the many comparators. Therefore, we present our results first for all the comparisons with nonspecific active controls (efficacy) and then for those with specific active controls (comparative effectiveness).

The direction and magnitude of effect is derived from the relative difference between groups in the change score. In our efficacy analysis (Figure 1A), we found low evidence of no effect or insufficient evidence that mantra meditation programs had an effect on any of the psychological stress and well-being outcomes we examined. Mindfulness meditation programs had moderate evidence of improved anxiety (ES, 0.38 [95% CI, 0.12- 0.64] at 8 weeks and 0.22 [0.02-0.43] at 3-6 months), depression (0.30 [0.00-0.59] at 8 weeks and 0.23 [0.05-0.42] at 3-6 months), and pain (0.33 [0.03-0.62]) and low evidence of improved stress/distress and mental health-related quality of life. We found low evidence of no effect or insufficient evidence of an effect of meditation programs on positive mood, attention, sleep, and weight. We also found insufficient evidence that meditation programs had an effect on health-related behaviors affected by stress, including substance use and sleep.

In our comparative effectiveness analyses (Figure 1B), we found low evidence of no effect or insufficient evidence that any of the meditation programs were more effective than exercise, progressive muscle relaxation, cognitive-behavioral group therapy, or other specific comparators in changing any outcomes of interest. Few trials reported on potential harms of meditation programs. Of the 9 trials reporting this information, none reported any harms of the intervention.

We could not conduct any quantitative tests (eg, funnel plots) for publication bias because few studies were available for most outcomes, and many were excluded from the meta-analysis owing to missing data. We reviewed the clinicaltrials.gov registration database to identify trials completed 3 or more years ago that prespecified our outcomes of interest and did not publish at all or did not publish all prespecified outcomes. We found 5 trials that appeared to have been completed before January 1, 2010, that did not publish all the outcomes they had prespecified and 9 trials for which we could not find an associated publication. Because only 6 outcomes were excluded from the analyses of the relative difference in change scores between groups, whereas 16 outcomes were

Table 2. Study Descriptions

Source	Meditation Program	Type of Active Control	Study Quality	No. of Hours		Program Duration/Study Duration	Outcomes (End of Treatment/End of Study)	Population	No. of Patients
				Program Training	Homework				
Henderson et al,[68] 2012	MBSR	NSAC	Fair	25	UC	8 wk/24 mo	Anxiety (NS/NS), depression (+/↑), positive affect (+/Ø)	Breast cancer	100
Gaylord et al,[43] 2011	MBSR	NSAC	Fair	23[a]	Y-NS	8 wk/3 mo	Anxiety (Ø/+), depression (Ø/Ø), stress/distress (Ø/+), pain (+/+)	IBS	75
Schmidt et al,[64] 2011	MBSR	NSAC	Fair	27	42	8 wk/4 mo	Anxiety (Ø/+), depression (Ø/↑), sleep (Ø/Ø), pain (↑/Ø)	Fibromyalgia	109
Gross et al,[44] 2010	MBSR	NSAC	Fair	27	Y-NS	8 wk/6 mo	Anxiety (↑/↑), depression (↑/↑), positive affect (Ø/↑), mental QOL (Ø/Ø), sleep (↑/+), pain (Ø/Ø)	Organ transplant	137
Morone et al,[55] 2009	MBSR	NSAC	Good	12	42	8 wk/6 mo	Pain (↑/Ø)	Low back pain	35
Whitebird et al,[72] 2013	MBSR	NSAC	Fair	25	26.7	8 wk/6 mo	Anxiety (Ø/Ø), depression (+/↑), stress/distress (+/+), mental QOL (+/+)	Dementia caregivers	78
SeyedAlinaghi et al,[67] 2012	MBSR	NSAC	Poor	25[a]	Y-NS	8 wk/14 mo	Stress/distress (↑/↓)	HIV	171
Pbert et al,[60] 2012	MBSR	NSAC	Good	26	24	8 wk/10 mo	Stress/distress (↑/+), mental QOL (↑/+)	Asthma	82
Oken et al,[58] 2010	MM	NSAC	Fair	9	Y-NS	7 wk/NA	Depression (↑/NA), stress/distress (↑ /NA), sleep (Ø/NA)	Dementia caregivers	19
Garland et al,[42] 2010	MM	NSAC	Fair	UC	17.5	10 wk/NA	Stress/distress (+/NA)	Alcoholism	37
Mularski et al,[56] 2009	MM	NSAC	Poor	8	Y-NS	8 wk/NA	Stress/distress (Ø /NA), mental QOL (↑/NA)	COPD	49
Lee et al,[50] 2007	MM	NSAC	Fair	8	Y-NS	8 wk/NA	Anxiety (+/NA), depression (↑/NA)	Anxiety	41
Malarkey et al,[52] 2013	MM	NSAC	Good	9	18.5	8 h/NA	Depression (NS/NA), stress/distress (NS /NA), sleep (NS/NA)	CRP level >3.0 mg/L	186
Chiesa et al,[39] 2012	MBCT	NSAC	Fair	16	UC	8 wk/NA	Anxiety (↑/NA), depression (+/NA), positive affect (+/NA)	Depression	18
Hoge et al,[78] 2013	MBSR	NSAC	Fair	20	18.7	8 wk/NA	Anxiety (+/NA), sleep (+/NA)	Anxiety	89
Nakamura et al,[79] 2013	MM	NSAC	Fair	6	UC	3 wk/3 mo	Depression (Ø/↑), stress/distress (↑/↑), positive affect (Ø/Ø), sleep (↑/↑)	Cancer and insomnia	38
Wong et al,[74] 2011	MBSR	Pain AC	Good	27	Y-NS	8 wk/6 mo	Anxiety (Ø/Ø), depression (Ø/Ø), mental QOL (Ø/Ø), pain (Ø/Ø)	Chronic pain	99
Gross et al,[45] 2011	MBSR	Drug	Fair	26	36	8 wk/5 mo	Anxiety (Ø/↑), depression (↓/↓), mental QOL (Ø/NA), sleep (↑/Ø)	Insomnia	27
Koszycki et al,[71] 2007	MBSR	CBGT	Poor	27.5	28	8 wk/NA	Anxiety (↓/NA), depression (Ø/NA)	Anxiety	53
Barrett et al,[34] 2012	MBSR	Exercise	Fair	20	42	8 wk/5 mo	Anxiety (Ø/Ø), stress/distress (Ø/Ø), positive affect (Ø/Ø), mental QOL (Ø/Ø), sleep (Ø/Ø)	Cold/URI in past year	98

(continued)

Table 2. Study Descriptions (continued)

Source	Meditation Program	Type of Active Control	Study Quality	No. of Hours		Program Duration/Study Duration	Outcomes (End of Treatment/End of Study)	Population	No. of Patients
				Program Training	Homework				
Jazaieri et al,[48] 2012	MBSR	Exercise	Poor	25	28.3	8 wk/5 mo	Anxiety (↑/Ø), depression (↑/↑), stress/distress (↑/NA), positive affect (↑/NA)	Social anxiety disorder	56
Moritz et al,[54] 2006	MBSR	Spirituality	Good	12[a]	Y-NS	8 wk/3 mo	Anxiety (−/NA), depression (↓/NA), stress/distress (−/↓), positive affect (−/NA), mental QOL (−/↓), pain (↓/NA)	Mood disturbance (POMS)	110
Plews-Ogan et al,[63] 2005	MBSR	Massage	Poor	20	Y-NS	8 wk/3 mo	Mental QOL (↓/↑), pain (↓/↓)	Chronic pain	23
Hebert et al,[46] 2001	MBSR	Nutrition education	Fair	45[a]	UC	15 wk/12 mo	Eating habits (Ø/Ø), weight (Ø/Ø)	Breast cancer	106
Philippot et al,[61] 2012	MBCT	Relaxation	Fair	13.5	Y-NS	6 wk/3 mo	Anxiety (↑/↑), depression (↑/Ø)	Tinnitus	25
Segal et al,[66] 2010	MBCT	Drug	Good	23[a]	Y-NS	8 wk/20 mo	Depression (NA/↑)	Depression	84
Kuyken et al,[49] 2008	MBCT	Drug	Good	24[a]	37.5	8 wk/15 mo	Depression (↓/NA), mental QOL (+/+)	Depression	123
Piet et al,[62] 2010	MBCT	CBGT	Fair	16	28	8 wk/NA	Anxiety (↓/NA), depression (↓/NA), stress/distress (↓/NA)	Social phobia	26
Delgado et al,[40] 2010	MM	PMR	Fair	10	Y-NS	5 wk/NA	Anxiety (Ø/NA), depression (↑/NA), stress/distress (Ø/NA), positive affect (Ø/NA)	Worriers	32
Wolever et al,[73] 2012	MM	Viniyoga	Fair	14	UC	12 wk/NA	Depression (↑/NA), stress/distress (Ø/NA), sleep (Ø/NA), pain (↓/NA)	Stressed employees	186
Miller et al,[53] 2012	MM	Smart Choices	Poor	25	Y-NS	12 wk/6 mo	Eating (↓/↓), weight (Ø/Ø)	Diabetes mellitus	52
Brewer et al,[37] 2011	MM	Lung Association FFS	Poor	12	Y-NS	4 wk/4 mo	Smoking (↑/+)	Smokers	71
Brewer et al,[36] 2009	MM	CBT	Poor	9	UC	9 wk/NA	Alcohol abuse (Ø/NA)	Alcoholism	118
Arch et al,[75] 2013	MM	CBT	Fair	18	29.2	10 wk/6 mo	Anxiety (Ø/↑), depression (↑/Ø)	Anxiety	105
Omidi et al,[80] 2013	MBCT	CBT	Poor	16	56	8 wk/NA	Anxiety (↓/NA), depression (↓/NA)	Depression	60
Ferraioli and Harris,[77] 2013	MM	SBPT	Poor	16	UC	8 wk/5 mo	Stress/distress (+/+)	Stressed parents	15
Paul-Labrador et al,[59] 2006	TM	NSAC	Good	39	Y-NS	16 wk/NA	Anxiety (Ø/NA), depression (↓/NA), stress/distress (↓/NA)	CAD	103
Jayadevappa et al,[47] 2007	TM	NSAC	Good	22.5[a]	90	12 wk/6 mo	Depression (↓/NA), stress/distress (Ø/Ø), positive affect (Ø/Ø), pain (Ø/↑)	CHF	23
Schneider et al,[65] 2012	TM	NSAC	Good	78[a]	1310	12 wk/5.4 y	Depression (NA/↑), weight (NA/NS)	CAD	201
Smith,[69] 1976	TM	NSAC	Poor	UC	87.5	4 wk/6 mo	Anxiety (NA/Ø)	Anxiety	41
Elder et al,[41] 2006	TM	NSAC	Fair	UC	90	UC	Weight (Ø/NA)	Diabetes mellitus	54
Castillo-Richmond et al,[38] 2000	TM	NSAC	Poor	UC	120.6	12 wk/NA	Weight (Ø/NA)	AA with hypertension	60
Chhatre et al,[76] 2013	TM	NSAC	Fair	24	112	12 wk/6 mo	Depression (NA/↑), stress/distress (NA/↑)	HIV	20

(continued)

Table 2. Study Descriptions (continued)

Source	Meditation Program	Type of Active Control	Study Quality	No. of Hours		Program Duration/Study Duration	Outcomes (End of Treatment/End of Study)	Population	No. of Patients
				Program Training	Homework				
Bormann et al,[35] 2006	Mantra	NSAC	Fair	7.5	Y-NS	10 wk/6 mo	Anxiety (↑/Ø), depression (Ø/↓), stress/distress (Ø/Ø)	HIV	93
Taub et al,[70] 1994	TM	Biofeedback	Fair	19	UC	4 wk/NA	Alcohol (Ø/NA)	Alcoholism	118
Lehrer et al,[51] 1983	CSM	PMR	Fair	7.5	Y-NS	5 wk/6 mo	Anxiety (Ø/NA), depression (↓/↓)	Anxiety	42
Murphy et al,[57] 1986	CSM	Running	Poor	8	37.5	8 wk/NA	Alcohol (−/NA)	Alcoholism	27

Abbreviations: AA, African American; AC, active control; CAD, coronary artery disease; CBGT, cognitive behavioral group therapy; CBT, cognitive behavioral therapy; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; CSM, clinically standardized meditation; FFS, Freedom From Smoking program; HIV, human immunodeficiency virus; IBS, irritable bowel syndrome; MBCT, mindfulness-based cognitive therapy; MBSR, mindfulness-based stress reduction; mental QOL, mental component of health-related quality of life; MM, mindfulness meditation; NA, not available; NS, not significant; NSAC, nonspecific active control; PMR, progressive muscle relaxation; POMS, Profile of Mood States; SBPT, skills-based parent training program; TM, transcendental meditation; UC, unclear; URI, upper respiratory tract infection; Y-NS, homework was prescribed but amount not specified; Ø, no effect (within ±5%); +improved and statistically significant; ↑favors meditation (>5% but nonsignificant); ↓favors control (>5% but nonsignificant); −, worsened and statistically significant.

SI conversion factor: To convert CRP to nanomoles per liter, multiply by 9.524.

[a] Indicates estimated.

excluded from the meta-analyses, our findings from the primary analyses are less likely than the meta-analyses to be affected by publication bias.

Discussion

Our review indicates that meditation programs can reduce the negative dimensions of psychological stress. Mindfulness meditation programs, in particular, show small improvements in anxiety, depression, and pain with moderate evidence and small improvements in stress/distress and the mental health component of health-related quality of life with low evidence when compared with nonspecific active controls. Mantra meditation programs did not improve any of the outcomes examined, but the strength of this evidence varied from low to insufficient. Although meditation programs generally seek to improve the positive dimensions of health, the evidence from a small number of studies did not show any effects on positive affect or well-being for any meditation program. We found no evidence of any harms of meditation programs, although few trials reported on harms. One strength of our review is the focus on RCTs with active controls, which should give clinicians greater confidence that the reported benefits are not the result of nonspecific effects (eg, attention and expectations) that are seen in trials using a waiting list or usual-care control condition.

Anxiety, depression, and stress/distress are different components of negative affect. When we combined each component of negative affect, we saw a small and consistent signal that any domain of negative affect is improved in mindfulness programs when compared with a nonspecific active control. The ESs were small but significant for some of these individual outcomes and were seen across a broad range of clinical conditions (Table 2). During the course of 2 to 6 months, the mindfulness meditation program ES estimates ranged from 0.22 to 0.38 for anxiety symptoms and 0.23 to 0.30 for depressive symptoms. These small effects are comparable with what would be expected from the use of an antidepressant in a primary care population but without the associated toxicities. In a study using patient-level meta-analysis, Fournier et al[81] found that for patients with mild to moderate depressive symptoms, antidepressants had an ES of 0.11 (95% CI, −0.18 to 0.41), whereas for those with severe depression, antidepressants had an ES of 0.17 (−0.08 to 0.43) compared with placebo.

Among the 9 RCTs* evaluating the effect on pain, we found moderate evidence that mindfulness-based stress reduction reduces pain severity to a small degree when compared with a nonspecific active control, yielding an ES of 0.33 from the meta-analysis. This effect is variable across painful conditions and is based on the results of 4 trials, of which 2 were conducted in patients with musculoskeletal pain,[55,64] 1 trial in patients with irritable bowel syndrome,[43] and 1 trial in a population without pain.[44] Visceral pain had a large and statistically significant relative 30% improvement in pain severity, whereas musculoskeletal pain showed 5% to 8% improvements that were considered nonsignificant.

Overall, the evidence was insufficient to indicate that meditation programs alter health-related behaviors affected by stress, and low-grade evidence suggested that meditation programs do not influence weight. Although uncontrolled studies have usually found a benefit of meditation, very few controlled studies have found a similar benefit for the effects of meditation programs on health-related behaviors affected by stress.[17-19]

In the 20 RCTs examining comparative effectiveness,† mindfulness and mantra programs did not show significant effects when the comparator was a known treatment or therapy. A lack of statistically significant superiority compared with a specific active control (eg, exercise) only addresses the question of equivalency or noninferiority if the trial is suitably pow-

*References 43, 44, 47, 54, 55, 63, 64, 73, 74

†References 34, 36, 37, 40, 45, 46, 48, 49, 51, 53, 54, 57, 61-63, 66, 70, 71, 73-75, 77, 80

ered to detect any difference. Sample sizes in the comparative effectiveness trials were small (mean size of 37 per group), and none appeared adequately powered to assess noninferiority or equivalence.

A number of observations provide context to our conclusions. First, very few mantra meditation programs met our inclusion criteria. This lack significantly limited our ability to draw inferences about the effects of mantra meditation programs on psychological stress–related outcomes, which did not change when we evaluated transcendental meditation separately from other mantra training.

Second, differences may exist between trials for which the outcomes are a primary vs a secondary focus, although we did not find any evidence of this. The samples included in these trials resembled a general primary care population, and there may not be room to measure an effect if symptom levels of the outcomes are low to start with (ie, a floor effect). This limitation may explain the null results for mantra meditation programs because 3 transcendental meditation trials[47,59,65] enrolled patients with cardiac disease, whereas only 1 enrolled patients with anxiety.[69]

Third, the lack of effect on stress-related outcomes may relate to the way the research community conceptualizes meditation programs, the challenges in acquiring such skills or meditative states, and the limited duration of RCTs. Historically, meditation was not conceptualized as an expedient therapy for health problems.[3,6,82] Meditation was a skill or state one learned and practiced over time to increase one's awareness and through this awareness to gain insight and understanding into the various subtleties of one's existence. Training the mind in awareness, in nonjudgmental states, or in the ability to become completely free of thoughts or other activity are daunting accomplishments. The interest in meditation that has grown during the past 30 years in Western cultures comes from Eastern traditions that emphasize lifelong growth. The translation of these traditions into research studies remains challenging. Long-term trials may be optimal to examine the effect of meditation on many health outcomes, such as those trials that have evaluated mortality.[65] However, many of the studies included in this review were short term (eg, 2.5 h/wk for 8 weeks), and the participants likely did not achieve a level of expertise needed to improve outcomes that depend on mastery of mental and emotional processes.

Finally, none of our conclusions yielded a high strength-of-evidence grade for a positive or null effect. Thus, further studies in primary care and disease-specific populations are indicated to address uncertainties caused by inconsistencies in the body of evidence, deficiencies in power, and risk of bias.

Limitations

Some of the trials we reviewed were implemented before modern standards for clinical trials were established. Thus, many did not report key design characteristics to enable an accurate assessment of the risk of bias. Most trials were not registered, did not standardize training using trainers who met specified criteria, did not specify primary and secondary outcomes a priori, did not power the trial based on the primary outcomes, did not use CONSORT recommendations for reporting results, or did not operationalize and measure the practice of meditation by study participants.[83]

We could not draw definitive conclusions about effect modifiers, such as dose and duration of training, because of the limited details provided in the publications of the trials. Despite our focus on RCTs using active controls, we were unable to detect a specific effect of meditation on most outcomes, with the majority of our evidence grades being insufficient or low. These evidence grades were mostly driven by 2 important evaluation criteria: the quality of the trial and inconsistencies in the body of evidence. Trials primarily had the following 4 biases: lack of blinding of outcome assessment, high attrition, lack of allocation concealment, and lack of intention-to-treat analysis. The reasons for inconsistencies in the body of evidence may have included the differences in the particular clinical conditions and the type of control groups the studies used. Another possibility is that the programs had no real effect on many of the outcomes that had inconsistent findings.

Clinical Implications and Future Directions

Despite the limitations of the literature, the evidence suggests that mindfulness meditation programs could help reduce anxiety, depression, and pain in some clinical populations. Thus, clinicians should be prepared to talk with their patients about the role that a meditation program could have in addressing psychological stress.

Future research in meditation would benefit by addressing the remaining methodological and conceptual issues. All forms of meditation, including mindfulness and mantra, imply that more time spent meditating will yield larger effects. Most forms, but not all, present meditation as a skill that requires expert instruction and time dedicated to practice. Thus, more training with an expert and practice in daily life should lead to greater competency in the skill or practice, and greater competency or practice would presumably lead to better outcomes. However, when compared with other skills that require training, such as writing, the amount of training or the dose afforded in the trials was quite small, and generally the training was offered during a fairly short period. These 3 components—trainer expertise, amount of practice, and skill—require further investigation. We were unable to examine the extent to which trainer expertise influences clinical outcome because teacher qualifications were not reported in detail in most trials. Trials need to document the amount of training instructors provide and patients receive and the amount of home practice patients complete. These measures will allow future investigators to examine questions about dosing related to outcome.

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Invited Commentary

Moving Toward Evidence-Based Complementary Care

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Therapies that lie outside the spectrum of traditional, science-based clinical medicine and surgery are often labeled as *complementary* or *alternative*. These therapies range from herbal remedies and dietary supplements to meditation and acupuncture, and they derive from Eastern and Western traditions. Use is widespread and often promoted by commercial interests and practitioners, with prevalence estimates exceeding 50%.[1] Their popularity derives in part from being available without prescription and the supposition that the label of *natural* makes them safe and preferable to pharmacologic and surgical treatments.[2] Despite widespread use, many complementary therapies still lack a rigorous evidence base.[3]

The relative scarcity of scientifically derived data on efficacy and safety stems from a number of factors, ranging from a lack of financial incentives for practitioners and suppliers (why study something that is already profitable and accepted by patients?) to difficulty measuring outcomes.[3] This unacceptable state of affairs for treatments that consume billions of health care dollars annually in the United States alone[1] provided the stimulus for establishing at the National Institutes of Health a National Center for Complementary and Alternative Medicine in 1991. Its mission is "to define, through rigorous scientific investigation, the usefulness and safety of complementary and alternative medicine interventions and their roles in improving health and health care."[4] The Agency for Healthcare Research and Quality shares this mission. Their sponsorship and funding have begun to generate and make available scientific evidence on a wide variety of complementary therapies.

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Among complementary measures, meditation has occupied a special position, revered in religious circles and Eastern societies for centuries and rediscovered in the West in the mid-20th century by psychologists such as Abraham Maslow who were interested in its potential for enhancing human consciousness and experience. Widespread medical application followed about 10 years later, popularized by such best-selling books as *The Relaxation Response* by Herbert Benson.[5] Mindfulness techniques, which seek to enhance self-awareness, and mantra methods, which aim for transcendence, have been applied widely to treat stress and stress-related conditions[1,6] and are becoming popular for use in everyday life by a public that finds itself increasingly distracted and disrupted by endless interruptions and stressors.[7]

In this issue, Goyal and colleagues[8] from The Johns Hopkins University report on their examination of best available evidence for the efficacy and comparative effectiveness of meditation. In their Agency for Healthcare Research and Quality–sponsored systematic review and meta-analysis of methodologically sound studies of mindful and transcendental forms of meditation, they attempt to address efficacy and comparative effectiveness with regard to psychological stress and well-being. They focus their review on best evidence, derived from randomized clinical trials involving patients with a mental health or physical condition and using active controls for determination of efficacy and comparative effectiveness. The active control studies are subcategorized by whether the control involves a nonspecific measure, such as education (which helps determine efficacy by controlling for time, attention, and expectation), or a specific intervention, such as exercise or progressive muscle relaxation (which provides for a comparative effectiveness assessment). They also grade studies for strength of evidence based on assessments for risk of bias, directness, consistency, and precision and categorized according to degree of confidence in the results by likelihood that further research would change the level of confidence.

Only 3% of published trials examined met their inclusion criteria, making for a review of 47 trials of mindfulness-based stress reduction (MBSR) or transcendental (mantra-based) meditation. With the exception of MBSR studies providing moderate evidence of improvement in anxiety, depression, and pain and low evidence of improvement in stress/distress and mental health-related quality of life, the investigators found low levels of evidence of no effect or insufficient evidence of effect for improvements by MBSR or transcendental meditation in any of the other variables of psychological stress or well-being examined. In the comparative-effectiveness analysis, they found little evidence of any benefit compared with specific active measures, such as exercise, progressive muscle relaxation, or cognitive behavioral therapy.[8]