Comparative Effectiveness Research Review Disposition of Comments Report

Research Review Title: *Meditation Programs for Psychological Stress and Well-Being*

Draft review available for public comment from December 4, 2012 to. January 2, 2013

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Comments to Research Review

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The tables below include the responses by the authors of the review to each comment that was submitted for this draft review. The responses to comments in this disposition report are those of the authors, who are responsible for its contents, and do not necessarily represent the views of the Agency for Healthcare Research and Quality.

Comment #	Reviewer	Section	Comment	Response
1.	[Peer reviewer 1]	General	They have taken a complicated topic and tried to make it understandable. The findings could be distilled down even more. Effects generally bigger when controls less well matched or not as active.	The comparison group was critical to the effects, and is the reason we chose to define and separate nonspecific active controls from specific active controls. The effects were generally bigger when compared with nonspecific active controls. In our discussion under KQ1, we write: " Sixth, all of the findings favoring an improvement in outcomes among the mindfulness groups as compared to control were found only when the comparisons were made against a nonspecific active control. In each comparison that was made against a known treatment or therapy, mindfulness did not show superiority for any outcome. This was true for all comparisons among any form of meditation for any key question. Out of 53 comparisons with a specific active control, we found only 2 that showed a statistically significant improvement: MBCT improved quality of life in comparison to antidepressant drug among depressed patients and mindfulness therapy reduced cigarette consumption in comparison to the Freedom from Smoking program .However, we also found five comparisons where the specific active control performed better, with statistically significant results, than the meditation programs. The comparisons with specific therapies led to highly inconsistent results for most outcomes (Figure C2), and indicated that meditative therapies were no better than the specific therapies they were being compared to. These include such therapies as exercise, yoga, progressive muscle relaxation, cognitive behavioral therapy, and medications."

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2.	[Peer reviewer 2]	General	The report pertains to clinical populations and indicates effects sizes based on mindfulness and concentration forms of therapeutic interventions; thus, it is clinically relevant. The phrasing of key constructs such as “stress” is somewhat vague and needs revision, see full set of comments below.	We have revised our conceptualization of stress under the subheading “Psychological Stress and Well Being” in INTRODUCTION pg 3: “As a mind-body method, meditation is believed to use mental processes to influence physical functioning and promote health. The potential effects on function and health are postulated to occur by reducing negative emotions, cognitions, and behaviors; increasing positive emotions, cognitions, and behaviors; and altering relevant physiological processes. While some of these effects can be immediate (i.e., observed within seconds of beginning meditation), the health effects are typically postulated to occur following longer-term practice (i.e., weeks, months, or even years). For the purpose of this review, we use the phrase psychological stress and well being to refer to a range of negative and positive emotions, cognitions, and behaviors that are known to change with exposure to acute or chronic stress. Emotions include the following: general negative affect, as well as specific emotions such as anxiety and depression; general positive affect, as well as psychological well being; perceived stress, which generally measures a perceived loss of control; and the mental health component of health-related quality of life. Cognitions include attention, and behaviors include a range of stress-reactive appetitive behaviors, such as eating, sleeping, smoking, and the use of alcohol or recreational drugs. Although not always directly linked to stress in the studies we include, these outcomes are generally studied in groups exposed to stress, either due to having a chronic health condition that could be construed as stressful (e.g., cancer, chronic pain, or an anxiety disorder) or due to caring for someone with a debilitating chronic medical condition (e.g., dementia). “

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3.	[TEP - Reviewer 4]	General	Overall, the report seems complete and logical, with the questions reasonably well defined. Referring to meditation as "mental exercise" seems inappropriate. I prefer the term "focused attention" or "sitting meditation". Although there is a practice component to meditation, "mental exercise" seems too much like crossword puzzles or brain teasers and gives the wrong impression to the reader. This review includes studies of a wide variety of medical conditions and looks at the fairly broad outcomes of negative and positive affect. In addition to the enormous heterogeneity of outcome measures, conditions, and to some extent "dose" of intervention, it's unclear to me how much "opportunity to improve" might be present in the various patient populations. This would make the findings fairly imprecise and might underestimate the value of the therapy. For example, if a study included only 20-30% of people who were clinically depressed, then we might not have enough room to measure meaningful improvement on a depression scale. Very often, behavioral medicine trials are quite specific about baseline criteria for enrolling patients with depression for example, but if it's not the focus of the study, then results on "depression" might not really be meaningful for persons who have the condition. I think the authors should consider how important this phenomenon might be in their systematic review (though I do note this on, for example, page 48, lines 11-18 and page 117, lines 30-32). I think this is particularly likely to be an issue in the analyses of "negative affect" and quite possibly in the pain studies (only five of which really focused on pain patients). I think this should be mentioned in the conclusions (pp 124-5) as well.	In INTRODUCTION, subheading "Forms of Meditation," we have extensively revised our description of meditation programs. In this description we have changed the phrase "mental exercise" to "mental activity," in addition to other descriptors such as "focused attention." We have reorganized our relative difference in change graphs to display the primary outcomes followed by the secondary outcomes so that readers can clearly see if there is a difference between trials for whom a particular outcome was primary vs secondary. In Figure C in the ES, we have added the number of trials for which the outcome was a primary outcome to the total number of trials. To the DISCUSSION section under KQ1, we have added the following paragraph: "The fifth observation is that although there may be differences between trials for which these outcomes are a primary versus secondary focus, although we did not find any evidence for this. While we did not conduct separate meta-analyses for primary versus secondary trials due to the small number of each, our analysis of the difference in change estimates did not suggest any difference. Some trials in which an outcome was a primary focus did not recruit based on high symptom levels of that outcome. Thus, the samples included in these trials more closely resemble a general primary care population, and there may not be room to measure an effect if symptom levels were low to start with (i.e. a "floor" effect)." Also, to the CONCLUSION we added the following paragraph: "Fifth, symptom levels may have been low to start with for many trials, not leaving much room to find a difference from an intervention. However, if one purpose of meditation interventions is to improve symptomatology at non clinical levels, this issue may not be as

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				relevant."
4.	[Peer reviewer 5]	General	From a research perspective, the report clearly identifies the lack of sufficient rigor in many studies and offers recommendations to improve designs and overcome methodological challenges. I think that most clinicians will find the report discouraging and of limited value. The weak case in support of mindfulness will challenge their clinical experience. I think that it would be helpful to identify clinical recommendations based on the findings and in consideration of risks and benefits. I thoroughly reviewed the document and apologize that I have not had sufficient time to write a more complete analysis. Honestly, I think that the report will be more valuable to researchers than clinicians.	The strength of evidence has changed with the addition of 10 new trials in our updated review. Our updated review shows low to moderate evidence that current mindfulness therapies have a small impact on negative affect and pain, which some may find more clinically relevant. In our discussion, we discuss the reasons for these findings, and lay out our thoughts which the research community should consider going forward. We do not make clinical recommendations in this report. EPC reports are intended to present the evidence. Partner organizations may use the evidence report as a foundation for their decisions, which may incorporate other factors such as resources, costs, and individual values and preferences.
5.	[Peer reviewer 6]	General	Yes, the report is clinically meaningful. The authors are to be commended in their work with such a conceptually challenging review topic. The focus on study designs with adequate attentional control was an important advance in the literature. Overall, the report is well-presented.	Thank you.
6.	[Peer reviewer 7]	General	The report is not clinically meaningful for several reasons. First, it lacks a conceptual-theoretical model. If I may use an analogy. If one were reviewing the effects of two sports, baseball and football, for their therapeutic outcomes on BMI, Blood pressure, Anxiety, depression and stress, you might expect to find some minor therapeutic effect, BUT most people do not engage in these sports for medical reasons. Similarly, meditation is a largely spiritual practice in which people engage for all sorts of reasons other than medical outcomes. Medical outcomes are generally secondary, so studies will be underpowered to detect those outcomes. Second the abstract does not follow the study questions, which were clearly described, though without any theoretical rationale. Did the authors choose these outcomes because these were the theoretical outcomes of interest (actually, I would think the primary outcomes would be MINDFULNESS or PEACEFULNESS, or CONNECTION with deepest parts of self).	Regarding theoretical rationale, please see response to Comment #2 and revision of how meditation is conceptualized below in this box. Regarding our study questions, these were specified a priori, and no data is presented that was not prespecified. Thus, we do not believe there is any "data-dredging." We agree that people may participate in meditation for nonmedical reasons, however the nomination of this review was to evaluate the effects on stress related health outcomes. Mindfulness, peacefulness, and connection with deepest parts of the self are not clearly defined health outcomes, and there is considerable debate about what mindfulness itself is. We have revised our text in Introduction, subheading Forms of Meditation: " Researchers have categorized meditative

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			The study questions did NOT a priori, compare mindfulness with mantra-type (which I assume includes relaxation response as well as TM), yet many analyses did divide types of meditation. If done after the studies were identified and abstracted, this means it was "data dredging" or "fishing expedition" analyses, NOT hypothesis-testing analyses. There seems to be a lot of mixing of apples and oranges, and the abstract does little to clarify the study questions and outcomes. Please use parallel construction to make it easier to follow. Unlikely to be useful to clinicians, teachers or policymakers. Looks like a methodologist field day.	techniques into two forms, those that emphasize "concentration," such as transcendental meditation (TM) and other mantra-based meditation programs, and those that emphasize "mindfulness," such as mindfulness-based stress reduction (MBSR) and mindfulness-based cognitive therapy (MBCT). However this distinction is overly simplistic and may not adequately differentiate the effects of the techniques or the particular skills they teach. Both forms appear to involve concentration or focused attention at some point in the training, although the object of attention may differ. Both forms prescribe a mental activity, or non-activity (which itself may be considered an activity by some), associated with the focused attention. Both forms appear to describe an attitude or intention associated with these practices. Furthermore, both forms appear to be dynamic. That is, as a student gains experience, understanding, and/or skill in the practice, their state of awareness and approach to the meditation may evolve. That being said, most descriptions of meditation do not account for this dynamic nature of meditation, and, in fact, some practitioners and instructors may not feel their particular form of meditation has an evolutionary component. Meditation training is rarely manualized and there are challenges to knowing whether teachers within a practice tradition differ in their understanding of the practice, or whether they emphasize different aspects of the practice. Since meditation is within the mind, and there is not an established way to measure precisely what is being done, there are also significant challenges to knowing what exactly a student is doing when practicing. The mantra-based techniques practiced in the U.S. primarily consist of TM, a program established by Maharishi Mahesh Yogi around

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				1955, and a few others that use a mantra as part of their meditative technique. Many consider TM instruction 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 also receive instructions for home practice and are expected to practice daily. While a mantra is given to each student, there is a dynamic nature to the practice in that the mantra is used as a vehicle to transcend mental activity. This process has been referred to as "automatic self-transcending"--a process of meditation where one attempts to reach a state of being through meditation. In spite of TM having previously been labeled as a "concentration" form of meditation, some TM experts believe "proper" technique should not teach one to focus attention on the mantra. Rather, one should use the mantra in such a way that the mantra is "innocently" transcended. However, it is not clear how a practitioner can use mantra without focusing attention on it at least initially, nor what other mental activities or attitudes one needs to innocently transcend the mantra. Experts maintain that TM is different from all other forms of mantra meditation, but it is not clear specifically how one transcends the mantra in TM but not in other mantra-style meditations. However, emphasis is placed on the effortlessness of the technique, and electroencephalography has indicated a difference between automatic self-transcendence, and mindful focused attention / nonjudgmental awareness of the present moment. While some meditative techniques require the ongoing development of skills, some experts feel this is not the case with TM. That is, the technique does not take long to learn, and once learned there is no further skill set to

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				develop. Mindfulness-based programs include MBSR and its adaptation 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 modified 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 the original practices from which MBSR and other mindfulness-based techniques are derived. Despite its growing popularity, there remains uncertainty as to what mindfulness exactly is and inconsistency as to how it is taught. Mindfulness has been described as self-regulating attention toward the immediate present moment and adopting an orientation marked by curiosity, openness, and acceptance.Others have described mindfulness as including five key components: nonreactivity, observing, acting with awareness, describing, and non-judging. Still others have criticized these descriptions, noting that originally the practice emphasized qualities of awareness, which are not adequately captured by these definitions. The number of mindfulness-based practices that have been created to target particular conditions, such as MBCT for depression, appear to be more focused on solving problems related to particular conditions

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				rather than cultivating the general qualities of awareness. Thus, the conceptual and practical heterogeneity of mindfulness programs further complicates an understanding of what mindfulness is and how it differs both between and within different programs. 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. And 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 physiological effects of the exercise component. Many of the yoga interventions, in particular, do not clearly indicate how much meditation is involved in the intervention. Qi gong is a broad term encompassing both meditation and movement, as such, we're faced with similar difficulties parsing the effects of movement from the effects of meditation. It should be noted that although this report evaluates the health effects of meditation programs, meditation historically was not necessarily practiced for a specific health benefit. For many the goal was either philosophical or spiritual enlightenment, a sense of mental and physical peace and calm, self-inquiry, or a combination of these. Our review does not include these more classic goals of meditation, but instead focuses primarily on health benefits. We respectfully acknowledge that some experts regard this focus on specific health outcomes as a diversion from what meditation research should ideally evaluate.
7.	[Peer reviewer 8]	General 1	a. General Comments: This report attempts to isolate the "specific effects of meditation programs separate from the non-specific effects of attention and expectation" on a variety of	The issue of control group selection is central to our review, as recognized by the reviewer in comment #1. This is not merely an academic

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			outcomes. This is counterintuitive to most, if not all, practitioners of these treatment forms and their patients. It appears to be an academic exercise which encounters considerable challenges in its attempt to isolate the efficacy of meditation within a treatment that employs a number of aspects intertwined with the meditation. The authors address this briefly when discussing yoga and qi gong, but do not fully expand on these challenges, other than excluding yoga and qu gong studies. The methods are, as the authors claim, rigorous, but have limited clinical relevance.	exercise, as described in our Introduction, subheading “Evidence to Date: “Studies and reviews to date have demonstrated that both “mindfulness” and “mantra” meditation techniques reduce emotional symptoms (e.g., anxiety and depression, stress) and improve physical symptoms (e.g., pain) to a small to moderate degree. The populations studied have included healthy adults as well as those with a range of clinical and psychiatric conditions. The meditation literature has significant limitations related to inadequate control comparisons. For the most part previous 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 from the suggestion from trainers that symptoms will likely improve with these increased efforts. Due to the heterogeneity of control groups used in past meditation research, we chose to focus this review on only those studies that included a well-defined control group so that we could draw conclusions about the specific effects of meditation on psychological stress and well-being. An informative analogy is the use of placebos in pharmaceutical or surgical trials.

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				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 nonspecific factors are particularly important to control when evaluation of outcome relies on patient reporting. Since double-blinding has not been feasible in the evaluation of the effects of meditation, the challenge to execute studies that are not biased by these nonspecific factors is more pressing. As inquiry in this field has advanced over the last few decades, a larger number of trials have moved to a more rigorous design standard by using higher quality controls and blinded evaluators. Thus, there is a clear need to determine the specific effects of meditation based on randomized trials in which expectations for outcome and attentional support from health care professionals are controlled. The clinical relevance is the consistency and magnitude of changes we see in these RCTs.

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8.	[Peer reviewer 8]	General 2	A report of this type is only useful for the meditation “profession” in its strive to refine its treatment tools. For patients the most important issue is whether a series of meditation sessions will help more than doing nothing or choosing a different line of treatment.	In general studies so far have shown that meditation is better than doing nothing. We don’t know whether it is better than the placebo effects of attention and expectation, or whether meditation programs are better than any known treatments. We address this in our Discussion, subheading Limitations of the Review, last paragraph: “ While this review sought to assess the effectiveness of meditation programs above and beyond the non-specific effects of time and attention, it did not assess the impact of the preferences of patients. For many patients, even though one therapy may not be better than another but is better than doing nothing, the patient may still prefer a particular therapy for personal or philosophical reasons. Further, by reviewing only trials with active controls, 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.”
9.	[Peer reviewer 8]	General 3	The report is therefore technically well done, but yields results that, for the reasons mentioned above, informs to a minor degree patients seeking help for their stress-related or other problems.	Please see response to comment #4.

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10.	[Peer reviewer 9]	General 1	The authors are to be congratulated on their commitment to methodological rigor. However, aspects of the review pose serious threats to its validity and downgrade its rating to "poor." The chosen study selection criteria, for example, restrict the pool of relevant studies to a small sample. That might not be a problem if the studies were homogeneous, but the few studies selected are highly diverse, seriously limiting the inferences that can be drawn. As a result, the goals of a meta-analysis and synthesis—reliably summarizing effect size and also evaluating dispersion of effects—are not able to be achieved (Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. Introduction to Meta-Analysis. Chichester, UK: Wiley, 2009). Because of these limited exclusion/inclusion criteria, the report reaches misleading conclusions regarding its stated goal—evaluating the current status of meditation research on stress and well-being—limiting the clinical meaningfulness of the report and running the risk of turning the medical community away from potentially useful technologies. The report as it stands is not clinically meaningful. The target population and audience were not consistently or explicitly defined.	The review is focused on a set of key questions. The target population of trials is defined in our inclusion/exclusion criteria (Table 1 in Methods). We reviewed the effects of meditation programs on clinical populations, and defined clinical population broadly to be as inclusive as possible. Upon re-evaluating the included trials after receiving these comments, we concluded that three trials we had previously included matched a "healthy" population more closely rather than a clinical one. These three trials by Pipe et al, Alexander et al and Sheppard et al have now been excluded. The populations are diverse, which improves the applicability of the report. It is not true that meta-analysis cannot be performed on this data set. We have presented two different ways of understanding the data (relative percent differences and standardized mean differences) so that readers can get a full picture of what the data shows. Mostly, the two methods show fairly consistent results. The main limitation in the inclusion criteria that restricted the pool of studies was RCTs with an active control. However, this requirement was necessary to evaluate effectiveness and comparative effectiveness. Thus, this synthesis should be meaningful to any populations that were studied, which were intentionally broad. Also see response to comment #4.
11.	[Peer reviewer 9]	General 2	Problems of study selection are compounded by the inappropriate aggregation of meditation practices that are distinctly different in their nature and effects. For mindfulness meditation, this included MBSR, MBCT, and other variants that may not qualify as mindfulness approaches. For "mantra meditation," the Transcendental Meditation technique is classified as "concentration meditation" although those who teach and practice the technique report that it does not involve concentration. In other words, trials with the Transcendental Meditation technique are combined with trials involving other mantra meditation approaches that appear to be quite different.	We have reviewed the MBCT handbook. It is mainly mindfulness with cognitive therapy added to it. We have revised our description of mindfulness and manta, and no longer classify TM as "concentration." Please see response to comment #6, for our revised discussion of the types of meditation programs and the challenges to categorizing and defining them. We did evaluate the effects of TM separately from other mantra programs to see if it changed our conclusions. However, there were no

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				instances in which it changed our conclusions. We note a limitation of the review as having very few mantra trials, including TM, to draw meaningful conclusions about their effects on these outcomes. Discussion, KQ1: " The first observation is that there were very few mantra meditation programs included in our review. This significantly limited our ability to draw inferences about the effects of mantra meditation programs on psychological stress-related outcomes. Of the four TM trials, three were well-designed trials with low risk of bias that studied cardiac patients, while one had a high risk of bias and studied anxiety patients. Among the other mantra trials, both had a medium risk of bias. Based on the available evidence from these trials, we found no evidence that mantra meditation programs have an effect on psychological stress and well-being as compared to a nonspecific active control. These conclusions did not change when we evaluated TM separately from other mantra. Apart from the paucity of trials, another reason for seeing null results may also be due to the type of populations studied (e.g. 3 TM trials enrolled cardiac patients, while only 1 enrolled anxiety patients), and whether these study participants had high levels of a particular negative affect to begin with. Also, Conclusion, 1st paragraph, we state: "There were also too few trials of mantra meditation programs to draw meaningful conclusions."

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12.	[Peer reviewer 9]	General 3	The assumption that the selected meditation approaches are comparable within these two general classifiers (“mindfulness based” and “mantra meditation”) is not supported by hard data. At least for Transcendental Meditation and other mantra meditations, there is strong evidence that they are not comparable (see Eppley K, Abrams AI, Shear J. Differential effects of relaxation techniques on trait anxiety: A meta-analysis. Journal of Clinical Psychology. 1989;45(6):957–74.). Thus, this type of aggregation may confuse rather than clarify the issues. Regarding combining the Transcendental Meditation technique with concentration techniques, important distinctions exist between the respective techniques, as recent reviews based on hard data have shown (see Travis F, Shear J. Focused attention, open monitoring and automatic self-transcending: Categories to organize meditations from Vedic, Buddhist and Chinese traditions. Conscious Cogn. 2010;19(4):1110-1118.) Therefore the available literature makes it clear that combining a variety of different approaches and the Transcendental Meditation technique into one category of “mantra meditation” obfuscates the review.	We reviewed the mantra trials to see if evaluating just the TM trials alone would make a difference to our conclusions, however it did not. Due to the small number of trials, we have not separated them. We do not feel there is conclusive evidence to suggest that one form is different from another, and have revised our introduction to reflect the various uncertainties around what exactly is being practiced in the different traditions. Other reviewers such as Reviewer #10 (below) feel they are all the same. Eppley is a meta-analysis from a quarter century ago, doesn’t describe all the studies in detail, and is unclear what design characteristics are being compared to what. The evidence the reviewer has provided from Eppley does not support the conclusion that they are not comparable. We appreciate the reference to Travis and Shear. We have incorporated their categorization of “automatic self transcending” into our Introduction (see comment #6), as well as the reviewer’s comments on what transcendental meditation is and is not. Although we have tried to respect the traditional separations between the different traditions, we do not believe that the available literature has the evidence or clarity to conclusively say how similar or different they are, and whether those similarities or differences warrant a specific synthesis or another. Given the difficulties with transparently knowing what is actually being taught and what is actually being practiced, our view is that the outcome data can eventually provide some guidance.

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13.	Peer reviewer 9]	General 4	It appears also that mindfulness meditation is interpreted too broadly. Are all the techniques described in this category really “meditation techniques?” For example, cognitive/intellectual approaches to problem solving—such as mindfulness-based CBT—are quite different from trying to maintain an observant, non-judgmental attitude in activity. Cognitive Behavioral Therapy (CBT) may well have benefits for focused, problem-oriented goals, especially short term, but is it really appropriate for inclusion in a comparison of “meditation techniques?”	We do believe it is appropriate to include (Please see response to comment #6). However, we have incorporated a sentence in that section (Introduction, “Forms of Meditation”, last half of 5th paragraph) to reflect the reviewer’s concern: “The number of mindfulness-based practices that have been created to target particular conditions, such as MBCT for depression, appear to be more focused on solving problems related to particular conditions rather than cultivating the general qualities of awareness. Thus, the conceptual and practical heterogeneity of mindfulness programs further complicates an understanding of what mindfulness is, and how it differs both between and within different programs.”
14.	[Peer reviewer 9]	General 5	The key questions in the review need to be examined in the light of the total body of evidence for health benefits of meditation. A major point of contention is leaving out studies on mortality and CVD. The largest and most well controlled studies on meditation have been done in these areas. The omitted studies are not only well controlled, but examine objective measures directly relevant to this review. Therefore the meta-analysis does not provide a balanced assessment of the questions it sets out to answer, and reduces the clinical meaningfulness of the review. It seems almost as if the study were planned as a means of discrediting meditation research, including the most defensible findings of this research, by excluding those critical findings.	We agree that biologic markers of stress were left out of our review. These are of equal importance, and people are welcome to nominate to AHRQ for a dedicated but separate assessment on those outcomes. We have modified our title to state “Meditation programs for PSYCHOLOGICAL stress and well being” We have also added a sentence to our Introduction, subheading Psychological Stress and Well Being: “While there are many physiological/ biological markers of stress, we did not include such intermediate markers in this report because we thought it was important to keep this report focused on outcomes that are clinically meaningful to patients. “ A separate review would be needed to give adequate attention to the effects on physiological and biological markers of stress. We have cited the absence of biologic markers as a limitation to our review. See Discussion, subheading Limitations of the Review, 4th paragraph: “Stress outcomes encompass both

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				psychological and biological markers, yet we focused only on the psychological markers. This may disappoint some readers and may have reduced the number of transcendental meditation trials included, since many recent trials have been more focused on physiologic markers of stress. However, studies that included measures of psychological stress and well being, even as secondary outcomes, were included and contribute to our overall inclusions. An interesting challenge for future work is raised by the findings of one particularly strong transcendental meditation study. Paul-Labrador and colleagues compared transcendental meditation to a health education control condition in patients with congestive heart failure and found reductions in adjusted systolic blood pressure, heart rate variability and insulin resistence in the absence of concurrent changes in anxiety, depression, or stress. Given the absence of changes in measures of psychological stress in this study, these authors postulate that meditation may alter the biologic stress response independently of psychological stress responses, a hypothesis that will need to be directly tested in future research."
15.	[Peer reviewer 9]	General 6	A further limitation of the review is its having been restricted to randomized controlled trials having "appropriate comparators." Due to the authors' narrow definition of appropriate comparators, a large number of relevant studies were excluded, with the loss of important results. The resulting paucity of trials for each outcome measure may have contributed to the inconsistent findings.	Please see response to comment #1 and #7.
16.	[TEP - Reviewer 10]	General	a. General Comments: This is a very interesting and useful report that reviews clinical evidence of meditation program as a therapy for stress reduction in clinical settings. Different from most previous reviews, this review (1) focus on the clinical studies among patient population only, (2) set a higher standard for inclusion so that only high-quality clinical studies with active control would be included in the review; and (3) evaluate a variety of health conditions (instead of one condition) that are	1) We have modified the title to reflect that only psychological stress is evaluated, not biologic markers of stress. However, due to the numerous ways meditation could be defined (i.e., in terms of length of program, involvement of movements, manner in which the program is administered such as in person vs remotely), we felt a full modification of the title to reflect all

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			related to stress and general well-being…. This reviewer can feel the amount of passion and efforts the authors have put into this special and complicated report, and sense the difficulties applying the western medicine standard to evaluate the clinical applications of an eastern traditional practice that was not meant to be used as a therapy. But I am not fully satisfied with the reviewing strategy and current presentation. I can probably give a lot of appraisal for its strength, significance, and uniqueness in the field; however, I think some critiques, comments or questions may help this report to become more useful and targeted. Here are my general impressions on the problems in the current draft of report: 1) The title is misleading, since it does not include all meditations, and not include all studies of meditation, it should be more specific on what this report is really about – something like: mindfulness and mantra meditation programs for stress reduction in clinical populations. 2) The definition of meditation does not take full use of available information or literature, and has not made progress in that direction, especially if it excludes popular mind-body practice like yoga and qigong, which are mostly meditative or just pure meditation, it needs a good rationale to do so. Given the limited high-quality studies available in the field, exclusion of many real meditation studies from the review, and separation of mindfulness and mantra meditations in analysis may not be a good idea to objectively assess the field, unless these meditations are really different -- by definition, or experts, or clinical evidence. The reality is that, even Buddhist and Daoist meditations, two very different traditions that have scientifically proved different in physiological responses, have much in common, it is hard to differentiate the two Buddhist meditation traditions by clinically measurable outcomes… By the end, this report finds almost exactly what many previous reviews have found – few qualified studies, diversified outcomes to combine studies, lack of evidence, and inconclusive in most of evaluated outcomes. 3) The stress-related outcomes are too board to include in one review, but it did not include some of key clinical outcomes, such as headache, hypertension, allergy and fatigue. Meanwhile, it may be difficult to find many quality studies in these areas (as in the case of reviewed conditions) since the	these issues would be too cumbersome. We have therefore left the details of the inclusion/exclusion criteria to the Methods section. We did not exclude all other forms of meditation. We were open to all forms as long as they fit our inclusion criteria of a "meditation program" which is defined in Table 1 (inclusion/exclusion criteria) of the main report. Our review did not come up with any RCTs with an active control using such a meditation program other than one trial from Korea. 2) We have added this limitation to Discussion, Limitations of the Review, 5th paragraph: "In addition to limiting our focus to psychological stress and well being outcomes, we also limited the types of meditation included. We chose not to include other eastern meditative traditions such as Qi Gong and yoga. These forms typically involve movement and published reports often do not clearly indicate whether the form practiced was purely or mostly meditative or not. In our initial review of papers for inclusion, we were unable to accurately identify QiGong trials that emphasized movement from those that did not. We also did not include studies in healthy populations." We have also added to Discussion, subheading Future Directions: "Sixth, we were unable to review biologic markers of stress comprehensively for meditation programs, nor were we able to evaluate the effects of meditation programs that involve more movement such as yoga and Qi Gong, nor did we review the effects on healthy populations. Numerous trials have been conducted in these areas, and meditation research may benefit from a comprehensive review covering these areas. Such reviews would allow for a cross validation of psychological and biological outcomes." 3) We included any clinical population including

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			review focus on clinical populations only. Therefore, it really needs a better rationale to layout the key questions and key outcomes, and make it manageable in one systematic review. 4) Each key question could become a separate systematic review with more through search and inclusion of other meditation programs, instead of one key question in a more comprehensive and complicated review. These questions are not explicit enough for the audience since it missed many related concepts or conditions, while reflecting some important key questions for the benefits of meditation, but not important for most clinical studies (such as well being and attention). 5) Well-being may not belong to the literature review for high-quality clinical studies since good clinical studies tend to mostly focus narrowly on the improvement of disease or illness, and do not provide a general well-being measure, unless the study is done among healthy population. The same problem may be present when focus on studies of meditation for attention problem among clinical samples since most clinical studies have specific outcomes for physical or mental health conditions, which leave little room to measure other possible outcomes like attention. Restriction of study population to those with medical conditions will significantly limit the kind of outcomes that will be reported. 6) The latest literature to be included in this review is October 2011, and now it is 14 months later, and I understand the review is on-going as we evaluate the draft. I just want to make sure that we will publish a more up to date version for this report. 7) Authors acknowledged in the discussion that meditation was not meant to be a clinical therapy, but a tool or skill for self cultivation, balance and spirituality… Since most meditation programs focus on quieting down the mind and reaching a state of calmness and peace, while stress or mind disturbance is the number one reason for people to go see doctor, it makes perfect sense to examine the clinical outcomes of these meditation programs. However, this background or perspective should be stated in the introduction so that readers would know before hand (and probably reached the wrong conclusion themselves) that meditation is supposed to train individuals for the peaceful mind state or for a calm lifestyle, it is not a clinical therapy for physical or mental conditions (especially so for	headache, hypertension, allergy and fatigue as long as it fit our other inclusion criteria. 4) We appreciate the interest in broadening the types of meditation programs while narrowing the key questions. However, this was not in line with the general comments we received from our panel of expert reviewers during the development phase of this report. We do recommend further reviews as you suggest in our Future Directions section as noted above in #2. 5) see #2 above. Also, we note in the problems of not seeing effects due to a floor effect in the Discussion under KQ1: "Fifth, there may be differences between trials for which these outcomes are a primary versus secondary focus, although we did not find any evidence for this. While we did not conduct separate meta-analyses for primary versus secondary trials due to the small number of each, our analysis of the difference in change estimates did not suggest any difference. Some trials in which an outcome was a primary focus did not recruit based on high symptom levels of that outcome. Thus, the samples included in these trials more closely resemble a general primary care population, and there may not be room to measure an effect if symptom levels were low to start with (i.e. a "floor" effect)." 6) yes, we have included 10 additional trials. 7) We have added a paragraph to Introduction, subheading Forms of Meditation, last paragraph: " It should be noted that although this report evaluates the health effects of meditation programs, meditation historically was not necessarily practiced for a specific health benefit. For many the goal was either philosophical or spiritual enlightenment, a sense of mental and physical peace and calm, self-inquiry, or a combination of these. Our review does not include these more classic goals of

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			Buddhist tradition of meditation), and it may not work well as it means to be during a short clinical observation or trial.	meditation, but instead focuses primarily on health benefits. We respectfully acknowledge that some experts regard this focus on specific health outcomes as a diversion from what meditation research should ideally evaluate.
17.	[Peer reviewer 11]	General	The report is well written. The methods are clearly described and carried out. The results, given the limited scope of this review are also well written. This reviewer finds that the discussion and the interpretation of the findings do not effectively assist the readers in putting these findings in perspective. A major concern this reviewer has with this report is that the title of this review implies that this is a very comprehensive review of the literature on meditation programs and their effects on well-being. Most readers will assume that this implies a review of all forms of meditation and effects on health and well-being. This is not the case. Some reviewers and subsequent readers may argue that other meditation forms should have been included. This reviewer's concern is more on the very limited set of outcomes included, and particularly the fact that health-related physiological outcomes are not included. The objective of the review, as described, indicates that the goal was to examine "stress-related outcomes." This focus on stress rather than on meditation and health-related outcomes may create a problem because there is considerable controversy as to what should be included in "stress-related" outcomes. There is a vast literature on the relationship between environmental and psychosocial stress and the prevalence and incidence of health outcomes, including, for example, diseases and risk-factors associated with cardiovascular disease and gastro-intestinal diseases. However, despite the size of this literature, there is controversy in some circles as to whether these physical health outcomes are "stress-related." Perhaps that is why the authors didn't include studies that focused on health-related outcomes. However, the title of the report implies that all outcomes are included and as this report is announced it is very likely that the conclusion will be drawn that meditation has no effect on physiological outcomes and indeed, these were not evaluated. One solution might have been to drop the focus on "stress" and instead focus on meditation and health-related outcomes. The	We agree that the title is broader than the review. See response to comment #14. We have revised it to say "Meditation programs for PSYCHOLOGICAL stress and well being." We have revised our conceptualization of stress under the subheading "Psychological Stress and Well Being" in introduction pg 3: "As a mind-body method, meditation is believed to use mental processes to influence physical functioning and promote health. The potential effects on function and health are postulated to occur by reducing negative emotions, cognitions, and behaviors; increasing positive emotions, cognitions, and behaviors; and altering relevant physiological processes. While some of these effects can be immediate (i.e., observed within seconds of beginning meditation), the health effects are typically postulated to occur following longer-term practice (i.e., weeks, months, or even years). For the purpose of this review, we use the phrase psychological stress and well being to refer to a range of negative and positive emotions, cognitions, and behaviors that are known to change with exposure to acute or chronic stress. Emotions include the following: general negative affect, as well as specific emotions such as anxiety and depression; general positive affect, as well as psychological well being; perceived stress, which generally measures a perceived loss of control; and the mental health component of health-related quality of life. Cognitions include attention, and behaviors include a range of stress-reactive appetitive behaviors, such as eating, sleeping, smoking, and the use of alcohol or recreational

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			inclusion of "stress" in the title and in the conceptualization of this review suggests that the authors are implying that meditation exerts it's effect through reducing psychological stress rather than through changes in physiological functioning. This reviewer believes that the mechanisms by which various forms of meditation, including both mindfulness and mantra may have effects on physiological and psychological outcomes is not known. The focus of this review is on the author's view of stress-related self-reported psychological states and not on the effects of meditation on physiological health outcomes. As a result, studies of meditation that focused on physical health or physiological outcomes are not included. A few of these studies are included because they included the assessment of psychological measures. Examining one of the included studies highlights this issue. The study by Paul-Labrador (Arch Intern Med, 166, 2006) evaluated mantra meditation in a study to explore the effects of meditation on physiological variables associated with the metabolic syndrome, which is thought to be a contributor to coronary heart disease. This study explicitly states that the main outcome measures were blood pressure, insulin resistance and lipoprotein profile. The study was included in this review because it happened to also measure changes in self-reported negative affect, which was used as a control variable. That is the interest of the authors was in the effects on meditation on the physiological variables, controlling for any changes in self-reported negative affect. The mantra meditation did have greater effects on systolic blood pressure and insulin resistance, compared to the active control but this is not mentioned in the meditation review. The reader of review of "Meditation, Stress and Well-being" would likely be interested in main finding of the Paul-Labrador research, but it is not included. Instead, the review evaluated only data on the effect of the mantra meditation on the self-reported negative affect that was included in the study as a control variable. This reviewer believes that this issue needs to be addressed either by including studies with physiological outcomes in the review or being even more explicitly clear that these studies were excluded. If the studies are excluded, this should be discussed with some detail and including this as a limitation in	drugs. Although not always directly linked to stress in the studies we include, these outcomes are generally studied in groups exposed to stress, either due to having a chronic health condition that could be construed as stressful (e.g., cancer, chronic pain, or an anxiety disorder) or due to caring for someone with a debilitating chronic medical condition (e.g., dementia). " We have also added this limitation to Discussion, Limitations of the Review: "Stress outcomes encompass both psychological and biological markers, yet we focused only on the psychological markers. This may disappoint some readers and may have reduced the number of transcendental meditation trials included, since many recent trials have been more focused on physiologic markers of stress. However, studies that included measures of psychological stress and well being, even as secondary outcomes, were included and contribute to our overall inclusions. An interesting challenge for future work is raised by the findings of one particularly strong transcendental meditation study. Paul-Labrador and colleagues compared transcendental meditation to a health education control condition in patients with congestive heart failure and found reductions in adjusted systolic blood pressure, heart rate variability and insulin resistance in the absence of concurrent changes in anxiety, depression, or stress. Given the absence of changes in measures of psychological stress in this study, these authors postulate that meditation may alter the biologic stress response independently of psychological stress responses, a hypothesis that will need to be directly tested in future research. In addition to limiting our focus to psychological stress and well being outcomes, we also limited the types of meditation included. We chose not

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			the Discussion. An option, which this reviewer mentions in the sections below would be to change the title to modify "well-being" to "Meditation Programs for Stress and Psychological Well-being."	to include other eastern meditative traditions such as Qi Gong and yoga. These forms typically involve movement and published reports often do not clearly indicate whether the form practiced was purely or mostly meditative or not. In our initial review of papers for inclusion, we were unable to accurately identify Qigong trials that emphasized movement from those that did not. We also did not include healthy populations." We have also added to Discussion, subheading Future Directions: "Sixth, we were unable to review biologic markers of stress comprehensively for meditation programs, nor were we able to evaluate the effects of meditation programs that involve more movement such as yoga and Qi Gong, nor did we review the effects on healthy populations. Numerous trials have been conducted in these areas, and meditation research may benefit from a comprehensive review covering these areas. Such reviews would allow for a cross validation of psychological and biological outcomes."
18.	[Peer reviewer 12]	General	In general, the quality of this report is outstanding. The detail and rigor in the methodology and analysis makes it a very important addition to the literature. Target population and audience are clearly defined. Key questions are also explicitly stated. The document shows consistency in the quality of the reporting across all areas: executive summary, introduction, data collection and analysis, discussion of results, tables, figures, appendices.	Thank you for your comments.
19.	[The public - Reviewer 3]	Executive Summary	"Meditation Programs for Stress and Well-being" David Orme-Johnson, Ph.D. The AHRQ's non-scientific process. The main problem with this report is that the AHRQ review process does not adhere to even the minimal standards of science that any professional journal requires. Peer-reviewed journals send submitted papers is to independent outside reviewers to critique, and the authors of the submission must address the weaknesses and flaws identified by the reviewers and incorporate changes into the	Non scientific process: This is not true. AHRQ's process is more transparent than the regular publishing process. After receiving a public/professionally nominated topic, we posted a Refinement document publicly. After receiving public and expert comments, we revised the document and developed a protocol. This protocol was publicly posted and we received more comments. This was then revised based

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			submission to the satisfaction of the reviewers before the paper in published in the journal. AHRQ does invite outside professional as well as public reviews. However, study authors are not required to make changes that satisfy the reviewers' criticisms before they publish their reports. They only promise to make revisions, "as appropriate" through some opaque internal process to be posted three months after the review is finalized. In any journal review, the researchers may even have to go back and do more research and analyses and completely revise the paper, with the reviewer's final signing off on it before it is acceptable for publication. The AHRQ reviews do not have such a transparent process of interaction with the reviewers in place, and consequently, there is no real accountability to the scientific community (1). As a scientist and taxpayer who has paid for this report, as well as paid for all the salaries of the AHRQ personnel, I have to say that the AHRQ review process is a sham, blatantly ignoring the most basic tenets of the scientific process, making it completely open to bias and vulnerable to the agendas of special interest groups. Bias in the inclusion criteria. Meta-analysis is a completely objective process, as far as the mathematics of quantifying the effects of a body of studies is concerned. There are indeed many choices and decisions on how to conduct it, but these are explicitly stated and transparent. Where subjectivity and bias can creep in is in the selection of what studies to include (2, 3). The guiding principle for what studies to include should be the best controlled and most relevant ones for addressing the major question being posed by the analysis, which is in this case: "This report reviews the efficacy of meditation programs on stress-related outcomes among those with a clinical condition." Yet this report excludes meditation studies on hypertension, chronic heart failure, arterial sclerosis and other aspects of cardiovascular disease, which are arguably the conditions most well-documented to be stress-related (4-6). The omitted meditation studies in this area used highly objective outcome measures, such as decreased blood pressure in hypertensive patients (7-12), arterial blockage in patients with blocked arteries (13), decreased mortality due to cardiovascular disease and by all causes in hypertensive patients over an 18-year period (12, 14, 15), reduction of enlarged hearts in patients with left ventricular hypertrophy (16, 17), and decreased strokes,	on comments and the research commenced. The draft report was posted publicly, and we are now responding to those comments. Sometimes one reviewer disagrees with another reviewer, in which case it may not be possible to satisfy both reviewers. However, we have done extensive edits in response to comments, far more than is typical for a journal review. AHRQ, as with many journals, uses an editorial review process which exercises editorial discretion over acceptance for publication and it is the responsibility of the associate editors for ensuring adequate response to peer review comments, which is similar to many journal processes. AHRQ associate editors are external from AHRQ and the authors. Bias in inclusion criteria: We agree that stress can have physiologic as well as biologic markers. Our review focused on psychologic markers and not biologic markers. This is not a bias, merely a focus of this review. We have changed our title to reflect this, as well as made revisions to our Introduction, Discussion, Limitations, and Future Directions. Please see response to comments # 11 and 12, comment #16, and comment # 17. We reviewed all meditation programs reporting on our outcomes of interest that satisfied our inclusion criteria. Adolescents, while not children, are also not adults. We understand that in the tradition of TM, adolescents are taught the technique with "minor" reductions in training. Given the heterogeneity of our review, adding adolescents would add another layer of complexity. Please see response to comments # 10-14. Please also see comment # 7 for issues relating to control groups. According to the meta-analysis the reviewer cites by Sedlmeier, a theoretical argument is made in the paper that all meditations could be

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			heart attacks and death due to all causes over a ten-year period in patients with at least 50% blockage one or more of the major arteries to their heart (18). All these studies used active treatment control groups to control non-specific effects, such as expectation, attention, social support, amount of contact time with the instructors, and other factors. All were on the Transcendental Meditation technique (TM) and there are no such studies on mindfulness. Yet, studies on mindfulness on much more subjective outcomes, such as pain perception, were included. The selection process of what studies to include in this AHRQ report suggests a bias that is not in the national interest. The review was initially presented as being on all types of meditation, yet the name given in the download of the preliminary report is simply "Mindfulness Meditation". Another exclusion criteria not favorable to the TM technique but favorable to mindfulness techniques was excluding studies on adolescents, who are not "children" using different techniques, as the report asserts. Learning to meditate in early adulthood could potentially reduce stress-related problems and diseases and increase the quality of life across the lifespan (5, 16, 19-21). The report also misclassifies the TM technique as "concentration" meditation, even though it is consistently characterized as an effortless technique requiring no concentration (22, 23), and recently as automatic self-transcending (24). The advantages and limitations of active controls in behavioral research and using cross-validation to solve the problem. The AHRQ report only included studies that used active control groups to control for non-specific effects, which is good. But there can be problems interpreting such studies. For example, in a study on anxiety prominently cited in the review as evidence that TM does not work, Smith (1976) carefully constructed a control group that had received all the expectation fostering features and procedural details as the TM program and found that both TM and the control group reduced anxiety (25). Does this mean that TM is just a placebo? Not necessarily. TM's reduction of anxiety is cross-validated by studies showing it reduces autonomic correlates of anxiety, such as respiratory rate, skin resistance, and plasma lactate, compared to sitting comfortably with eyes closed as in TM practice (26). It also reduces cortisol, a major stress hormone in	lumped together. Since the effect sizes were quite similar for different meditation types for these outcomes, this is yet another argument that one could lump them together since there isn't a significant difference in effect. The Sedlmeier review notes that the effect size of the studies using TM was greater than the others, but it does not appear to be clinically significant (TM=.32 vs Mindful = .24). Furthermore, this difference was not found after this comparison was limited to articles (.27 vs .26). Further, we aren't shown information how the TM and other studies might have differed regarding study population or quality. Please see response to comment #12 regarding paper by Eppley. We agree that a cross validation of outcomes is an important step in meditation research. While we searched for psychological markers of stress, we did not find many transcendental meditation trials that had cross validated biological outcomes with psychological ones, and we did not assess the degree to which mindfulness trials cross validated psychological outcomes with biological ones. We have added a paragraph to Limitations of the review (4th paragraph): "Stress outcomes encompass both psychological and biological markers, yet we focused only on the psychological markers. This may disappoint some readers and may have reduced the number of transcendental meditation trials included, since many recent trials have been more focused on physiologic markers of stress. However, studies that included measures of psychological stress and well being, even as secondary outcomes, were included and contribute to our overall inclusions. An interesting challenge for future work is raised by the findings of one particularly strong transcendental meditation study. Paul-Labrador

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			humans (27), and reduces stress reactivity (21, 28, 29). Coronary heart disease is a correlate of anxiety (30, 31) and TM practice reduces coronary heart disease (4). Physiological cross-validating evidence should be included in evaluating outcomes such as Smith's. The abstract of the AHRQ report states: "We need more research using adequately powered high-quality randomized controlled trials that address the effects of meditation programs on stress and its correlates." Yet, the review ignored precisely that information, the physiological and medical correlates of stress. The review should also be broadened to take into account the results of previous meta-analyses. To continue with the example of Smith's study, it is relevant that a recent metaanalysis, conducted by researchers at Chemnitz University in Germany, who are completely independent of any TM organization, found that TM practice reduces anxiety more than mindfulness and other meditation techniques (32). The studies included were not limited to randomized controlled trails (RCTs), but they do replicate an earlier meta-analysis, which also found that TM practice reduced anxiety more than other meditation and relaxation techniques, even when only RTC's conducted by researchers who were neutral or negative were included (33). The other meditation and relaxation treatments that TM has been compared with in these meta-analyses provides a wide range of controls for attention, expectation, social support, etc. that support the conclusion that TM has non-specific effects on reducing anxiety, regardless of the conclusions from Smith's study. Tunnel vision. This AHRQ report used a set of exclusion/inclusion criteria that severely limited its perspective on the current status of meditation research on stress and well-being, which led to highly distorted conclusions. I was invited to be a key informant at the beginning of this study, and I emphasized to the study group that they needed to include studies on objective outcomes on stress, such as cardiovascular disease, and needed to examine cross-validating physiological evidence of stress reduction. Apparently, they had another agenda than to provide a balanced picture of the evidence.	and colleagues compared transcendental meditation to a health education control condition in patients with congestive heart failure and found reductions in adjusted systolic blood pressure, heart rate variability and insulin resistance in the absence of concurrent changes in anxiety, depression, or stress. Given the absence of changes in measures of psychological stress in this study, these authors postulate that meditation may alter the biologic stress response independently of psychological stress responses, a hypothesis that will need to be directly tested in future research." We have also added to our future directions subsection of the Discussion (Main report): "Sixth, we were unable to review biologic markers of stress comprehensively for meditation programs, nor were we able to evaluate the effects of meditation programs that involve more movement such as yoga and Qi Gong, nor did we review the effects on healthy populations. Numerous trials have been conducted in these areas, and meditation research may benefit from a comprehensive review covering these areas. Such reviews would allow for a cross validation of psychological and biological outcomes."

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20.	[Peer reviewer 9]	Executive Summary 1	As discussed in the general comments section, the definition of meditation needs to be clarified. The current one is vague and non-specific. It could, for example, include other cognitive approaches than meditation – e.g. CBT or biofeedback.	Please see response to comment #6.
21.	[Peer reviewer 9]	Executive Summary 2	In the Transcendental Meditation technique, one does not "focus attention." Instructors of this technique hold that focusing attention is "wrong meditation." It would be better to state in the review, "In some forms of meditation, a person learns to focus attention. However, this is not the case with Transcendental Meditation. In this technique, the mantra is used in such a way that the mantra is innocently transcended."	Please see response to comment #6.
22.	[Peer reviewer 9]	Executive Summary 3	Some researchers have categorized meditative techniques as emphasizing "mindfulness" or "concentration." Because the TM technique does not involve concentration, the reader is misled by this statement. I suggest describing the TM technique as follows: "Researchers have categorized meditative techniques into three categories, those that emphasize "mindfulness, open monitoring," those that emphasize "focused attention or concentration" and those that emphasize "automatic self-transcending." The Transcendental Meditation technique, which involves no effort to hold the mantra, is classified as automatic self-transcending to distinguish the technique from those that are "concentration" focused, that is, focused attention meditation that entails voluntary and sustained attention on a chosen object. Travis and Shear (2010) provide data supporting the distinctive descriptions of the Transcendental Meditation practice, expressly stating that the technique does not involve concentration. The EEG data they review show pronounced differences in brain wave activity in subjects practicing these different techniques of meditation. The general definition of meditation provided by the authors of this review might appear to favor mindfulness because the concept of mindfulness is embedded in their definition, followed by a sentence about potential benefits.	The main report has been modified. Please see response to comment # 6. The ES has less room for modification due to word limits, but has also been modified to say (ES-1, "Forms of Meditation, 2nd paragraph): "Researchers have categorized meditative techniques as emphasizing "mindfulness," "concentration," and "automatic self-transcendence." Popular techniques like Transcendental Meditation (TM), emphasize use of a mantra in such a way that it transcends one to an effortless state where there is no focused attention. 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 psychosocial stress outcomes."
23.	[Peer reviewer 9]	Executive Summary 4	Watch out for typographical errors such as not leaving a space between sentences, as in the first sentence of 'Stress Outcomes' (page 14).	Thank you.
24.	[Peer reviewer 9]	Executive Summary 5	On page 15, the citations 5-16 17-25 could be combined to 5-25.	We have fixed this

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25.	[Peer reviewer 9]	Executive Summary 6	P. 16. Bias due to limited inclusion criteria for physical outcomes — Why are pain and weight but not other physical conditions like hypertension included? No logical reason is given for this choice of outcomes. Hypertension and CVD are arguably more reliably linked to stress/psychological distress than weight, which can go down as well as up with depression/anxiety/stress. See the evidence re: CVD and stress/distress — plus see the following recent BMJ paper and editorial re: dose-response relation of psychological distress and mortality (all-cause, but primarily CVD). Russ TC, Stamatakis E, Hamer M, Starr JM, Kivimäki M, Batty GD. Association between psychological distress and mortality: individual participant pooled analysis of 10 prospective cohort studies. BMJ 2012;345:e4933. Also see Lewis G. Editorial: Psychological distress and death from cardiovascular disease. BMJ 2012;345:e5177.	We originally had two KQ on biologic outcomes (Jan 2012): KQ4: What is the efficacy of meditation programs on biologic processes among those with a clinical condition? KQ5: What is the time course and pattern of changes in these various outcomes (positive / negative affect; stress-related health behaviors; stress-related biologic processes) associated with meditation programs among clinical populations? Based on TEP/AHRQ input, we decided to delete KQ5 and add the evaluation of pain and weight. Due to issues of scope within a tight time-frame, it was not felt feasible to complete a review on all the psychologic and physiologic outcomes. We had received feedback from TEP/AHRQ that our physiologic outcomes looked more like intermediate outcomes and may not be that worthwhile to pursue. For these reasons, the physiologic outcomes, were dropped. We have revised the report to state that the lack of biologic outcomes is a limitation on the effects of meditation programs on stress-related outcomes, as already noted in responses above (see comment # 14). Also see response to comment #68.
26.	[Peer reviewer 9]	Executive Summary 7	P. 17. – 'with a clinical condition' – the definition of a clinical condition seems rather arbitrary.	We kept the definition of clinical condition as broad as possible to be inclusive of as many trials as possible. This was an intentional decision, not an arbitrary one.
27.	[Peer reviewer 9]	Executive Summary 8	P. 19. Exclusions. The exclusion criterion 'Studies of otherwise healthy individuals' was not applied consistently. 'Usual care control': This is a standard approach for medical trials when testing a new intervention against current best available care, so it may be inappropriate to exclude such studies, especially when the remit specifies a clinical context. Regarding exclusion of RCTs on adolescents and young adults, adolescents and young adults are not children. The review states that: 'The type and nature of meditation children receive	RE exclusion of healthy individuals, please see response to comment #10. RE Adolescents: Adolescents, while not children, are also not adults. We understand that in the tradition of TM, adolescents are taught the technique with "minor" reductions in training. Given the heterogeneity of our review, adding adolescents would add yet another layer of complexity, which is something this reviewer

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			is significantly different from adults,' However, this is not true for the Transcendental Meditation technique after the age of 10 years, except for small differences in the length of each practice session. Excluding studies on adolescents severely limits the credibility of the review. Learning some techniques of meditation in early adulthood has been found to reduce stress-related problems and to increase the quality of life into adulthood. Specifically, the studies using the Transcendental Meditation technique in adolescent age groups should not have been excluded because the technique is the same in anyone over the age of 10 as it is for older adults. See: Barnes VA, Orme-Johnson DA. Prevention and Treatment of Cardiovascular Disease in Adolescents and Adults through the Transcendental Meditation Program®: A Research Review Update. Current Hypertension Reviews. 2012;8(3):227-242. Barnes VA, Kapuku GK, Treiber FA. Impact of Transcendental Meditation on left ventricular mass in African American adolescents. Evidence-Based Complementary and Alternative Medicine 2012 (article ID 923153):1-6. Barnes VA, Treiber FA, Davis H. Impact of Transcendental Meditation on cardiovascular function at rest and during acute stress in adolescents with high normal blood pressure. Journal of Psychosomatic Research 2001 51(4):597-605. Barnes VA, Treiber FA, Johnson MH. Impact of stress reduction on ambulatory blood pressure in African American adolescents. American Journal of Hypertension 2004 17(4):366-369. Barnes VA, Bauza LB, Treiber FA. Impact of stress reduction on negative school behavior in adolescents. Health and Quality of Life Outcomes 2003 1(1):10. So KT, Orme-Johnson DW. Three randomized experiments on the holistic longitudinal effects of the Transcendental Meditation technique on cognition. Intelligence 2001 29:419-440. Wenneberg SR, Schneider RH, McLean C, Levitsky DK, Walton KG, Mandarino JV, Salerno JW, Wallace RK, Waziri R. A controlled study of the effects of Transcendental Meditation on cardiovascular reactivity and ambulatory blood pressure. International Journal of Neuroscience 1997 89(1/2):15-28.	argued against doing in an earlier comment (comment #10).

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28.	[Peer reviewer 9]	Executive summary 9	P 36. Definition of meditation. As mentioned previously, not all kinds of meditation require focus of attention. The Transcendental Meditation technique does not, even considering focus of attention on the mantra to be counter to correct meditation. In the section on kinds of meditation, again this technique is erroneously categorized as a concentration technique. It should be identified as a technique of effortless self-transcending, as mentioned earlier. This needs to be corrected in the first and third paragraphs of this section, as well as in the first line of the 'Evidence to date' section.	Please see response to comment #6. Corrections made to ES (see response to comment #22)
29.	[Peer reviewer 1]	Introduction	Line 44: Are you suggesting no difference in effect?	I assume this comment refers to structured abstract. Negative affect is a psychological term (see KQ 1)
30.	[Peer reviewer 1]	Introduction	Line 45: Is the focus on weight gain or loss?	We evaluated either.
31.	[Peer reviewer 1]	Introduction	Line 54: pain here	We are unable to tell what is being asked or commented on here (pg 14).
32.	[Peer reviewer 1]	Introduction	P 14, line 18: Pain relief not mentioned line 38: Are these the two types to be reviewed?	It is not known whether meditation results in pain relief. Please see response to comment #6. Yes, we review any meditation that fits our inclusion criteria and definition of a meditation program.
33.	[Peer reviewer 1]	Introduction	P 15, line 33: Was this a factor in selecting studies?	Trials needed to have an active control. Please see comment #7.
34.	[Peer reviewer 1]	Introduction	P 16, line 40: Is the focus on over- or under-eating?	It is typically on over-eating, but could theoretically be either. We describe in the paragraph on Scope and Key Questions: "They measure eating using food 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."

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35.	[Peer reviewer 1]	Introduction	P 17: surely eating and weight are related	Yes, but eating is more of a behavioral outcome and weight a biologic outcome. Also, studies may not measure both.
36.	[Peer reviewer 2]	Introduction	The introduction is lacking sufficient rationale based in previous research and can be strengthened, see full set of comments below.	See response to your "Overall" comments at the end of this document. Also see response to your General comment above (comment #2), and comment #6.
37.	[TEP-Reviewer 4]	Introduction	Overall, the introduction is a clear synopsis of the scope of the review. Page ES-1, line 34 – replace "mental activity" with "focused attention" as meditation is not normally considered "mental activity", even though there are measurable brain waves. Page 2, line 5, replace "mental exercises" with "sitting meditation" or "focused attention".	This issue is more complicated and contentious (see various other reviewer comments #6, 12, 13, 19). We have little room to modify the ES due to word count limitations. We have made revisions to meditation in the main report. Please see comment #6.
38.	[Peer reviewer 6]	Introduction	ES1/Pg 1: I believe the limited conceptual development will detract from the review's contribution. The background section starts with the medicalized perspective of meditation, then focuses immediately on the subgroup of meditation comprised of standardized meditation programs that have been developed for healthcare settings. This subgroup is a legitimate one, so that isn't a problem. But the background section doesn't locate this subgroup within meditation itself, not does it allow enough conceptual model to support all of the inclusion/exclusion criteria. I'm going to lay out in the following paragraphs my initial reaction to the background material. I'm sure the team members and TEP are well-verse in different aspects of this topic – my goal here is to help the authors focus on the communication process. That a person practicing meditation learns to focus attention is true. Meditation most often differs in the *object* of meditational focus. Thus, the object of meditation may be one's own experiences – mental and sensory, or "mindfulness". Other objects of focus may be single-pointed in nature, that is, holding attention steady on a single object, for example, a silent mantra, an imagined visual image, a candle flame, speaking aloud a mantra, even the contents of one's own mindstream. There are a number of fields deeply involved in understanding meditation, from comparative religion to humanistic to cognitive and neurosciences to pragmatic health interventionalists. Where the lines are drawn to create categories is determined by the question of interest and the understanding of the inquiring person – there is no absolute one right way.	Due to space limitations in the ES, we have made substantive revisions to the background in the main report. Please see comment #6 above. HeartMath's methods are very brief, and do not fit our definition of a "meditation program." This is listed in Table 1 as "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."

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			Mindfulness-based programs doe health were developed by, for the most part, practitioners of Vipassana techniques from the Theravedan Buddhist traditions. True, Zen, a Mahayana Buddhist tradition, also teaches a meditation with mindfulness as the object. True, TM developed from a Hindu tradition and has been systematized for teaching and health practices as well. However, the conceptualization does not provide a reader a way to make sense of meditation if their initial experiences, or even basic learning, come from other sources or traditions (such as Tibetan Buddhist, or Sufi, or Sikh, or even Christian contemplative meditation practices). So while I understand and agree with leaving physical yoga, pranayama, tai chi out of scope due to confounding factors, I'm not sure that a reader would necessarily understand why other types of visualization meditations would be excluded. While I understand why biofeedback using feedback equipment would be out of scope, I'm not clear why HeartMath's freeze-frame or heart-lock techniques would be (can be much shorter meditation techniques, initially developed by a person trained in Tibetan Buddhism). I'm not advocating that the scope be changed or that new studies be included. I am advocating for some revision of the background material so that the conceptual development and subsequent narrowing of scope to systematized approaches involving similar training programs are clear.	

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39.	[Peer reviewer 6]	Introduction	ES1/Pg 1: I'm confused by the PROMIS citation for meditation-related outcomes. I wouldn't have picked PROMIS as a site I'd expect to cover mind-body treatments and therapies, and I couldn't find anything useful when I searched the site. (If there is a specific page on the site I missed that is helpful, please give the URL detail.) I don't have a problem with the idea of stress and well-being. Is there a reason why Richard Davidson's work on MRIs of practitioners were not cited as preliminary evidence?	This was an error. We have deleted citation #4 in the ES. We describe the PROMIS framework in Methods, Study selection. It has nothing to do with meditation, but rather with categorization of self-reported outcomes. In METHODS, Study selection, paragraph 6 we write: "We evaluated the effect of these meditation programs on a range of stress-related outcomes and used the framework from the Patient Reported Outcomes Measurement Information System (PROMIS) to help guide our categorization of outcomes. 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, pain, and health-related behaviors affected by stress such as substance abuse, sleeping, and eating. Based on input from technical experts, we also evaluated the effect of meditation programs on weight, that is an additional stress-related outcome we deemed important."
40.	[Peer reviewer 6]	Introduction	ES2/Pg 3: Clinical/Policy relevance – I'd suggest that the bigger challenge is in fact matching the patient to the practice for most likely patient acceptance and practice, rather than conditions for which it may be helpful (since the outcomes being assessed are fairly ubiquitous). One could conceive that patient concordance (patient aims to optimize health gain and chooses to follow lifestyle practices within a medical context) would increase if attention is paid to matching meditation technique to the patient. But assessing if in fact there are no major differences in outcomes should be first.	Yes, we are focused on assessing whether there are any differences in outcomes. We do discuss the issue of patient preferences in Discussion: Limitations of the Review. Please see comment # 8.

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41.	[Peer reviewer 6]	Introduction	ES2/Pg 3: I like that the authors chose to use specific/nonspecific effects terms rather than placebo. However, later in the report, control groups are categorized as specific and nonspecific as well, and this leads to some confusion for the reader. Pg 7, paragraph beginning line 31, the paragraph begins using non-specific to refer to the type of control, then later uses non-specific to refer to the effect. Perhaps the report could use explicit and non-explicit for control groups? Or something similar? Alternatively, devote a para to explain the different uses of same terms.	Yes, we already did. Please see ES: Table A: Comparisons of Interest. " 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. • 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.
42.	[Peer reviewer 6]	Introduction	ES3/Pg 3: Wonder if it would help to suggest that the attention outcomes are similar to intermediate outcomes. An increase in attention control would show the person is attain a level of skill, but it doesnot necessarily (unless for ADHD pop) mean as much to the patient as a reduction in negative affect.	It is not clear that attention outcomes are intermediate outcomes for all cases, and due to the uncertainty of whether psychological or biological effects come first, we have refrained from suggesting this as an intermediate outcome in our report.
43.	[Peer reviewer 6]	Introduction	Please see attachment. Introduction could be revised to more clearly separate conceptual model of meditation as health intervention from report scope of meditation as defined as standardized meditation training programs. This would provide a more solid foundation for the inclusion/exclusion criteria.	Please see response to comment #6.
44.	[Peer reviewer 7]	Introduction	Rationale for analyzing these particular outcomes is unclear. This report would be more useful clinically if it had a theoretical basis. Separate reports on separate outcomes may have helped avoiding confusion for clinically-oriented readers.	Please see response to comment # 2, comments #10 and 14, and comment # 7.
45.	[Peer reviewer 8]	Introduction	b. Introduction: 1. In the first paragraph of the background (page 1, lines 15-18) it is unclear whether a practitioner is the patient or the instructor. These sentences are formulated better in the ES.	It does not matter which it is; however, we have revised the sentence to read: Some forms of meditation instruct the student to become mindful of thoughts, feelings, and sensations and to observe them in a nonjudgmental way. Practitioners generally believe this results in a state of greater calmness, physical relaxation, and psychological balance

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46.	[Peer reviewer 8]	Introduction	2. Under the heading "Current practice and prevalence of use" the authors should avoid using terms like "many people" and "A number of hospitals and programs". Indicate either the actual numbers or refrain from stating these meaningless expressions.	We feel that the wording is meaningful and expresses what we wish to convey, and have kept the original language.
47.	[Peer reviewer 8]	Introduction	3. In line 43 and 44 of page 1 one could get the impression that MBCT is only used in depression. If that is correct this should be stated clearly at the outset when describing MBCT.	We have changed the phrase slightly to say "...but instructors *modified* MBCT for the particular condition of depression." We don't make a claim that this is only what it is used for, just that this is what it has been modified for use for.
48.	[Peer reviewer 9]	Introduction	Page 6. Structured Abstract Objectives Note that, as mentioned above, the Transcendental Meditation technique is not a "concentration-based" meditation technique. The term "mantra-based" is used later in the review. Based on available hard data, the term "automatic self-transcending" would be the most accurate descriptor for this technique [See above citation for Travis and Shear (2010)].	We have deleted the phrase and the sentence now reads: "We aimed to determine the effectiveness and safety of 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) compared to an active control in clinical adult populations."
49.	[TEP - Reviewer 10	Introduction	The definition of meditation does not take full advantage of available literature, and has not made much progress in the field, especially if it excludes popular mind-body practice like yoga and qigong, which are mostly meditative, it needs a good rationale to do so. The mindfulness and mantra meditations are both from Buddhist tradition or practice, with a focus on mind nurturing and cultivation of peace. The meditation with more benefits for physical health would be among the Daoist (Taoism) tradition (like nei-dan or Inner elixir, and nei-yang or inner nourishing meditation) and medical tradition (like inner smile, lower-blood-pressure meditation, and five-element practice), unfortunately, there are not many high-quality clinical studies yet from those meditation traditions. The introduction should acknowledge the fact that Buddhist tradition of meditation has been most popular in this country or around the world, and most studied in clinical settings, but not the most effective in improvement of physical health conditions since Buddhism itself does not emphasize physical health in its practice. It may be helpful to have a joint discussion among meditation researcher and master meditaters on this issue – what are the true differences and what are the same? Although the introductory forms or techniques of various meditations may	Most of these comments were already addressed under your General comments (comment #16). With respect to the comment about acknowledging which form is most beneficial for physical health conditions, since our main focus is psychological health we have refrained from commenting on what is known about physical health effects.

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			seem different a lot, almost all meditation practices lead to the same mind state – restful alertness, feel empty or nothingness but stay highly alerted. The mindfulness, the mantra, the imagery, and the postures are all but different means to reach that same mind state. The stress-related outcomes are too board for one review, and not well defined here. Many other illnesses or diseases can be stress related. For example, the common stress-related clinical outcomes, such as headache, hypertension, allergy and fatigue, are not included in this review; therefore, it needs a good rationale to layout the key questions and key outcomes, as it is reviewed here. The key question is good and reasonable from meditation perspective, but each question could become a separate systematic review with more through search and inclusion of other meditation programs, instead of one question in a more comprehensive and complicated review. These questions are not explicit enough for the audience since it missed some related concepts or conditions. It would be nice if the introduction can clearly state that meditation is supposed to be a mind-body exercise to train individuals for the peaceful mind state or for a calm lifestyle, not a clinical therapy for physical or mental conditions, and it may not work well as it is supposed to be during a short clinical observation or trial, especially when taking it as a stand-alone therapy. Meditation may work better if it is adjunct to other existing therapies, or as part of rehabilitation and recovering therapies, which could be more difficult to study and evaluate its efficacy. Historically most traditional meditations were created for mind cultivation and spirituality, instead of healing or a therapy. There are some specific meditation forms created for health and healing purposes (like many medical qigong forms), but they are not very popular, and have not been well studied yet.	

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50.	[Peer reviewer 11]	Introduction	The introduction is well written. It defines the focus of this review on meditation using meaningful definitions and provides ample background to justify the strategies subsequently taken. The introduction cites some of the key papers to provide the appropriate background to this review and to support some of the methodological decisions to be made. The stated objective -- "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)" is clear but does not match this reader's expectation from reading the title, "Meditation Programs for Stress and Well-being." What seems to be missing is any recognition of physiological indicators of "well-being." The definition of "well-being" is not limited to self-reported reports of psychological states and pain, but also refers to general health. There is a large literature on the impact of perceived or actual stress and an impact on physiological outcomes in cardiovascular and other conditions. This literature seems to be entirely lacking. Readers of this meditation report, particularly physicians and other health professionals are equally, if not more interested in physical well-being, and these are studies not included. The decision to only include studies with active controls and within those studies to focus primarily on the relationship between the treatment and the active control throughout the analysis impacts the entire report. Given this, the introduction could benefit from include some of recent papers that highlight issues regarding the challenges of using active controls in trials for treatments of conditions where emotional or cognitive processes play an essential role -- which is particularly true in studies of depression and pain. When a treatment is a drug as opposed to psychotherapy, for example, the differences between the active treatment - the drug vs. an inert pill is straight forward. This report faces the same challenges as have faced reviews of psychotherapy.	We have changed the title as noted in our response to your General comments above (comment # 17), as well as our conceptualization and description of stress. We highlight the issues related to control groups in the Introduction, subheading "Evidence to Date" with relevant references.

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51.	[Peer reviewer 12]		I object to the use of the word “concentration” to refer to transcendental meditation. In reality, the recommended practice of TM emphasizes easiness in the repetition of the mantra, allowing thoughts throughout the process. Using concentration brings strain to the practice and instructors specifically warn against it. TM should not use concentration because it changes the nature and the results of the practice. Calling TM a mantra meditation is preferable and more appropriate. Other elements of the introduction I find appropriate.	We have revised this, please see comment #6.
52.	[Peer reviewer 1]	Methods 1	Line 15: Presumably these RCTs would have a great deal of patient self-selection.	Self selection is a ubiquitous problem for all RCTs. The advantage of using RCTs is that participants are randomized, despite being self-selected, so should have good internal validity.
53.	[Peer reviewer 1]	Methods 2	Line 45: But presumably did not use funnel plots P 22,	Yes, see ES Results, subheading 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. We reviewed the clinicaltrials.gov registration database to assess the number of trials that had been completed three or more years ago and that prespecified our outcomes but did not publish at all, or did publish but didn’t publish all outcomes that were prespecified. We found 5 trials on clinicaltrials.gov that appeared to have been completed before Jan 1, 2010 that were published but did not publish the results of all outcomes they had prespecified on the registration website. We also found 9 trials that appeared to have been completed before January 1, 2010 but that we could not find any publication for, and had prespecified at least one of our outcomes. Ten registered trials had prespecified one or more KQ1 outcomes but did not publish them, 2 registered trials had prespecified attention as an outcome but did not

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				publish, 5 registered trials prespecified one or more KQ3 outcomes but did not publish, and 5 registered trials prespecified one or more KQ4 outcomes but did not publish. For 8 of the 9 registered trials for which we could not find a publication, it was not possible to tell if those trials had actually been conducted or completed. Among 109 outcomes in 41 trials, trials did not did not give enough information to calculate a relative difference in the change score (our primary analysis) for six outcomes due to statistically insignificant findings. Trials did not give enough information to conduct a meta-analysis on 16 outcomes. Our findings from the primary analysis are therefore less likely to be affected by publication bias than the meta-analysis”
54.	[Peer reviewer 1]	Methods 3	Line 53: Why is 5% clinically significant?	We describe in our Discussion, Limitations of the Review, 6th paragraph: “We selected 5 percent difference in the outcome change scores as being potentially clinically significant and this decision 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 most of these scales, there is variability across measures, and even for those measures that have clinical cut-offs (e.g., many measures of depression) the change in proportion of study participants meeting these cut-offs following participation in the meditation programs was rarely reported. Some may consider a higher threshold as being clinically relevant.”
55.	[Peer reviewer 1]	Methods 4	P 18, line 31: Did you exclude those without attention controls? Table A suggests that you did P 20, line 29: relative differences based on mean values?	Yes. Yes.

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56.	[Peer reviewer 1]	Methods 5	P 21, Table B: assessors may be blind but participants were not. How could you conceal allocation? How do you assess credibility?	Allocation concealment would refer to all the parties not knowing the group assignment until the time of allocation. This does not require single or double blinding. Credibility is evaluated by certain scales assessing how much the individual believes the intervention they are in is going to help them.
57.	[Peer reviewer 2]	Methods	The methods used appear rigorous and meticulous, and the review only reports on the most valid RCTs, and provides bias ratings, making this a rigorous review, see full set of comments below.	Thank you
58.	[TEP - Reviewer 4]	Methods	In general the methods are reasonable. I have the following more specific comments: On page ES-5, the authors suggest they will update the report with newer citations, but on page 6, they do not mention this. Given the small number of articles and the wide scope of outcomes, an updated literature search is critical. The section on Study Selection is a little confusing in the first two paragraphs because there are multiple layers of excluding studies. I suggest the authors use the terminology in ES-10 (results of search strategy) and indicate how articles were eliminated during article screening and Key Question Applicability screening. For example, on page 6, line 56, the sentence could read: Citations remaining after title and abstract screening underwent article screening. In that process, two reviewers independently reviewed a full-text copy of each article (Appendix C, Article Review Form).	This review has been updated with 10 new trials. We have revised the sentence.
59.	[TEP - Reviewer 4]	Methods	Page 14, lines25-28: this sentence needs a better illustration since “greater than 20 percent attrition” is one of the Major Criteria.	We have modified the sentence to read: “In addition, if there were other issues with the studies that were not captured by the above criteria, such as significantly greater than 20 percent attrition (e.g. 40 or 50% attrition) or significant errors in reporting, we categorized such studies as high risk of bias on a study-by-study basis.”

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60.	[TEP - Reviewer 4]	Methods	Page 15, lines 20 – 23 describe the recommended domains that are used for assigning evidence grades. Each of the four subsequent paragraphs should describe the details of these four domains in the order they were listed in the first sentence. Therefore the paragraph describing "precision of individual studies (lines 40 to 49) should be moved so that it is after the paragraph describing "directness of the evidence (lines 50 to line 7 on page 16).	Rather than switching the paragraphs we modified the parent sentence to read: "In assigning evidence grades, we considered the four recommended domains, including risk of bias in the included studies, consistency across studies, and precision of the pooled estimate or the individual study estimates, and directness of the evidence."
61.	[TEP - Reviewer 4]	Methods	Page 7, line 26, replace mental exercise" with "sitting meditation" or "focused attention".	We have made replacements elsewhere in the text to this reference. However, in describing our conceptualization of a meditation program we feel the use of "... brief mental exercise..." is appropriate for this particular context.
62.	[Peer reviewer 6]	Methods 1	ES7/Pg 12 Data Synthesis: Consider adding to ES7, last paragraph, the explanation given on Pg 12 line 38 regarding short interventions and low doses for why using 5% relative difference for clinical significance.	This was added. The sentence now reads: "We considered a five percent relative difference in change score to be potentially clinically significant, since these studies were looking at short interventions and relatively low doses of meditation. "
63.	[Peer reviewer 6]	Methods 2	ES7/Pg 9 Data Abstraction/Management: Especially for an intervention like meditation training, I'd prefer the term "adherence" to "compliance". I'd prefer the term "concordance" overall, but it is not as well-recognized a term, perhaps.	Compliance was changed to adherence throughout the report.
64.	[Peer reviewer 6]	Methods 3	ES8/Pg 14: Table B/3 – please clarify what credibility is being evaluated.	We have added the following text to this section in main report: "Credibility is evaluated by administration of a scale that measures a participant's expectations of benefit before or during the trial. If credibility scores are similar in both arms of a trial, it suggests that those in the control group had similar beliefs and expectations of benefit as the treatment arm. We only gave a point for this if the trial specified administration of a measure of credibility."
65.	[Peer reviewer 6]	Methods 4	Methods are reasonable, especially given the complexity of the topic.	Thank you

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66.	[Peer reviewer 6]	Methods 5	Pg 14: Risk of Bias – Blinding the outcome assessor is only possible if the outcome is not patient reported. The net result would be rating a study as lower risk of bias if it incorporated some form of clinical measure, which is not necessarily possible for all of the studies as conceived. This would necessarily then, all else being equal, rate risk of bias lower for, say, a study assessing stress/change in weight than a study assessing negative affect. Did the review team assess other ways the study may have accounted for expectations, for example, asking study participants about their expectations?	This is not true. The idea of blinding of the assessor is that the assessor should not be able to influence the outcome reported. There are a variety of ways to execute this, such that the patient reports what they genuinely feel without any influence from a study team member watching over them, answering questions or guiding them, etc. If a trial reported their assessors were blinded, we took their word for it for self-reported as well non self-reported outcomes.
67.	[Peer reviewer 6]	Methods 6	Pg 19-20: Please check figures/text numbers for math and included articles. Sometimes it looks like there should be 33 articles (text if one does the exclusion subtraction), sometimes 34 (numbers in tables). Article review level is 1506 or 1507?	We have fixed it
68.	[Peer reviewer 6]	Methods 7	Pg 6: Topic Development – if you recruited Tai Chi and Qi Gong experts, then you must have initially meant to start with a bigger topic and narrowed it down? So – I can imagine a number of reasons why this might be, and I have great sympathy for the process. However, I still would have preferred the report gave a better accounting of the actual process rather than what in the end looks like reconstructed logic after the fact.	We have added the following sentence to this section: "Initially we planned to include physiologic outcomes as well as the various movement based meditation programs. Based on expert panel input we eliminated the biological outcomes due to need to limit the scope of this broad review, as well as a concern that a number of them, such as inflammatory markers, were felt to be more intermediate outcomes. We also eliminated the movement based meditation programs because we felt their relevance would be greatest on the physiologic markers."
69.	[Peer reviewer 7]	Methods	The rationale for the exclusion criteria is poor. Why exclude adolescents in the pediatric studies? Meditation and other lifestyle interventions are not drugs and studies about them should not use the same criteria as drug studies. We were able to ascertain that smoking was bad and breastfeeding is good without RCTs. Similarly, epidemiologic and cohort studies can yield powerful information about the benefits of other lifestyle practices, like meditation, and should not be excluded from analysis. It was wrong to exclude studies that evaluated wait list/usual care control groups. Yoga and tai chi should have been included if you are casting a broad net, as yoga is actually part of MBSR training and both are considered moving meditations. Pranayama is a meditative	Please see response to comment # 19 and 27. While there may be some controversy around which study designs to include, we do believe RCTs are the best design to assess whether an intervention is having an effect on a particular outcome. RCTs often show different or reduced effects from nonRCTs, and this suggests that non RCTs can be less reliable. Furthermore, RCTs are not limited in any way to drugs. A number of behavioral/lifestyle interventions have been successfully assessed through an RCT design. We describe the rationale for excluding waitlist/usual care controls in main report, sub

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			technique also. So is centering prayer, and it is not mentioned at all. Being unnecessarily rigorous (ie applying drug trial methodology to studies of lifestyle interventions) is likely to substantially under-estimate the effectiveness of these therapies as they are used in the real world, reducing the real world relevance of the analysis.	heading: Evidence to date. “Studies and reviews to date have demonstrated that both “mindfulness” and “mantra” meditation techniques reduce emotional symptoms (e.g., anxiety and depression, stress) and improve physical symptoms (e.g., pain) to a small to moderate degree. The populations studied have included healthy adults as well as those with a range of clinical and psychiatric conditions. The meditation literature has significant limitations related to inadequate control comparisons. For the most part previous 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. Due to the heterogeneity of control groups used in past meditation research, we chose to focus this review on only those studies that included a well defined control group so that we could draw conclusions about the specific effects of meditation on psychological stress and well being. An informative analogy is the use of placebos in pharmaceutical or surgical trials. Researchers typically design placebos to match

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				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. Since double blinding has not been feasible in the evaluation of the effects of meditation, the challenge to execute studies that are not biased by these non-specific factors is more pressing. As inquiry in this field has advanced over the last few decades, a larger number of trials have moved to a more rigorous design standard by using higher quality controls and blinded evaluators. Thus, there is a clear need to determine the specific effects of meditation based on randomized trials in which expectations for outcome and attentional support from health care professionals are controlled.” RE: yoga/tai chi. We do mention them in ES Table 1, and included meditative program including prayer if meditation was the main focus of the program, had at least 4 hours of training with homework exercises given. Yoga/Tai Chi were excluded due to the large component of movement as well as difficulty with being able to tell how much was meditation vs movement. We discussed whether to include Pranayama with experts and their feeling was that it was more of a breathing exercise and not really a meditation program. We did not find any RCTs of centering prayer in which at least 4 hours of training with instructions to practice at home were given.

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70.	[Peer reviewer 8]	Methods	Methods: The methods are described in admirable detail. If one accepts the basic assumptions (see my comments under general comments), the authors have done an excellent job in sifting through all the necessary issues to determine which studies to include, and to classify the included studies according to risk of bias.	Thank you.
71.	[Peer reviewer 9]	Methods	The justification of the inclusion/exclusion criteria was not clear, and these criteria were not consistently applied. For example, studies with adolescents were excluded with insufficient reason. Although the authors have selected only studies done on clinical populations, the outcomes they have chosen to focus on are often only tangentially related to the clinical syndromes that are the main focus of these studies. Thus, for example, for Transcendental Meditation there are a number of RCTs focusing on various dimensions of cardiovascular health, with reported significant and clinically relevant outcomes. Some of these studies are included in the review and others are not. For these studies, the outcome variables chosen by the authors of this review serve primarily as moderator variables, rather than the variables of primary interest.	Please see our response to your general comments above (comment # 10-14).
72.	[Peer reviewer 9]	Methods	Regarding the definitions of or diagnostic criteria for the outcome measures (and this applies more broadly than to the studies just alluded to), the outcome variables chosen by the authors are not necessarily clinically relevant to the sample of a study. For example, the sample of one study may not have, prior to treatment, high levels of anxiety or depression, while the subjects of another study may have been chosen explicitly for high levels of these stress indicators. In the latter case, the study will be more amenable to finding treatment effects on the chosen variables. At the same time, the four classes of outcome measures selected may be very relevant to 'normal' populations, who are also subject to stress, anxiety, depression, attention problems, substance use problems, and sleep or weight problems. Such groups might in fact have elevated levels of these problems prior to clinical intervention, and amelioration of these problems using an effective meditation technique at this early date can contribute to health.	Please see our response to your comment # 10 above regarding exclusion of healthy. Re levels of symptomatology, please our response to comment #3 above.

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73.	[Peer reviewer 9]	Methods	The search strategies are logical and explicitly stated, however, too much emphasis was placed on reactive subjective measures.	We describe our "Topic Development" in the Methods section: "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. Initially we planned to include physiologic outcomes and the various movement based meditation programs. Based on expert panel input we eliminated the biological outcomes due to need to limit the scope of this broad review, as well as a concern that a number of them, such as inflammatory markers, were felt to be more intermediate outcomes. We also eliminated the movement based meditation programs because we felt their relevance would be greatest for the physiologic markers. We uploaded the protocol to the Effective Health Care Program Web site on February 22, 2012."

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74.	[Peer reviewer 9]	Methods	The following studies may need to be re-evaluated for inclusion. Alexander et al 1989 included elderly subjects (mean age 81 years) and as such falls under the category of medical or psychiatric condition under your broad definitions on page 18, however it is debatable as to whether or not advanced age should serve as a medical condition, when young age groups are excluded.	Please see our response to your general comment (comment # 10) above regarding exclusion of healthy.
75.	[Peer reviewer 9]	Methods	Pipe et al 2009 included normal subjects, but they were 'stressed'. Under your broad definitions on page 18 this may be permissible.	We have excluded this study.
76.	[Peer reviewer 9]	Methods	Smith JC 1976 included normal college students that did not fall under the category of medical or psychiatric condition. The subjects were not specifically screened for anxiety level. Rather, they were recruited for a study to reduce anxiety. Even under the review's broad definition on page 19, this study may not be permissible. The risk of self-selection bias in this study needs to be carefully examined.	We did not apply a criterion to any of the trials that they had to specify screening cutoffs. If the trial said they recruited anxious students, we took their word for it. Regarding "self-selection bias," all trials, including all TM trials, are subject to self selection as long as people volunteer to participate. However, since participants are randomized, there is good internal validity to such designs.
77.	[Peer reviewer 9]	Methods	Elder et al 2006. Treatment for the experimental group included exercise, an Ayurvedic diet, Transcendental Meditation instruction, and an Ayurvedic herb supplement (MA 471). In this combo intervention, we do not know what specific aspect was largely responsible for the treatment effect. It could have been the combination of all. Control patients attended standard diabetes education classes with primary care clinician follow-up.	Sometimes TM studies use supplements such as chawan prash, and it hasn't been clear if this is a standard part of every TM protocol or an optional one.
78.	[Peer reviewer 9]	Methods	Note that MBSR is a combination intervention that includes a number of different techniques of meditation as well as yoga asanas, and as this is an exclusion criterion, should be reconsidered for exclusion.	In Methods:Table 1, in our exclusion criteria, we state that we exclude " Meditation programs in which the meditation is not the foundation and majority of the intervention." MBSR did not fit into this exclusion criteria.

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79.	[Peer reviewer 9]	Methods	Sheppard et al 1997. The subjects were not pre-screened for stress levels, but were normal healthy volunteers who worked in a high security US government agency setting that was reputed to be highly stressful. It is debatable whether these subjects fall under the category of medical or psychiatric condition. Page 19. Again, inclusion/exclusion criteria come into question in that studies of children are excluded. The rationale that meditation is different for children is flawed. The Transcendental Meditation technique is the same for youth (age ≥10 years) as it is for adults. With this technique, students starting at age 10 practice the same technique as adults; however, as mentioned previously, the "dosage" (time spent practicing meditation each day) may be less.	We have excluded this study. Please see prior comments to you on adolescents (comment #27)
80.	[Peer reviewer 9]	Methods	Page 20. Most of the RCTs on the Transcendental Meditation technique are studies in which the control group was matched in time and attention to the intervention group for the purpose of matching expectations of benefit. Early meditation studies did not provide information on measures of intervention fidelity, including dose, training, and receipt of intervention, duration and maximal hours of structured training in meditation, amount of home practice recommended, description of instructor qualifications, and description of participant compliance.	Yes, we merely report who has and hasn't described the amount of dose, and suggested that all studies do this in the future.
81.	[Peer reviewer 9]	Methods	The statistical methods appear to be appropriate for the review, but if the sample of studies does not include the most important outcomes to answer the question, then even the best statistics are of no avail. Sometimes a published manuscript is limited by word limits imposed by the journal and may have not have space to include the randomization procedure. If a trial was said to be randomized but did not report on the randomization procedure, it was rated the same as if it was not randomized.	We have come across various trials that say they are randomized, but in their description of allocation it is clear that they are not randomized. While older trials may not have been explicit about mentioning the randomization process, newer ones should. Irrespective of word count limits, in deciding bias criteria, we felt this was an important criterion. We do not say that the trials have a particular level of bias, but rather that they have a particular level of risk of bias, since we are relying on their reporting.
82.	[TEP - Reviewer 10]	Methods	The research design and methods are generally acceptable. I especially like the revised criteria in assessing risk of bias. However, I have some questions on the exclusion criteria since many true meditation programs – such as yoga, qigong and breathing exercise – are excluded from the review, when the actual number of studies included in the review are relative small. This makes readers wonder what exactly other	We have addressed the issue of exclusion of yoga, Qigong in our response to a previous comment (#16). Regarding voluntary vs prescribed practices: In a clinical trial, all participants will still be volunteers. No one is forcing them to meditate. We agree that there is insufficient data to say

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			meditation is supposed to be. I have tried to clarify the definition or concept of qigong for a while since all meditations will be called Qigong in China, while it seems that some people in America misperceive qigong as the slow movement mind-body exercise only, which was actually called Dao Yin in the history, just one of Qigong practices. Inclusion of randomized controlled trials with an active control in a review is definitely a good step to evaluate the strength of clinical evidence. However, this good strategy may exclude many really good studies in meditation programs since meditation is not meant to be used for clinical settings, and never fully supported by conventional medical community to do so (partially due to lack of evidence, and partially due to ideological bias). The randomized controlled study with an active control may not be the best way, or best choice by a true meditator, to evaluate the efficacy of this mind-body exercise that is supposed to be chosen by the practitioner voluntarily, not prescribed by a doctor. In other words, you cannot force a patient to meditate by randomizing them into meditation training if he/she prefers just taking a pill for his/her condition and go home. No matter how good the instructor is, if the patient does not like meditation, it would not work for him/her since he/she will not be complied with the meditation protocol. By the way, this raises another issue that has not been fully addressed in the review: Have the protocol compliance or quality of meditation be evaluated and considered in correlation with individual clinical outcomes? I have personally run into this problem that some residential patients in addition treatment chose meditation program over other existent programs because they could fall asleep during meditation time… Of course, this fact should be a necessary note to the reader, but not stop us from doing a systematic review of the clinical evidence. After reading the various scales for clinical outcomes in Table 2, I had the feeling that the diagnostic criteria for the stress-related outcomes are way too board for one systematic review to handle, not mention there are many more missed clinical outcomes, like hypertension and fatigue, which may make this systematic review more difficult to complete…. A more focused review with the consideration that meditation is really not a clinical therapy may make more sense to the research	whether the different meditation therapies should be separated or lumped together. However, given the conceptual differences (see response to comment #6), we feel it is safest to separate mindfulness and mantra approaches currently, and let the data guide researchers over time about the true similarities and distinctions between the various forms. Regarding language issues, we did review a number of foreign language articles. We have added the following text to Methods, subheading Search Strategy, 2n d paragraph: "For articles written in non-English languages, we either used individuals familiar with the language or used the Google Translate website to assess whether an article fit our inclusion criteria."

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			community and clinicians. Given the limited high-quality studies available in the field, I am not sure the separation of mindfulness and mantra meditations in data analysis is a good idea to objectively assess the field, unless these meditations are really different, by definition, or experts, or by physiological evidence. Conducting separate examination or statistical analysis with very limited number of studies will definitely weaken the small amount of clinical evidence we have. One comment to the search strategy, I believe this review is for English literature only, therefore, it actually has a language limitation since many meditation studies were done and published in Chinese, Korean and Japanese, and not included in this review yet.	
83.	[Peer reviewer 11]	Methods	The inclusion and exclusion criteria for selection of the studies included in the review are justified given the limited focus of this review. These criteria are far more restrictive than the title of the report implies and this creates an important issue. The search strategies are clearly stated and logical, given the very restricted scope of this report – which only includes self-reported psychological well-being and pain. The definitions and diagnostic criteria are appropriate, given the restricted scope. The data synthesis is well described, and the statistical methods are appropriate. The sections on methodological quality and bias are also well presented. The section on determining the strength of evidence is thoughtful and well described. The emphasis on patient outcomes is where there is a challenge in that only a subset of outcomes in meditation studies are reported and in some cases, they are not the primary outcomes in the studies reviewed. The decision to not include publication bias in the evidence grade but to take it into consideration where there was low strength of evidence is appropriate. Selected trials of patients with medical conditions are included. It appears that these happened to be included because, in addition to physiological outcomes, the studies included measures of affect or pain. What is not clear to the reader is the rationale for focusing only on affect (negative and positive) and on pain while including patients with medical conditions. This is discussed at length in the "General Comments" section. For example, patients with cardiovascular conditions are included.	Regarding reasons and process of excluding the outcomes involving physiologic markers of stress, please see: Comments # 14 and 25, Comment # 68 While trials reported on a number of primary outcomes, we only reported on those outcomes if they were a focus of our review. We have modified our review to report which outcomes were primary and which were secondary, as well as the proportion which were primary. Please see: Comment # 3

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			Many readers, including professionals and the public, will be particularly interested in physiologically relevant outcomes such as blood pressure or insulin resistance. A patient with cardiovascular disease may be particularly interested in whether his or her cardiovascular risk factors are lowered by participating in mindfulness or mantra meditation. This is likely to be a more valued patient outcome than lower negative affect. This is particularly relevant, given that these outcomes might be thought as less influenced by social desirability than self-reports. To this reviewer, it appears that these outcomes were not seemed to be relevant to this review. If these outcomes were evaluated and all were found to not show even low evidence, this should be stated. The problem probably arises that there are other studies of meditation programs for physiological outcomes that were excluded perhaps because they didn't report the psychological outcomes. Were physiological outcomes not included because an assumption was made that "stress," affect, and the like mediate ALL physiological outcomes of meditation? If so, this assumption should be discussed. The problem is that it is likely that this would be readily challenged. Meditation may change physiological parameters that could influence medically relevant physiological outcomes independent of "stress," affect and pain. In general, throughout the report, the rationale for the outcomes included is presented but the rationale for NOT including physiological outcomes in the included studies was not stated as clearly.	
84.	[Peer reviewer 12]		: Inclusion criteria is well thought and justified. The use of only randomized studies is well supported. The exclusion criteria is also rigorous and well supported. The evaluation of bias, strength of evidence and its algorithm, the definition of precision, consistency and directness add to the rigor and strength of the paper.	Thank you
85.	[Peer reviewer 12]		Outcomes measures are well defined and consistent. Statistical methods: the use of multiple approaches (grading of strength of evidence, meta-analysis, contrast of relative differences) are clearly demonstrated and lead to clear conclusions	Thank you

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86.	[Peer reviewer 1]	Results	Line 17: Where are studies divided by these types? Looks like Mindfulness and Mantra only Figures C1 and C2: Effects marginally stronger for non-specific controls but SOE does not reflect control issues.	The ES has a summary figure of the results (Figure C1 & C2). The main report clearly divides studies by these types throughout the results section. SOE is not intended to reflect control issues since all controls are an active control.
87.	[Peer reviewer 1]	Results	P 23, line 10: huge exclusion. Were screening criteria too broad?	No, we felt they were appropriate.
88.	[Peer reviewer 1]	Results	P 28, line 12: You said a magnitude of 5-10% was clinically significant P 31, line 21: "positive outcomes are a key focus of meditative practices" What does this mean? Of course, one wants positive outcomes.	Yes We are referring to positive mental health outcomes such as well being.
89.	[Peer reviewer 1]	Results	P 37, line 31: What kinds of subjects enroll in these studies? How are they recruited? I suspect lots of self-selection.	See response to prior comment about self selection (comment #52)
90.	[Peer reviewer 1]	Results	P 45, Table 2: How were various measures of the same domain combined?	Please see methods: Data synthesis, where this is already described in detail.
91.	[Peer reviewer 1]	Results	P 47, line 21: Relative difference not used statistically? Line 29: standardized mean differences across measures? Line 55: "only one scale per outcome per trial" but different scales for different trials?	Please see methods: Data synthesis
92.	[Peer reviewer 1]	Results	P 48, line 15: "we prioritized using the scale that was most common in the group of studies" What does this mean?	Please see methods: Data synthesis.
93.	[Peer reviewer 1]]	Results	P 50, line 52: Weren't a lot of the outcomes intermediate?	We did not categorize outcomes as intermediate or not.
94.	[Peer reviewer 1]	Results	P 53, line 14: Were they highly selected? Figure 3: Why is not randomized used twice?	See prior comments on self selection (comment # 52). Articles on further review that appeared not randomized were excluded
95.	[Peer reviewer 1]	Results	P 72, line 14: Not much available on self-selection.	See prior comments on self selection.
96.	[Peer reviewer 2]	Results	There are several studies published in 2012 that should be incorporated in the review, and these are provided in the full set of comments below.	See our response to your detailed comments at end of document (comment #165)

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97.	[TEP - Reviewer 4]	Results	The general discussion in each section seems reasonable. Given the heterogeneity and small numbers, most comparisons have low or inconclusive strength of evidence. The main value is in summarizing the literature and providing data for future research. Overall, the figures and tables seem reasonable and easy to understand. The authors should update any tables and sections with new studies, if any were published in the time since the lit review was completed. I wonder if it would be helpful to have one summary table – perhaps with colors – to summarize the weight of the evidence by domain and type of meditation with the number of trials and total subjects – just as a visual way to display the findings in one table for non-specific controls and one table (or a 2nd part of the table) for active treatments.	We already do this in the ES Figure C1 & C2.
98.	[Peer reviewer 6]	Results	ES10: line 44 mentions a sensitivity analysis. Information is available in body of text but not ES methods for that. Either add to ES methods, or delete from the ES (I don't think the detail is critical to the ES.)	Sentence on sensitivity analysis was deleted from ES.
99.	[Peer reviewer 6]	Results	I find it easier to absorb and understand the key points in the body of the text with the number of trials and subjects included. Otherwise I keep going back and forth between the tables and the key points.	This information is already included in the summary Figure C1 & C2, as well as in the individual tables of SOE. We have added the figures C1 and C2 to the main report, along with more detailed synthesis tables for each outcome.
100.	[Peer reviewer 6]	Results	Results are reasonably described and displayed. Please see attachment for specific comments.	Thank you
101.	[Peer reviewer 7]	Results	The studies are well described. They simply did not include all the relevant cohort, waiting list, and TAU control group studies. They used the wrong criteria for evaluating studies of lifestyle interventions.	Please see prior response to comment #7.
102.	[Peer reviewer 8]	Results	d. Results: On page 21 a summary is presented of the trials that are included. There is one striking observation: There seems to be such a great variety in outcomes, clinical conditions, meditation techniques, geography, duration of treatment and training of instructors that one would recommend already at this stage to not proceed with further detailed analyses. The heterogeneity is striking, as the authors themselves describe when presenting results under each key question.	The greater heterogeneity makes the findings that much more generalizable.

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103.	[Peer reviewer 9]	Results	The amount of detail presented in the results section is appropriate, but the results may be seen as 'penny wise but pound foolish', that is, there is a lot of detail on an inadequate data set. The characteristics of the studies are clearly described. The key messages are explicit, but the focus on harmful effects may be inappropriate for the key questions because no such effects are reported. Perhaps this could be relegated to a separate section where this aspect can be summarized.	Some trials did report that they assessed harms as an outcome. We have conveyed this information to the reader in a separate section titled "Harms for all Key Questions" in both the ES and main report.
104.	[Peer reviewer 9]	Results	Page 24 "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."	See comment #103.
105.	[Peer reviewer 9]	Results	Page 28. It remains to be determined whether MBCT is a meditation technique or a cognitive therapy. As mentioned on page 37, it is difficult to ascertain the effects of meditation itself on various outcomes, separate from the effects of the exercise component.	See response to your comments #11 and 13.
106.	[Peer reviewer 9]	Results	The analysis combines the Transcendental Meditation technique with other techniques based on their use of a mantra, i.e., "mantra meditations." This common factor is not a defensible choice of aggregation because the techniques for using the mantras are in many cases quite different. The review is severely limited by a shortage of studies, but this might be remedied by a somewhat different set of selection criteria. The findings point to the need for further studies, and the review provides guidelines in terms of a best practice for meditation trial study design.	See response to your prior comments #10-14.
107.	[Peer reviewer 9]	Results	The authors deserve appreciation for their attempt at a comprehensive review article and for their attempts to clearly define inclusion/exclusion criteria for outcome measures and study design.	Thank you.
108.	[Peer reviewer 9]	Results	P. 41. Again, instruction in the Transcendental Meditation technique for adults and for youth above age 10 is essentially the same, so the rationale for excluding studies on adolescents is flawed.	See response to your previous comment # 27
109.	[Peer reviewer 9]	Results	P. 53. Remove the dash on line 26.	This was removed.

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110.	[Peer reviewer 9]	Results	P. 55. 417 articles were excluded due to movement-based meditation; should not this also exclude MBSR, which includes yoga?	No, see previous comments #16, 25, 68.
111.	[Peer reviewer 9]	Results	Also 49 articles were excluded based on healthy population, yet a number of other articles on healthy populations were included. Criteria should be followed consistently.	See previous comment #10.
112.	[Peer reviewer 9]	Results	P. 56. Some articles on subjects with cardiovascular disease (hypertension and congestive heart failure, for example) were included yet a number of equally qualified articles on hypertensives were excluded.	They were excluded based on our exclusion criteria, such as not having an active control.
113.	[Peer reviewer 9]	Results	P. 68. The article by Castillo et al. is rated high risk of bias. This is questionable as this was an NIH-funded study, but may not have reported the criteria required for passing the bias test.	We used the same criteria consistently across all trials. Funding source was not one of our criteria.
114.	[Peer reviewer 9]	Results	P. 84. The large percent improvement in depression in the Henderson et al and Gross et al trials should be checked. Using 'relative percent difference' may be a misleading method of presenting the data.	We have presented the data in two ways. See previous comment #3. Data has been checked.
115.	[Peer reviewer 9]	Results	P. 74. Including meditation techniques basically different from the Transcendental Meditation technique in one category of 'mantra meditation' obfuscates understanding of these different methods, and should be avoided. Page 97, line 18, needs a space after the period.	Please see prior comments #11,12, 22 Space was added after the period.
116.	[Peer reviewer 9]	Results	Page 113, line 14. 'Beck Anxiety Index' should be capitalized.	The Beck Anxiety Index was changed to its abbreviated form, "BAI," throughout the document.
117.	[Peer reviewer 9]	Results	Page 126 line 24. The rationale provided, i.e., "Given that the trials only substantially represented two continents, and the racial and ethnic makeup of the populations was not always specified" does not support the conclusion that it is unlikely that these findings would be applicable to a diverse patient population, especially given that the origin of many of the meditation techniques being studied is Asia, and the studies are done mostly in North America and Europe.	We have modified this statement to say: "Given that the trials only substantially represented two continents, and the racial and ethnic makeup of the populations was not always specified, it is unclear whether these findings would be applicable to more diverse patient populations."
118.	[Peer reviewer 9]	Results	Page 126 line 28, a number of studies have shown daily sessions of the Transcendental Meditation technique for the first week to be practical in outpatient settings. See Schneider et al, Circulation, 2012, for examples. Page 128. The Alexander et al. (1989) study also reported survival findings which are relevant to the review outcomes. Note that this study used a 'no treatment, delayed start control.'	We agree, and have modified the statement to say: Regarding the applicability of an intervention to a medical practice, both transcendental meditation and mindfulness trials involved training for about 10-40 hours over several weeks, , which makes them fairly practical in a typical outpatient setting.

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119.	[Peer reviewer 9]	Results	Page 129. Is the definition of outcomes measuring 'attention' too limiting – are there other studies that assess attention (in clinical populations)? Page 130 line 44, The acronym 'KQ' should be spelled out. Page 146 line 16 should read "…strength of evidence is low that mantra meditation programs have an effect on pain…"	We included any objective measure of attention, but found only one study. We have fixed this The statement on pain is correct in the original version.
120.	[Peer reviewer 9]	Results	Page 147. Pain is not as central a feature of CHF as dyspnoea, exercise intolerance, general lassitude, fatigue, fluid retention; the major positive outcome on improving CHF functional capacity is ignored.	Yes, please see response to comment #3 on primary vs secondary outcomes.
121.	[Peer reviewer 9]	Results	The description of the Taub et al. results as mainly favoring control ignores the very high rate at 18 months of total abstinence in the meditation group in this extreme population. Total abstinence is arguably the most important sign of successful rehab in severe alcoholism.	Tables 1-4 on pages 203-206 of the paper give the data for percent of days not drinking for each of the arms of the trial. There is no separate data for percent of individuals who were completely abstinent.
122.	[TEP - Reviewer 10]	Results	The results are comprehensive and details in general. Again we run into the issue that too many clinical conditions need to be covered, and it lacks of details for each specific condition to understand the true story a physician or a researcher is looking for. If the review is done by each specific question separately, and the results of different meditation programs are combined first, and then separate only if it makes sense, the result section could be more detailed and interesting. I did not get chance to read the entire results section carefully, but get that impression by reading the summary and conclusion.	Thank you

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123.	[Peer reviewer 11]	Results	The results are clearly stated, the figures are very clear and interpretable. The text might be strengthened if the meditation strategies employed in the trials among patients with irritable bowel syndrome could be identified. For those two sentences (page 23, lines 49 -52) the meditation strategies are not identified. Given that some of the trials reviewed also had no-treatment controls or usual care controls, it would seem meaningful to also report the differences between the treatments, the non-specific active controls and the third less active controls – when they were available. This would seem to add significantly to the report and to the potential interpretation. From the perspective of comparative effectiveness, it would seem particularly relevant to compare the effects of the three conditions when they were available. Although there were only about 7 studies included that addressed medical conditions in addition to pain or mood states, including the studies with patients at cardiovascular risk. For these studies, it seems relevant to report the effects of meditation on physiological outcomes. There is a note in the Discussion about one of these studies, where the effects of mindfulness-based cognitive therapy was described in terms of effects on relapse rates in patients in full or partial remission from a major depressive episode.	We have specifically focused on comparisons with the active controls, so only report on those comparisons. In this heterogeneous data set, this provides the most straightforward comparison across outcomes and studies. This comparison is also the basis for why we chose active control RCTs, and feel that is one of the most important contributions of the report. Regarding reporting on other outcomes: While trials reported on a number of primary outcomes, we only reported on those outcomes if they were a focus of our review. We have modified our review to report which outcomes were primary and which were secondary, as well as the proportion which were primary. Please also see: Comment # 3 We were unable to find the following comment. we suspect there is page error "For those two sentences (page 23, lines 49 -52) the meditation strategies are not identified"
124.	[Peer reviewer 12]	Results	On line 14 of page ES-16, the authors state: ..."four trials evaluated the effect of meditation on substance abuse...", and include references 33 through 38. These are actually 5 different studies. Similar inconsistencies are found elsewhere in the text. For example, on page 38, line 55, please review the references listed to ensure they properly match the text. Similarly review statements and corresponding references on page 96, lines 4, 5, 12, 13, 25, 16, 42. Please, review similar inconsistencies in other parts of the text. On page 66 line 24 the text states that there are "imprecise estimates. However, on Table 15, line 36 the Precision is described as "Precise". The Results are well organized, clearly presented, very detailed; studies are well described, conclusions well supported. Figures, tables, appendices cover are exhaustive in the description and synthesis of data.	Thanks for pointing out the reference mis-numbering. These have been corrected. Pg ES 16: This section was deleted and rewritten. Page 38: Text was rewritten and there are now 10 references. Page 96: These references were updated. Page 66: The table was corrected to say "Imprecise."

Comment #	Reviewer	Section	Comment	Response
125.	[Peer reviewer 13]	Results	First, in the table on page 32, you listed that ITT was not used, and the credibility was not comparable. We stated clearly in the report that ITT was indeed used, and the control group is the gold-standard for smoking cessation, so are not sure why this is considered not comparable (Q8).	For a trial to get points for using ITT, it could not merely state that it did ITT, it had to impute the missing data. We state this in our Methods, Assessment of Methodological Quality of Individual Studies, 2nd paragraph: “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.” While the smoking cessation paper indicates that all the individuals allocated were also analyzed, the methods section reports that “Incomplete data were handled using casewise deletion...” which indicates missing data were not imputed but rather discarded. Finally, the data we needed to estimate treatment effects is presented in Figure 2. The text indicates that this is only treatment exposed data. Due to these issues, and that the data we needed from this trial was not ITT, this paper unfortunately was not given those points. Credibility is a separate issue, explained in response to comment #64 Trials had to use a credibility scale to assess credibility.

Comment #	Reviewer	Section	Comment	Response
126.	[Peer reviewer 13]	Results	Second, the summary statement (below) misquoted the number of randomized subjects (n = 88), and also stated that there was a high risk of bias, and lack of direct measures and precise results. We are unclear as to how the risk of bias was deemed “high” as this was an URN randomized trial, with allocation concealed until subjects started their first group, using objective measures of abstinence. Also, the gold standard for precision using direct measures is carbon monoxide verified point prevalence abstinence, which we used. Finally, they report that there was a 21% higher abstinence, but unless they report this as an absolute difference, it can be misleading, as most reports base this relative number on the % of one group –in this case it would be a >100% higher level of abstinence as the mindfulness group had 36% abstinence and the Freedom From Smoking group had a 15% abstinence at that timepoint.	For all of our trials, we used the actual N that represented the effect size estimates. Since the treatment exposed sample were the raw data that were presented (n=71), that is the N we reported. The risk of bias assessment was applied consistently across trials. This trial had an attrition of 28 people (88-60) or 32% at the first follow up. It did not get points for this. Outcome assessors were not blinded. The paper itself does not mention anything about allocation concealment. For these reasons it scored 5/12 on our risk of bias. We rated trials with a score of 6-8 as medium risk of bias, and 9-12 as low risk of bias. We have modified the text to state that the percent abstinence differences are absolute differences, and have made a similar footnote on the difference in change graphs. Precision in our strength of evidence rating refers to statistical precision for the group of trials being evaluated under an outcome category.

Comment #	Reviewer	Section	Comment	Response
127.	[Peer reviewer 13]	Results	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.	See comment #126
128.	[Peer reviewer 1]	Discussion/Conclusion	Discussion/ Conclusion: Not a lot of insights on future research. Five points but no real discussion of what needs to be done.	This section has been revised.
129.	[Peer reviewer 1]	Discussion/Conclusion	P 153, line 19: Two trials of depression relapse patients worthy of more investigation. Specific subgroup.	This entire section has been revised due to updated evidence from newer trials.
130.	[Peer reviewer 1]	Discussion/Conclusion	P 158, line 41: Types of controls matter. What is a non-specific active control? It may induce reporting bias. Line 54: see comments on positive outcomes above (p 31 - Results)	This is described in detail in Methods.
131.	[Peer reviewer 1]	Discussion/Conclusion	P 159, line 20: Conclusions seem strong for a review that shows mostly no effect. Important to note the high risk of bias. Observation the ROB did appear to affect outcomes is interesting. Would like to see more about participants and applicability.	These have been revised based on updated evidence from new trials.
132.	[Peer reviewer 1]	Discussion/Conclusion	P152, line 43: What do you want to make of the Korean study?	When we took it out of the anxiety analysis, it did not change our conclusions. This is reflected in the results section.

Comment #	Reviewer	Section	Comment	Response
133.	[Peer reviewer 2]	Discussion/Conclusion	This section can be strengthened by tying in the review with previous reviews on the topic and comparing program effects to other gold standards of treatment such as CBT, see full set of comments below.	See below at end of this document.
134.	[TEP Reviewer 4]	Discussion/Conclusion	Overall, the discussion seemed very complete and "even". If the authors have any idea which of their limitations, for example, is likely to be most important, that would be helpful information. As it stands now, we do not have a clear sense of how important the various potential limitations are in practice. On page 124, line 29 "to review the highest standards of behavioral randomized controlled" is confusing and should be reworded.	We do not suggest that there was a main limitation. We do discuss several limitations that we believe readers should be aware of. We've described in detail the important issue of control selection which is a high bar for behavioral RCTs in our introduction and methods. The statement appeared appropriate to us, and has been left unchanged as others have not commented on it being confusing.
135.	[Peer reviewer 6]	Discussion/Conclusion	ES18/Pg 123 Future research directions – We may not yet have an appropriate understanding of outcome measures to use. Current measures have been developed under medical/health rubrics that emphasize cure and improvement where possible. Meditation practices have developed, in contrast, not for health purposes and general emphasize ending suffering through observing what is real and promoting an acceptance that is quite different from Western philosophical traditions. As an example, current research into constructs such as the self-compassion scale may be beneficial. Likewise, our developed pain scales may or may not be appropriate to anticipated meditation outcomes. It is a cautious balance to walk – maintaining pragmatic support within healthcare settings for a lifestyle practice that is not itself contained within a Western health rubric. Meditation is about human flourishing.	We note in our introduction subheading "Forms of Meditation": " It should be noted that although this report evaluates the health effects of meditation programs, meditation historically was not necessarily practiced for a specific health benefit. For many the goal was either philosophical or spiritual enlightenment, a sense of mental and physical peace and calm, self-inquiry, or a combination of these. Our review does not include these more classic goals of meditation, but instead focuses primarily on health benefits. We respectfully acknowledge that some experts regard this focus on specific health outcomes as a diversion from what meditation research should ideally evaluate. We do not elaborate on this further.
136.	[Peer reviewer 6]	Discussion/Conclusion	Yes. Future research section focused appropriately on methodological lessons learned that will help the field to generate stronger and more useful research.	Thank you
137.	[Peer reviewer 7]	Discussion/Conclusion	Basically, the study was set up to find that existing research lacks methodologic rigor and more research needs to be done in the drug-trial model. This is a tautology since lifestyle therapies are not drugs and should not be evaluated on the same basis as drug trials.	Please see prior response to comment # 69.

Comment #	Reviewer	Section	Comment	Response
138.	[Peer reviewer 8]	Discussion/Conclusion	e. Discussion/ Conclusion: 1. The authors use the discussion section to again reiterate the results described in detail under the results section and in the executive summary. This is totally unnecessary.	We have re-written much of the discussion section.
139.	[Peer reviewer 8]	Discussion/Conclusion	2. The authors do describe in the discussion section most of the challenges that I have outlined above, but they avoid drawing the most obvious conclusion: This report cannot inform clinical practice in any meaningful way with regard to potential benefits of meditation. Their conclusion should have been that the research literature currently gives little or no guidance with regard to the clinical benefits of meditation.	We do not share this view. Please see our revised discussion and conclusion.
140.	[Peer reviewer 9]	Discussion/Conclusion	Discussion/ Conclusion: The implications of the major findings are clearly stated, and some limitations were adequately described—not the important ones listed in this critique. Important literature is omitted. The review should also be broadened to take into account the results of previous meta-analyses, which may contradict/support the current findings. There has been 40 years of research on meditation. For example, a recent meta-analysis conducted by researchers at Chemnitz University in Germany evaluated anxiety reduction from meditation practice. The studies included were not limited to RCTs. Other meditation and relaxation treatments in these meta-analyses provide a wide range of controls for attention, expectation, social support, etc. that support conclusions regarding non-specific effects on reducing anxiety. See: Sedlmeier P, Eberth J, Schwarz M, Zimmermann D, Haarig F. The Psychological Effects of Meditation: A Meta-Analysis. Psychological Bulletin. 2012;Online First Publication, May 14(doi: 10.1037/a0028168). Also Eppley et al. included RCTs, as well as weaker designs in their review. Eppley K, Abrams AI, Shear J. differential effects of relaxation techniques on trait anxiety: A meta-analysis. Journal of Clinical Psychology. 1989;45(6):957– 974.	Please see response to comment # 19 regarding the Seldmeier review, and response to comment #12 regarding Eppley review.

Comment #	Reviewer	Section	Comment	Response
141.	[Peer reviewer 9]	Discussion/Conclusion	The AHRQ report included only studies that used active control groups to control for non-specific effects, which is laudable. But there can be problems interpreting such studies. For example, in a study on anxiety prominently cited in the review, Smith (1976), reduction of anxiety might have been cross-validated by studies showing it reduces autonomic correlates of anxiety, such as respiratory rate, skin resistance, and plasma lactate. Some types of meditation also reduce cortisol, a major stress hormone in humans, and reduce stress reactivity. The abstract of the AHRQ report states: "We need more research using adequately powered high-quality randomized controlled trials that address the effects of meditation programs on stress and its correlates." Yet, the review ignored precisely the studies that included that information, the physiological and medical correlates of stress.	Please see response to prior comments on these issues (comment 19 on cross validation, and comments 2, 16, 17 on emphasizing psychological stress).

Comment #	Reviewer	Section	Comment	Response
142.	[Peer reviewer 9]	Discussion/Conclusion	I feel one of the most valuable aspects of this review is that a future research section will be an important guide for those planning future studies and publishing in these areas. The future research section should be clarified so it can be better translated into new research by addressing the complexities of active control group design and suggesting ways to cross-verify conclusions, e.g., with physiological measures which address the questions being posed, e.g., survival is an important variable to consider when addressing the issue of well-being.	The following paragraphs have been added to the future directions section: "Second, trials need to document the amount of training clinicians provide and patients receive, in addition to documenting 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. With this type of data, analyses of "dosing" can address the question that remains unclear: how much is enough to accomplish each outcome of interest? As the literature develops and these dosing issues are addressed, randomized trials may be indicated to test the effects of dosing on outcome. Amount of training interacts with time to follow-up and few trials in our review assessed long-term outcomes. One notable exception was the trial by Schneider et al., which followed patients for up to nine years and assessed effects on mortality. Additional high quality studies with long-term follow-ups are needed to fully examine the effects of "dosing" and the potential impact of meditation on objective indices of health including mortality. "Sixth, we were unable to review biologic markers of stress comprehensively for meditation programs, nor were we able to evaluate the effects of meditation programs that involve more movement such as yoga and Qi Gong, nor did we review the effects on healthy populations. Numerous trials have been conducted in these areas, and meditation research may benefit from a comprehensive review covering these areas. Such reviews would allow for a cross validation of psychological and biological outcomes."
143.	[TEP - Reviewer 10]	Discussion/Conclusion	The discussion and conclusion is thorough and reasonable. The major findings based on the planned framework are stated	1) We have reported teacher characteristics where it was available, and indicated the

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			clearly. The limitations are well discussed. On the limitations of the primary studies, one of them could be that, most of these clinical studies are designed by experienced clinicians or researchers who are not really meditaters themselves, and hardly any true master meditaters were involved in research design or meditation training so that the clinical outcomes reflected mostly the interests of scientists or clinicians, not the mind-body practitioners. When researchers and clinicians tried to standardize the meditation program (like MBSR) to fit into the need of massive training and randomized controlled trial, the process of training individual for stress management differently so as to fit individual's need, personality and situations was not even mentioned in most research design. In a true stress management program by meditation, the trainer or master would be able to identify the patient's primary problem, rate it and work on it first with a more feasible and acceptable way to help patient to reach the mindfulness state effectively. In many meditation programs, it is the actual mind state (such as be aware of here and now, acceptance, or let go) that makes a big difference in the practitioner's health or life, not necessarily the form or amount of meditation practice. I have noticed that studies from eastern countries (Indian, Korean and China) tend to report stronger effects of meditation than those from western countries, it could be related to quality of studies, but it could also reflect the fact that researchers in eastern countries may understand the meditation better, or had good training themselves before conducting meditation research. One of the limitations of the review could be the general strategy chosen for this review – when you try to focus on studies among clinical populations with active control, many outcomes relevant to meditation may not be measured in clinical studies since most quality clinical trials, especially those with active control, tend to be focused on improvement of clinical conditions, not general perceived stress, well-being or attention issues. In order to evaluate the outcomes relevant to meditation programs, the review need expand to the studies with general population, instead of clinical population only. The future directions are laid out well, I agree with most of them, except the amount of training clinicians provide and patients receive, which may not be directly related to clinical	importance of paying attention to teacher qualifications (Discussion, Future Directions): "Third, studies should report teacher qualifications in detail. A highly-experienced teacher may have a very different effect than an inexperienced teacher, yet the current literature does not provide enough detail to examine this systematically. 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 or practice likely plays a role in outcomes." 2) We cite not including healthy populations as a limitation (Limitations of the Review): "Stress outcomes encompass both psychological and biological markers, yet we focused only on the psychological markers. This may disappoint some readers and may have reduced the number of transcendental meditation trials included, since many recent trials have been more focused on physiologic markers of stress. However, studies that included measures of psychological stress and well being, even as secondary outcomes, were included and contribute to our overall inclusions. An interesting challenge for future work is raised by the findings of one particularly strong transcendental meditation study. Paul-Labrador and colleagues compared transcendental meditation to a health education control condition in patients with congestive heart failure and found reductions in adjusted systolic blood pressure, heart rate variability and insulin resistence in the absence of concurrent changes in anxiety, depression, or stress. Given the absence of changes in measures of psychological stress in this study, these authors postulate that meditation may alter the biologic

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			outcomes, since a truly effective meditation program does not need a lot of trainer-trainee interaction or a lot of time in training; it may need some practice and it needs touch the key quickly to reach the specific mindset – either being mindful, let go or being positive & grateful. If we have "better measurement tools", as the authors pointed out, we would be able to see that different trainers may create different outcomes even with the similar meditation program, not necessarily correlated with length of training or practice. Another dilemma frequently encountered in meditation studies is balance of available resources and high research standard. There have been very limited funding for meditation studies, many researchers conducted clinical studies without funding or with very limited funding, even many NIH funded clinical trials of meditation still used waiting-list control or usual care as control since it was the most affordable way to carry out the protocol with the limited funds. The demand for high quality studies with active control in design need the support of more research funding to this field so that serious scientists can afford to conduct large scale and high quality clinical studies that meet both clinicians' demand for good evidence and the practitioners' demand for true meditation practice.	stress response independently of psychological stress responses, a hypothesis that will need to be directly tested in future research. "In addition to limiting our focus to psychological stress and well being outcomes, we also limited the types of meditation included. We chose not to include other eastern meditative traditions such as Qi Gong and yoga. These forms typically involve movement and published reports often do not clearly indicate whether the form practiced was purely or mostly meditative or not. In our initial review of papers for inclusion, we were unable to accurately identify QiGong trials that emphasized movement from those that did not. We also did not include healthy populations." 3) amount of training - earlier you commented that short training spans may not be enough time to see effects, suggesting that one is looking for some level of training to become proficient? It appears this may depend on the type of meditation program. We discuss this theoretical issue in the introduction (Introduction, Forms of Meditation) and discuss this in Future direction first paragraph. 4) We agree that funding of trials is a barrier to conducting high quality trials, but this is related to several other factors that are beyond the scope of this review.
144.	[Peer reviewer 11]	Discussion/Conclusion	The Discussion included, as noted above, specific notes about certain trials or sets of trials. It seems like it would be helpful to add some detail as to whether these studies had any effect on physiological outcomes. If there is an effect on physiological outcomes, it would be important to note this. If there is no effect, it would add important information to the conclusion that the effects of mantra meditation on the outcomes were, as the authors state, "consistently null." The discussion of limitations is fine as far as it goes. If it is not possible to report on the effects of meditation on outcomes other than mood states and pain, this reviewer would recommend that a limitation be added the states that the effects	RE physiological outcomes: We have added this as a Limitation of the Review, 3rd para. Please see response to comment #143 above, item #2. We also added a related paragraph to the Future Directions section: "Sixth, we were unable to review biologic markers of stress comprehensively for meditation programs, nor were we able to evaluate the effects of meditation programs that involve more movement such as yoga and Qi Gong, nor did we review the effects on healthy populations. Numerous trials have been

Comment #	Reviewer	Section	Comment	Response
			of meditation on physiological outcomes were not evaluated in this report. This limitation needs to be made very clear to avoid misinterpretation. Please see additional comments in the "General Comments" Section. In making recommendations about future directions, in addition reporting on amount of training participants received and the amount of home practice recommended, a relative weakness in much of the meditation research to date is that self-report of adherence to home practice is often not included. Just as research is needed to validate the scales used in these studies, such as the mindfulness scales, there is a need for validating home practice diaries or for more direct measures of adherence to prescribed practice.	conducted in these areas, and meditation research may benefit from a comprehensive review covering these areas. Such reviews would allow for a cross validation of psychological and biological outcomes." RE home practice, we have modified our paragraph in the Future Directions section to read: "Second, trials need to document the amount of training clinicians provide and patients receive, in addition to documenting 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. With this type of data, analyses of "dosing" can address the question that remains unclear: how much is enough to accomplish each outcome of interest? As the literature develops and these dosing issues are addressed, randomized trials may be indicated to test the effects of dosing on outcome. Amount of training interacts with time to follow-up and few trials in our review assessed long-term outcomes. One notable exception was the trial by Schneider et al., which followed patients for up to nine years and assessed effects on mortality. Additional high quality studies with long-term follow-ups are needed to fully examine the effects of "dosing" and the potential impact of meditation on objective indices of health including mortality."

Comment #	Reviewer	Section	Comment	Response
145.	[Peer reviewer 12]	Discussion/Conclusion	There is a comprehensive review of the limitations of the studies and the review itself. The future directions give important considerations to the practices that need to be in place to improve the quality and relevance of meditation studies, to make them comparable and elevate their standards to those by which other behavioral interventions are judged. These recommendations can only help to give credibility to the studies and to improve their applicability in more diverse settings, conditions and populations.	Thank you
146.	[TEP - Reviewer 4]	Future research needs	the paragraph (p 123, 18-27) on developing meditation skills is a little confusing. If the authors aim to suggest that we need to measure "skill at meditation" more directly, they should be more specific about this.	We have revised this paragraph to read: " First, all forms of meditation, including both mindfulness and mantra, imply that more time spent meditating will yield larger effects, especially in changing health outcomes including psychological stress and well being. Most forms, but not all, also present meditation as a skill in which skill development occurs over time and is most efficiently achieved by learning from an expert. 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. When compared with other skills that require training, the amount of training in the trials we reviewed was quite small and generally offered over a fairly short period of time. Some of this is due to the challenging logistics of conducting RCTs, and some of this is due to the meditation programs tested (e.g., MBSR is a standardized 8-week program). There was little delineation on exactly what skill novice practitioners are acquiring, or measurement or validation that the skill was being practiced and applied. Given that meditation in its historical forms has been a long-term practice, consideration should be given to placing a greater emphasis on developing the skill. To facilitate this, we need better measurement tools. The currently available mindfulness scales have not been well validated and do not appear to distinguish

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				different forms of meditation.26 Thus, further work on the operationalization and measurement of mindfulness or the particular meditative skill is needed. For those meditation programs that do not believe they are training students in a skill, such as TM and certain mindfulness programs, there is still a need to be able to transparently assess whether a student has attained the mental state or is correctly executing the recommended mental activities (or absence of activities).
147.	[Peer reviewer 8]	Future research needs	3. The authors' recommendations for the future are a mixture of clinical recommendations to the meditation field, and methodological improvements in the research. All recommendations are well-justified, and again underline the lack of meaning in the results obtained in the review.	If having clinical meaning implies we must see large effect sizes, we are certainly not seeing that. However, we do see small and relatively consistent effect sizes for some outcomes, and feel it is important for readers to know that.
148.	[Peer reviewer 9]	Future research needs 1	Page 30 Future directions "Meditation is a skill, more training with an expert and more practice in daily life should lead to greater competency". It seems the authors have a misunderstanding of the concept of meditation, as certain techniques of meditation, such as Transcendental Meditation, may not be considered a skill. Once learned, it is not greater competency that is gained with daily practice but something entirely different. For example, Travis and Arenander (2006) found that EEG coherence increases during this technique over the first two months as a step function, and does not increase further with extended practice. However, EEG coherence outside of meditation during a computer task continues to increase linearly over the year-long study. See: Travis FT, Arenander A. Cross-sectional and longitudinal study of effects of Transcendental Meditation practice on interhemispheric frontal asymmetry and frontal coherence. International Journal of Neuroscience 2006 116(12):1519-38.	These have been revised. Please see comment #146 and comment # 6.

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149.	[Peer reviewer 8]	Future research needs 2	Page 153 line 47 “Although it would appear that mantra meditation programs do not have an effect on stress,” should be qualified with “ … in the two studies examined, in which stress was not the primary outcome measure…” Page 157 line 20. The assertion that —”Also, because meditation requires behavior change and skill development...” does not apply to the Transcendental Meditation technique and may not apply to most other types of meditation.	Pg 153: this paragraph was deleted and new section added. Pg 157: Although it does not affect the issue of self selection we are trying to make, we have revised this statement to say: “Also, because some meditation programs require 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.”
150.	[Peer reviewer 9]	Future research needs 3	Page 157, line 50. The same precaution applies to the assertion that — “The personal characteristics of individuals (e.g. personality, spirituality, education, etc.) may influence their understanding and skill in performing meditation....” This is not true with respect to the Transcendental Meditation technique and may not apply to other types of meditation.	We have modified this statement (under Limitations of the Review, 7th paragraph) to read: “The personal characteristics of individuals (e.g. personality, spirituality, education, etc.) may influence their understanding and skill or abilities in performing meditation.”
151.	[Peer reviewer 9]	Future research needs 4	Page 158 line 18. The assertion that —”since meditation is a skill, more training with an expert and practice in daily life should lead to greater competency in the skill...” As noted above, this is misleading and does not apply to Transcendental Meditation and may not apply to other types of meditation. Shear distinguishes practice-makes-perfect approaches and state-enlivening approaches (Shear, 2011). In practice-makes-perfect approaches, during meditation one practices the benefits one wants to gain in activity, for example, non-judgmental awareness, compassion, or focused attention during meditation, to gain those qualities in daily life. For these approaches, meditation is practicing a skill, and more training will lead to more competency. By contrast, in the ‘state enlivening’ approach the goal is to settle into the state of pure consciousness that transcends practicing anything. It is a state of ‘no doing’. Yet in activity one gains benefits such as greater focus, broader comprehension, more compassion, etc. because of enlivening a more integrated state of functioning of the nervous system. See: Shear, J. (2011). State-enlivening and practice-makes-perfect approaches to meditation. Biofeedback, 39(2), 51-55.	We have modified the first paragraph of this section. Please see comment #146.

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152.	[Peer reviewer 9]	Future research needs 5	Page 158, line 38. "...the range of experience in meditation and competence as a teacher of this skill likely plays a role in outcomes..." again may not apply to TM, where teachers undergo intensive training such that a newly trained teacher is expected to provide the same instruction in the technique as an experienced teacher. This is based on over five decades of use of a well-standardized teacher training protocol. Therefore this assertion does not apply to all types of meditations. Page 158, line 47. "require" should be "requires".	The idea that the TM organization *expects* newly trained teachers to provide the same instruction as experienced teachers has nothing to do with our statement about whether we can transparently tell if they actually do provide the same, similar, dissimilar, different emphasis, or completely different training to certain students. It also tells readers nothing about what they are actually teaching, how they are teaching it, what variations exist within the teaching paradigms, how differently the teachers themselves understand the concepts, and what it is that makes TM teachers think they are innocently transcending but users of other mantra traditions not transcending. Despite the number of decades of this program has been in place, it has not shed any light on these issues. Require was changed to requires.
153.	[Peer reviewer 6]	Minor	ES11: Line 28- "These are represented as solid grey boxes…" These boxes are found in tables in the body of the text. Consider either removing the sentence or amending to direct reader to full report.	This was deleted.
154.	[Peer reviewer 6]	Minor	This is completely silly, but for some reason kept pulling my attention away – the report is missing commas between reference numbers. Entirely something that can be handled at final edit clean-up, but there you have it.	We have fixed it
155.	[Peer reviewer 9]	Minor	"Recipients" is misspelled in the first paragraph of the discussion.	Entire section rewritten
156.	[Peer reviewer 1	Clarity and usability	Report is well organized and thoughtful. I am not sure there is much there to inform policy, but that is not the fault of the reviewers.	Thank you
157.	[Peer reviewer 2]	Clarity and usability	The manuscript structure is organized in a pattern that can be readily understood.	Thank you

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158.	[TEP - [Reviewer 4]	Clarity and usability	Overall, the report is fairly clear and appropriately organized. Unfortunately, the studies have so many heterogeneous features and the number of studies is sparse for many comparisons that clear conclusions are lacking for virtually all of the domains. This diminishes the practicality of the report, although it is a clear summary of the literature for future researchers.	The updated review provided 10 more trials, which provided more evidence for more domains. However, the lack of evidence is more true for the mantra trials, and is acknowledged in Discussion for KQ1: "First, there were very few mantra meditation programs included in our review. This significantly limited our ability to draw inferences about the effects of mantra meditation programs on psychological stress-related outcomes. Of the four transcendental meditation trials, three were well designed trials rated as low risk of bias and conducted in cardiac patients, while one was rated as high risk of bias and conducted in anxiety patients. Among the other mantra trials, both were rated as medium risk of bias. Based on the available evidence from these trials, we found no evidence that mantra meditation programs have an effect on psychological stress and well being as compared to a nonspecific active control. These conclusions did not change when we evaluated transcendental meditation separately from other mantra. Apart from the paucity of trials, another reason for seeing null results may also be due to the type of populations studied (e.g. three transcendental meditation trials enrolled cardiac patients, while only one enrolled anxiety patients), and whether these study participants had high levels of a particular negative affect to begin with."
159.	[Peer reviewer 8]	Clarity and usability	Clarity and Usability: The report is technically well structured. The main challenges of the meditation research literature are communicated, but at the same time the authors attempt to get meaningful results out of this heterogeneous and low-quality volume of research papers. The conclusions about clinical effect are thereby not as clinically meaningful as one would hope (see my previous comments)	Thank you

Comment #	Reviewer	Section	Comment	Response
160.	[Peer reviewer 9]	Clarity and usability	f. Clarity and Usability: Comment on the AHRQ's review process. A major problem in this and other AHRQ reviews is that the AHRQ review process does not adhere to the accepted standards of science that professional journals require. When peer reviewed journals send submitted papers to independent outside reviewers to critique, the authors of the submission must address the weaknesses and flaws identified by the reviewers and incorporate changes into the submission to the satisfaction of the reviewers before the paper is published. AHRQ invites outside professional as well as public reviews, but meeting the reviewers' criticisms and incorporating them into their review does not happen. These steps need to involve the reviewer beyond the submission of his/her review. Revisions must be made that satisfy the reviewers' criticisms before publication. It should be mandatory that research issues identified by invited outside reviewers be resolved to the satisfaction of the reviewer and incorporated into the report before it is published. This may include extensive reanalysis of data as well as rewriting of the report before it is issued. Otherwise, there is no accountability to the scientific community.	We disagree. Please see response to comment # 19.
161.	[TEP-Reviewer 10]	Clarity and usability	The structure and organization of this report is generally good, and highly readable. It may partially reflect the current state of evidence in meditation studies for stress reduction among clinical populations. However, it may not really add much to the literature or our knowledge of meditation programs due to its self-imposed restrictions and selection criteria, and a unique framework to examine a variety of stress-related outcomes among clinical populations with a high standard of inclusion. It is not clear on its usefulness to inform policy makers or healthcare professionals on whether or not to adapt meditation program in standard care since there is still a lack of high level of evidence, although many patients and practitioners reported miraculous results. It does point out, or need to point out the need for more high-quality studies in the field, which need more funding and sophisticated research design.	Our intent was to summarize the strength of evidence for our key questions, and feel the information does provide a greater understanding of the magnitude and direction of effects for various outcomes.

Comment #	Reviewer	Section	Comment	Response
162.	[Peer reviewer 11]	Clarity and usability	Please see General Comments. The report is well organized but has the problem this reviewer has highlighted which has to do with the fact that it is very circumscribed, focusing on an important but limited set of outcomes that do not reflect "health and well-being" as the term is used -- that is to reflect physical (and psychological) well-being. The report, when abstracted and reported in the media is vulnerable to being over-interpreted as having included physical health outcomes. Thus the very modest effects observed for the limited number of outcomes, i.e., negative affect and pain, will be assumed to be the only effects of meditation programs. It is likely to be assumed that meditation did not have effects on physiological or physical health related outcomes. Thus, unless the title is changed or the point is made exceptionally clear that this report is very limited and CANNOT be interpreted as saying anything about physical health outcomes, some conclusions, policy and practice decisions regarding a broader definition of well-being, including physical health, drawn from a quick reading of this report are likely to be misinformed.	We have made these changes to reflect that the report focuses on psychological stress outcomes.
163.	[Peer reviewer 12]	Clarity and usability	The report is very well structured, very comprehensive and well organized. It elevates the standards by which to model future reviews. Its conclusions serve to inform better research and clinical practices; the ability to inform policy, however may require that the the field of meditation research address first all the limitations that this review highlights.	Thank you
164.	[Peer reviewer 9]	Additional comments	References listed as 'Not relevant to key questions' Meta-analysis is an objective process, as far as the mathematics of quantifying the effects of a body of studies is concerned. Where subjective bias can creep in is in the selection of what studies to include. The guiding principle for what studies to include should be the best controlled and most relevant ones for addressing the major question being posed by the analysis, which in this case is stated as follows: "This report reviews the efficacy of meditation programs on stress related outcomes among those with a clinical condition." Yet this report excludes meditation studies on hypertension, chronic heart failure, arterial sclerosis, and other aspects of cardiovascular disease, which are documented to be stress-related. These RCTs used active treatment control groups to control for non-specific effects such as expectation, attention, social support,	W e have reviewed these studies but only included any that fit our inclusion criteria. We included the following studies in our review: Schneider RH, Grim CE, Rainforth MV, Kotchen T, Nidich SI, Gaylord-King C, Salerno JW, Kotchen JM, Alexander CN. Stress reduction in the secondary prevention of cardiovascular disease: randomized, controlled trial of Transcendental Meditation and health education in blacks. Circulation: Cardiovascular Quality and Outcomes 2012: 5(6):750-758. Paul-Labrador M et al. Effects of a randomized controlled trial of Transcendental Meditation on components of the metabolic syndrome in subjects with coronary heart disease. Archives

Comment #	Reviewer	Section	Comment	Response
			amount of contact time with the instructors, and other factors. Yet, studies with subjective outcomes, such as pain perception, were included. Exclusion of studies on hypertension, CVD outcomes, and mortality data does not seem logical when weight and pain are included. Some or all the following should be reconsidered with new criteria. Barnes VA, Orme-Johnson DW. Prevention and treatment of cardiovascular disease in adolescents and adults through the Transcendental Meditation Program: a research review update. Current Hypertension Reviews 2012 8(3):227-242. Barnes VA, Schneider RH, Alexander CN, Rainforth M, Staggers F, Salerno, J. Impact of Transcendental Meditation on mortality in older African Americans with hypertension—eight-year follow-up. Journal of Social Behavior and Personality 2005 17(1):201-216. Barnes VA, Treiber FA, Turner JR, Davis H, Strong WB. Acute effects of Transcendental Meditation on hemodynamic functioning in middle-aged adults. Psychosomatic Medicine 1999 61(4):525-531. Schneider RH, Alexander CN, Staggers F, Orme-Johnson D, Rainforth M, Salerno J, Sheppard W, Castillo-Richmond A, Barnes VA, Nidich SI. A randomized controlled trial of stress reduction in African Americans treated for hypertension for over one year. American Journal of Hypertension 2005 18(1):88-98. Schneider RH, Alexander CN, Staggers F, Rainforth M, Salerno JW, Hartz A, Arndt S, Barnes VA, Nidich SI. Long-term effects of stress reduction on mortality in persons >/=55 years of age with systemic hypertension. American Journal of Cardiology 2005 95(9):1060-1064. Schneider RH, Staggers F, Alexander CN, Sheppard W, Rainforth M, Kondwani K, Smith S, King CG. A randomized controlled trial of stress reduction for hypertension in older African Americans. Hypertension 1995 26(5):820-827. Alexander CN, Schneider RH, Staggers F, Sheppard W, Clayborne BM, Rainforth MV, Salerno J, Kondwani K, Smith S, Walton K, Egan B. Trial of stress reduction for hypertension in older African Americans: II. Sex and risk subgroup analysis. Hypertension 1996 28(2):228-237 P. 306 right column – referencing error: latter two of three Schneider hypertension references are missing journal name: Hypertension, and American Journal Cardiology, respectively.	of Internal Medicine 2006 166:1218-1224.

Comment #	Reviewer	Section	Comment	Response
			Schneider RH, Alexander CN, Staggers F, Rainforth M, Salerno JW, Hartz A, Arndt S, Barnes VA, Nidich SI. Long-term effects of stress reduction on mortality in persons >/=55 years of age with systemic hypertension. American Journal of Cardiology 2005 95(9):1060-1064. Schneider RH, Staggers F, Alexander CN, Sheppard W, Rainforth M, Kondwani K, Smith S, King CG. A randomized controlled trial of stress reduction for hypertension in older African Americans. Hypertension 1995 26(5):820-827. With regard to RCT studies that may have been overlooked, the following are suggested: Brooks JS, Scarano T. Transcendental Meditation in the treatment of post-Vietnam adjustment. Journal of Counseling and Development 1985 64:212-215. This study has a clinical population and active treatment control. This study was listed on p. 285 as 'not randomized' – but the paper says it was randomized, even in the abstract. The randomization procedure is described in the paper, allocating to TM or psychotherapy by odd and even recruitment numbers respectively. Nidich S, Rainforth M, Haaga D, Hagelin J, Salerno J, Travis F, Tanner M, Gaylord-King C, Grosswald S, Schneider R. A randomized controlled trial on effects of the Transcendental Meditation program on blood pressure, psychological distress, and coping in young adults. American Journal of Hypertension 2009 22(12):1326-1331. This is a wait-listed study that showed decreased total psychological distress, anxiety, depression, and anger/hostility; and improved coping. A number of other studies were done with college students, such as the Nidich (2009) study above, but these may have been excluded for lack of a clinical population. Schneider RH, Grim CE, Rainforth MV, Kotchen T, Nidich SI, Gaylord-King C, Salerno JW, Kotchen JM, Alexander CN. Stress reduction in the secondary prevention of cardiovascular disease: randomized, controlled trial of Transcendental Meditation and health education in blacks. Circulation: Cardiovascular Quality and Outcomes 2012: 5(6):750-758. This study had an active control, clinical population, found reduced anger expression as well as significant outcome for primary end-point on major reduced CV events and BP reduction. Nidich SI, Fields JZ, Rainforth MV, Pomerantz R, Cella D,	

Comment #	Reviewer	Section	Comment	Response
			Kristeller J, Salerno JW, Schneider RH. A randomized controlled trial of the effects of Transcendental Meditation on quality of life in older breast cancer patients. Integrative Cancer Therapies 2009 8(3):228-234. This study had active control – specifies controls given literature on breast cancer from official sources (so not just 'usual care'), clinical population, improved QOL, mental health, emotional well-being, social well-being. Nidich SI et al. Reduced symptoms of depression in older minority subjects at risk for cardiovascular disease: randomized controlled mind-body intervention trials. Paper presented at 31st Annual Meeting of the Society of Behavioral Medicine, 9 April 2010, Seattle, Washington, USA. Had active control, clinical population, decreased depression. (Two randomized controlled trials investigated depression levels in subjects aged over 55 who were at increased cardiovascular risk: respectively, Native Hawaiians with at least one other major cardiovascular risk factor; and African Americans with ultrasound evidence of carotid artery atherosclerosis. TM decreased depressive symptoms over a 9-12 month period compared to controls who received health education.) Paul-Labrador M et al. Effects of a randomized controlled trial of Transcendental Meditation on components of the metabolic syndrome in subjects with coronary heart disease. Archives of Internal Medicine 2006 166:1218-1224. TM also increased stability of the cardiac controlling autonomic nervous system – should this result have been mentioned? Broome JRN et al. Worksite stress reduction through the Transcendental Meditation program. Journal of Social Behavior and Personality 2005 17:235-276. A controlled prospective study of employees at a South African firm found that TM was effective in reducing psychological stress and decreasing both systolic and diastolic blood pressure over a five-month period. Other RCTs to consider: Travis F, Haaga DA, Hagelin J, Tanner M, Nidich S, Gaylord-King C, Grosswald S, Rainforth M, Schneider RH. Effects of Transcendental Meditation practice on brain functioning and stress reactivity in college students. International Journal of Psychophysiology 2009 71(2):170-176 This study was wait-	

Comment #	Reviewer	Section	Comment	Response
			listed controlled. Wilson AF, Honsberger RW, Chiu JT, Novey HS. Transcendental Meditation and asthma. Respiration 1975 32(1):74-80. Fields JZ, Walton KW, Schneider RH, Nidich SI, Pomerantz R, Suchdev P, Castillo-Richmond A, Payne K, Clark ET, Rainforth M. Effect of a multimodality natural medicine program on carotid atherosclerosis in older subjects: a pilot trial of Maharishi Vedic Medicine. American Journal of Cardiology 2002 89(8):952-958. Note that Elder et al., was included which was also multimodal. MacLean CR, Walton KG, Wenneberg SR, Levitsky DK, Mandarino JV, Waziri R, Hillis SL, Schneider RH. Effects of the Transcendental Meditation program on adaptive mechanisms: changes in hormone levels and responses to stress after four months of practice. Psychoneuroendocrinology 1997 22(4):277-295. Brautigam E. Effects of the Using the Transcendental Meditation program on drug abusers: a prospective study. In DW Orme-Johnson, JT Farrow. Scientific Research on Maharishi's Transcendental Meditation and TM-Sidhi programme: Collected Papers, Volume 1 (pp.506-514). Rheinweiler, West Germany: MERU Press, 1977.	
165.	[Peer reviewer 2]	OVERALL	OVERALL Comment 1: Indicate in abstract and title that the review findings represent "clinical adult populations" Comment 2: The Background section can be strengthened to develop a stronger rationale describing why such a review is needed at this very time in the history of science on meditation. A main concern is that a variety of outcomes are assessed and grouped as "stress-related outcomes"; however this presentation may be too simplistic. If all outcomes were assessed among those people who reported high stress at baseline, then the argument may be somewhat grounded. Yet, if these are not high stressed samples at baseline, the foundation of the review lacks a connection to the prosed theme, which is psychological stress and a variety of health outcomes. This issue should be carefully considered and addressed in the manuscript. ABSTRACT Comment 1, Page 6, Line 10: The statement that the effect of meditation on stress outcomes is unknown is only partially true	Comment 1: "Clinical adult populations" has been added to the end of Objectives in the Structured Comment 2, Main concern: We have revised the conceptualization of stress and stress-related outcomes in the Introduction: Psychological Stress and Well-Being. Since stress is not a "0/1" phenomenon, and exists on a continuum, we chose medical populations as a marker of some level of stress. We have identified all the trials for which it was a primary or secondary outcome, and we have attempted to describe where there are differences if we saw them. The primary outcomes are shown first on the relative difference in change graphs, so that the reader can draw their own conclusions about whether there is a difference between those trials. We did not find any significant differences. ABSTRACT

Comment #	Reviewer	Section	Comment	Response
			(also the term "stress" is vague--is the intent to review "psychological stress"). Several reviews indicate a beneficial effect of meditation on stress-related outcomes; consider rewording to account for the previously published evidence. See, for example: Chiesa, A. & Serretti, A. (2009). Mindfulness-Based stress reduction for stress management in healthy people: A review and meta-analysis. Journal of Alternative and Complementary Medicine , 15(5), 593-600. Grossman, P., Niemann, L., Schmidt, S., & Walach, H. (2004). Mindfulness-based stress reduction and health benefits. A meta-analysis. Journal of Psychosomatic Research, 57(1), 35-43. Black, D. S., Milam, J., & Sussman, S. (2009). Sitting-Meditation interventions among youth: A review of treatment efficacy. Pediatrics, 124(3), 532-541. Marchand, W. R. (2012). Mindfulness-based stress reduction, mindfulness-based cognitive therapy, and zen meditation for depression, anxiety, pain, and psychological distress. Journal of Psychiatric Practice, 18(4), 233-52. Regehr, C., Glancy, D., & Pitts, A. (2012). Interventions to reduce stress in university students: A review and meta-analysis. Journal of Affective Disorders. Krisanaprakornkit, T., Krisanaprakornkit, W., Piyavhatkul, N., & Laopaiboon, M. (2009). Meditation therapy for anxiety disorders (review). The Cochrane Library, (3). Also, "stress outcomes" also include stress-related biological markers. Thus, if it is the intent of the review to look at only psychosocial outcomes, it is important to indicate that the review looks at self-reported and objective psychosocial outcomes. For examples, see: Barnes studies regarding cardiovascular outcomes in "Black, D. S., Milam, J., & Sussman, S. (2009). Sitting-Meditation interventions among youth: A review of treatment efficacy. Pediatrics, 124(3), 532-541." For examples, see studies on stress-associated inflammatory markers such as: Malarkey, W. B. & Klatt, M. (2012). Workplace based mindfulness practice and inflammation: A randomized trial. Brain, Behavior, and Immunity. Rosenkranz, M. A., Davidson, R. J., MacCoon, D. G., Sheridan,	Comment 1: While a number of previous reviews have found meditation to be helpful, they included trials with wait-list or usual care controls. Since such controls do not control for attention and expectation, they may overestimate the beneficial effects of meditation programs. We therefore sought to focus on high quality RCTs in which the control group was an active control to assess the effects specific to meditation programs. Please see Introduction: Evidence to Date for further details. Comment 2: We have reworded the sentence to read, "We aimed to determine the effectiveness and .... compared to an active control in clinical adult populations." Comment 3:Due to time restrictions, we were not able to add a search from this database to our existing search of the other 8 databases. Comment 4: Note of clinical adult populations was made to the Objectives section of the abstract. EXECUTIVE SUMMARY Comment 1 : Due to limited word space, the main report has been extensively modified. Please see response to your General comment above. Comment 2: We have changed the title to psychological stress. Also see comment # 6. Comment 3: The article presented percentages. The reader can multiply 10% by the US population if they wish. Comment 2: "psychosocial stress" was added OBJECTIVES Comment 1: We have modified the objectives in the abstract slightly to read: "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

Comment #	Reviewer	Section	Comment	Response
			J. F., Kalin, N. H., & Lutz, A. (2012). A comparison of mindfulness-based stress reduction and an active control in modulation of neurogenic inflammation. Brain, Behavior, and Immunity. Black, D. S., Cole, S. W., Irwin, M. R., Breen, E., St Cyr, N. M., Nazarian, N., et al. (2012). Yogic meditation reverses nf-κb and irf-related transcriptome dynamics in leukocytes of family dementia caregivers in a randomized controlled trial. Psychoneuroendocrinology. Creswell, J. D., Irwin, M. R., Burklund, L. J., Lieberman, M. D., Arevalo, J. M., Ma, J., et al. (2012). Mindfulness-based stress reduction training reduces loneliness and pro-inflammatory gene expression in older adults: A small randomized controlled trial. Clinical Psychology Review, 26(7), 1095-1101. Comment 2, P6 L11: Clarify wording to indicate if “comparative effectiveness” refers to comparing mindfulness and concentration forms, or if they are being compared to non-meditation active control conditions. Comment 3, P6 L17: You may consider searching and citing the most comprehensive database on mindfulness meditation for completeness -- MINDFO found at http://www.mindfulexperience.org/mindfo.php Comment 4, P6 L36: Note that the analysis only included clinical adults and not pediatric populations. EXECUTIVE SUMMARY Comment 1, P14 L5: Consider that mindfulness meditation practice teaches a person how to focus, sustain, and regulate attention in order to gain greater clarity of mental phenomena, rather than just focus. The current definition is too simplistic. Comment 2, P14 L 23: Please consider using the more descriptive term “psychological stress” and cite its definition clearly early in the report and throughout the manuscript, as stress can also be environmental, social, etc. For concepts see, Cohen, S., Janicki-Deverts, D., & Miller, G. E. (2007). Psychological stress and disease. JAMA, 298(14), 1685-87. Comment 3, P14 L 25: Please indicate the raw number represented by 10% so the readership gets a a clearer picture of meditation prevalence in the US. Comment 2, P14 L 45: Clarify, “which these distinctions actually influence [psychosocial stress] outcomes.” OBJECTIVES	aimed to determine the effectiveness and safety of 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) compared to an active control in clinical adult populations.” We believe this is quite similar to what is presented in the main body of the report. DATA SYNTHESIS Comment 1: This was modified to: “We considered a five percent relative difference in change score to be potentially clinically significant, since these studies were looking at short interventions and relatively low doses of meditation.” DISCUSSION Comment 1: This change has been made in several locations, but we do not feel this level of specificity is needed in this particular location as it appears to change the character of our message. Comment 2: In discussion, we have included the following paragraph which sheds some light on how our effect sizes compare with antidepressant pills. “Fourth, the effect sizes are small. However, they are fairly comparable with what would be expected from the use of an antidepressant in a primary care population. In a study using patient-level meta-analysis, Fournier and colleagues found that for patients with mild to moderate depressive symptoms antidepressants had an effect size of 0.11 (-0.18, +0.41), while those with severe depression had an effect size of 0.17 (-0.08, +0.43) compared with placebo. Over the course of 2-6 months, mindfulness meditation program effect size estimates range from 0.22 to 0.40 for anxiety symptoms and 0.23 to 0.32 for depressive symptoms, and were statistically significant.”

Comment #	Reviewer	Section	Comment	Response
			Comment 1, P15 L51: The objectives stated appear somewhat different than the wording in the abstract. Please make the objectives consistent. across both of these sections It appears the wording on P15 and P16 better describes the intent of the paper than the current abstract. DATA SYNTHESIS Comment 1, P20 L53: Indicate why 5% difference was selected as clinically significant and cite support for this criteria, perhaps from previous clinical authoritative reviews. DISCUSSION Comment 1, P28, L6: Remain consistent and refer to “psychological stress” effects rather than just “effects”. Comment 2, P28 L 13: This is an important opportunity to tie in the 5-10% and 25-50% clinical changes and compare it with gold standards of clinical treatment for these conditions, such as Cognitive Behavioral Therapy (are the % changes similar when compared to other programs?). Comment 3, P31 L53: The last sentence is somewhat speculative and does not follow given the limitations outlined; delete or rephrase. REFERENCES Several controlled trails with psychosocial outcomes published in 2012 may be relevant to add to the review, see (these have been retrieved from MINDFO at http://www.mindfulexperience.org/mindfo.php): Britton, W. B., Shahar, B., Szepsenwol, O., & Jacobs, W. J. (2012). Mindfulness-based cognitive therapy improves emotional reactivity to social stress: Results from a randomized controlled trial. Behavior Therapy, 43(2), 365-80. Goldin, P., Ziv, M., Jazaieri, H., & Gross, J. (2012). Randomized controlled trial of mindfulness-based stress reduction versus aerobic exercise: Effects on the self-referential brain network in social anxiety disorder. Frontiers in Human Neuroscience, 6, 295. Hoffman, C. J., Ersser, S. J., Hopkinson, J. B., Nicholls, P. G., Harrington, J. E., & Thomas, P. W. (2012). Effectiveness of mindfulness-based stress reduction in mood, breast-and endocrine-related quality of life, and well-being in stage 0 to III breast cancer: A randomized, controlled trial. Journal of Clinical Oncology. Netterstrøm, B., Friebel, L., & Ladegaard, Y. (2012). The effects	Comment 3: There is some debate about whether certain forms of meditation are actually a skill or not. Thus far, no one has made a convincing case that a skill is not learned. We do not feel the point made is speculative, but rather a reality which meditation researchers need to consider seriously. We have modified the final paragraph of conclusion in main report to read: “ Sixth, the reasons for a lack of a significant reduction of stress-related health behavior outcomes may have to do with the way the research community conceptualizes meditation programs, the difficulties of acquiring such skills or meditative states, and the limited duration of RCTs. Historically, the general public did not conceptualize meditation as a quick fix toward anything. It was a skill or state one learns and practices over time to increase one’s awareness; through this awareness one gains insight and understanding into the various subtleties of their existence. Training the mind in awareness, nonjudgementalness, or in the ability to become completely free of thoughts or other activity, are daunting accomplishments. While some meditators may feel that these are easy tasks to do, they likely overestimate their own skills due to a lack of awareness of the different degrees to which these tasks can be done or ability to objectively measure their own progress. Becoming an expert at simple skills such swimming, reading, or writing (which can be objectively measured by others) take a considerable amount of time, so it only follows that meditation would also take a long period of time to master. However many of the studies included in this review were short term (e.g., 2.5 hours a week for 8 weeks) and the participants likely did not achieve a level of expertise needed to improve outcomes that depend on a mastery of our mental and emotional processes. Trials of short duration and training may be insufficient to

Comment #	Reviewer	Section	Comment	Response
			of a group based stress treatment program (the kalmia concept) targeting stress reduction and return to work. A randomized, wait-list controlled trial. Journal of Environmental and Occupational Science, 1(2). Nyklíček, I., van Beugen, S., & Denollet, J. (2012). Effects of mindfulness-based stress reduction on distressed (type D) personality traits: A randomized controlled trial. Journal of Behavioral Medicine. Robins, C. J., Keng, S. L., Ekblad, A. G., & Brantley, J. G. (2012). Effects of mindfulness-based stress reduction on emotional experience and expression: A randomized controlled trial. Journal of Clinical Psychology, 68(1), 117-31. SeyedAlinaghi, S., Jam, S., Foroughi, M., Imani, A., Mohraz, M., Djavid, G. E., et al. (2012). Randomized controlled trial of mindfulness-based stress reduction delivered to human immunodeficiency virus-positive patients in iran: Effects on CD4+ T lymphocyte count and medical and psychological symptoms. Psychosomatic Medicine. Whitebird, R. R., Kreitzer, M. J., Crain, A. L., Lewis, B. A., Hanson, L. R., & Enstad, C. J. (2012). Mindfulness-Based stress reduction for family caregivers: A randomized controlled trial. The Gerontologist. Wolever, R. Q., Bobinet, K. J., McCabe, K., Mackenzie, E. R., Fekete, E., Kusnick, C. A., et al. (2012). Effective and viable mind-body stress reduction in the workplace: A randomized controlled trial. Journal of Occupational Health Psychology. Wong, S., Mak, W., Cheung, E., Ling, C., Lui, W., Tang, W., et al. (2011). A randomized, controlled clinical trial: The effect of mindfulness-based cognitive therapy on generalized anxiety disorder among chinese community patients: Protocol for a randomized trial. BMC Psychiatry, 11(1), 187. Zangi, H. A., Mowinckel, P., Finset, A., Eriksson, L. R., Høystad, T., Lunde, A. K., et al. (2012). A mindfulness-based group intervention to reduce psychological distress and fatigue in patients with inflammatory rheumatic joint diseases: A randomised controlled trial. Annals of the Rheumatic Diseases, 71(6), 911-7. Zernicke, K. A., Campbell, T. S., Blustein, P. K., Fung, T. S., Johnson, J. A., Bacon, S. L., et al. (2012). Mindfulness-Based stress reduction for the treatment of irritable bowel syndrome symptoms: A randomized wait-list controlled trial. International	develop the meditative skills or states necessary to affect stress related outcomes in substantial ways. REFERENCES Five of these fit our inclusion criteria and were included in our updated review (articles by SeyedAlinaghi, Whitebird, Wolever, Chiesa, Pbert) TABLES Comment 1:This was edited as suggested. Comment 2: we have referenced this sentence. We recognize that there may be differing opinions on this issue. REFERENCES: We have not formally reviewed this literature, and therefore cannot comment on it. Comment 4:corrected

Comment #	Reviewer	Section	Comment	Response
			Journal of Behavioral Medicine. Chiesa, A., Mandelli, L., & Serretti, A. (2012). Mindfulness-based cognitive therapy versus psycho-education for patients with major depression who did not achieve remission following antidepressant treatment: A preliminary analysis. Journal of Alternative and Complementary Medicine (New York, N.Y.). Geschwind, N., Peeters, F., Huibers, M., van Os, J., & Wichers, M. (2012). Efficacy of mindfulness-based cognitive therapy in relation to prior history of depression: Randomised controlled trial. The British Journal of Psychiatry. Josefsson, T., Lindwall, M., & Broberg, A. (2012). The effects of a short-term mindfulness based intervention on self-reported mindfulness, decentering, executive attention, psychological health, and coping style: Examining unique mindfulness effects and mediators. Mindfulness. Shawyer, F., Meadows, G. N., Judd, F., Martin, P. R., Segal, Z., & Piterman, L. (2012). The DARE study of relapse prevention in depression: Design for a phase 1/2 translational randomised controlled trial involving mindfulness-based cognitive therapy and supported self monitoring. BMC Psychiatry, 12(1), 3. Pbert, L., Madison, J. M., Druker, S., Olendzki, N., Magner, R., Reed, G., et al. (2012). Effect of mindfulness training on asthma quality of life and lung function: A randomised controlled trial. Thorax. Creswell, J. D., Irwin, M. R., Burklund, L. J., Lieberman, M. D., Arevalo, J. M., Ma, J., et al. (2012). Mindfulness-based stress reduction training reduces loneliness and pro-inflammatory gene expression in older adults: A small randomized controlled trial. Clinical Psychology Review, 26(7), 1095-1101. TABLES Comment 1 Page 57 Table 4: Under the column “study objective” it is unnecessary to indicate “the goals of the study were...” for all studies listed; this is inherent. To save space just indicate, “To assess group MT...” Comment 2 Page 158 Line 2: The comment that mindfulness scales are not well validated is debatable. There are currently several psychometric validity papers out on the topic, see http://www.mindfulexperience.org/measurement.php. Please comment on the validity of the scales and how increases in mindfulness appear to be a significant mediator in some studies.	

Comment #	Reviewer	Section	Comment	Response
			REFERENCES Although this review concerns adults, it may be important, in the Background, to make the readership aware that reviews have collected empirical evidence for children and youth in clinical contexts, refer to: Black, D. S., Milam, J., & Sussman, S. (2009). Sitting-Meditation interventions among youth: A review of treatment efficacy. Pediatrics, 124(3), 532-541. Burke, C. A. (2010). Mindfulness-Based approaches with children and adolescents: A preliminary review of current research in an emergent field. Journal of Child and Family Studies, 19(2), 133-144. Comment 4, P397 L4: Differences has a typo	